Cascade Synthesis in Water: Michael Addition/Hemiketalization/Retro-Claisen Fragmentation Catalyzed by CatAnionic Vesicular Nanoreactor from Dithiocarbamate

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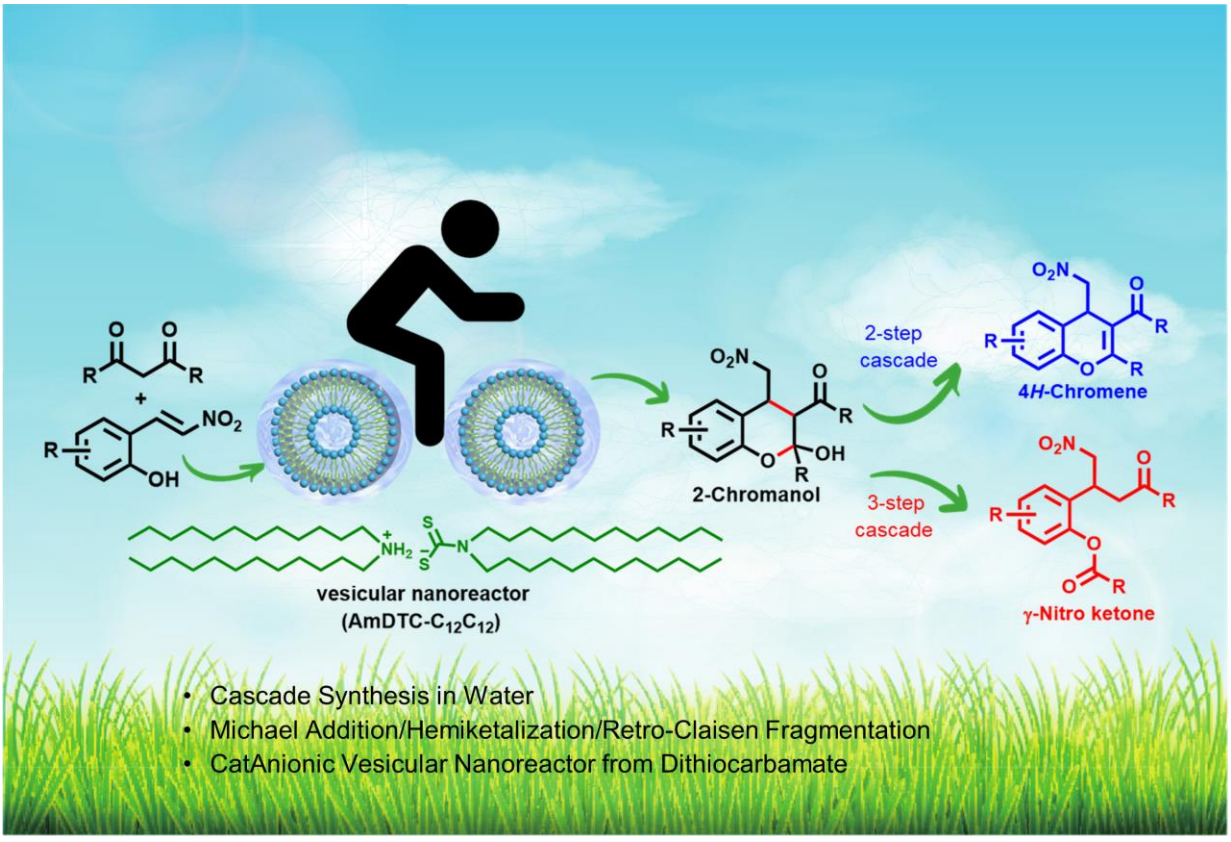
Graphical Abstract



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Abstract

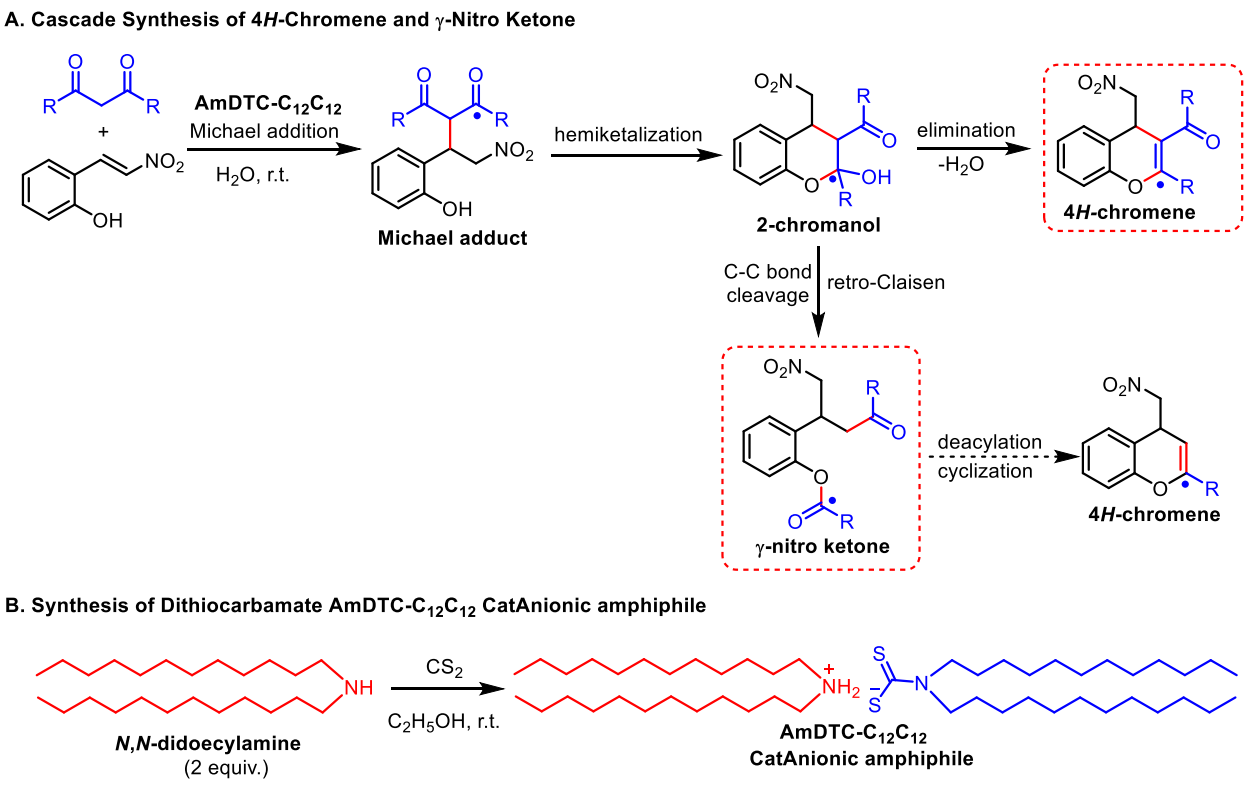
N,*N*-didodecylammonium *N*,*N*-didodecyldithiocarbamate (**AmDTC-$C_{12}C_{12}$**) underwent self-assembly to form a CatAnionic vesicular nanoreactor in water. **AmDTC-$C_{12}C_{12}$** can be readily prepared by condensation between *N*,*N*-didodecylamine and carbon disulfide. Previously, the cascade Michael addition/hemiketalization/retro-Claisen fragmentation was reported, but it required petroleum-based organic solvents as reaction media. Herein, the application of **AmDTC-$C_{12}C_{12}$** in aqueous cascade synthesis is investigated. Initially, we explored the catalytic activity of **AmDTC-$C_{12}C_{12}$** (10 mol%) in the synthesis of 4*H*-chromene through a 2-step cascade Michael addition/hemiketalization. The reaction occurred in water at room temperature using 2-hydroxy-*trans*-β-nitrostyrene as Michael acceptor and acetylacetone as Michael donor yielding 2-chromanol intermediates. Subsequent acidic dehydration of 2-chromanols produced 4*H*-chromenes with moderate yields (34–60%) and phenyl acetates of γ-nitro ketone as co-products (13–27%), deriving from retro-Claisen fragmentation. Surprisingly, using Michael donors with aromatic moieties on the 1,3-dicarbonyls resulted in spontaneous 3-step cascade Michael addition/hemiketalization/retro-Claisen fragmentation in water, without the need for acidic dehydration. The γ-nitro ketones were obtained as sole products, with no detection of 4*H*-chromenes, in moderate to high yields (31–84%) for symmetrical 1,3-dicarbonyl containing two aromatic groups. Unsymmetrical 1,3-dicarbonyl bearing aromatic/aliphatic or aromatic/aromatic groups afforded γ-nitro ketones in favorable yields (73–97%).

Introduction

Nanoreactors are specialized environments at the nanoscale designed to host and accelerate chemical reactions. They can mimic natural catalytic environments, such as enzymes, offering enhanced control over reaction pathways and selectivity. [1] The use of vesicular nanoreactors presents a significant advancement in green chemistry, enabling efficient catalysis in aqueous media. Vesicular nanoreactors provide a hydrophobic interior that can accommodate non-polar reactants, while their hydrophilic exterior interacts favorably with water, facilitating various organic transformations under environmentally benign conditions. Nanoreactors play a crucial role in overcoming limitations associated with traditional catalytic systems. By providing a confined reaction environment, they can stabilize reactive intermediates, control the local concentration of reactants, and create favorable conditions for multi-step reactions. [2, 3] This capability is particularly valuable for complex organic syntheses, where precise control over reaction conditions is essential for achieving high yields and selectivity. [4]

Cascade synthesis, also known as domino or tandem reactions, involves a series of consecutive reactions where the product of one reaction becomes the substrate for the next. [5] This approach improves synthetic efficiency by minimizing the need for intermediate purification steps and reducing the overall reaction time. [6] Cascade reactions are particularly valuable in complex molecule synthesis, as they can construct intricate structures in a single operational sequence. The integration of nanoreactors in cascade synthesis enhances these processes by providing a controlled environment that can facilitate multiple reaction steps in tandem. [7]

4*H*-Chromenes are heterocyclic compounds featuring a benzopyran ring structure (**Scheme 1A**). 4*H*-Chromenes are prevalent in various natural products and pharmaceuticals, exhibiting a wide range of biological activities, including antitumor, antioxidant, anti-inflammatory, and antiviral properties. In addition to their pharmacological applications, 4*H*-chromenes are also valuable intermediates in the synthesis of more complex organic molecules, enabling the construction of diverse chemical libraries for biological screening and drug discovery. [8, 9] Previous studies have demonstrated the cascade Michael addition/hemiketalization for the synthesis of 4*H*-chromenes. For example, Andres's[10] group and Wang's[11] group highlighted the use of squaramide-based organocatalyst for cascade Michael addition/hemiketalization, efficiently producing enantioselective 2-chromanol intermediates under neat conditions. These intermediates were subsequently transformed into 4*H*-chromenes *via* acid-catalyzed elimination in high yields. In a related study, Ramachary and Sakthidevi employed quinine-based organocatalysts for cascade Michael addition/hemiketalization in CH_2Cl_2, producing 2-chromanol intermediates for 4H-chromene synthesis. [12] Zhou and co-workers demonstrated the use of manganese dioxide-mediated C-H oxidation followed by squaramide-catalyzed Michael addition and cyclization in $CHCl_3$ to synthesize chiral 2-amino-4*H*-chromenes. [13]



Scheme 1. (A) Cascade synthesis of 4H-chromene and γ-nitro ketone. (B) Synthesis of dithiocarbamate **AmDTC-C$_{12}$C$_{12}$** CatAnioinic amphiphile.

γ-Nitro ketones serve as important building blocks for the synthesis of complex natural products and pharmaceuticals (**Scheme 1A**).[14] Their unique chemical properties allow for diverse transformations, including reductions, condensations, and cyclizations, making them highly valuable in synthetic organic chemistry.[15] The retro-Claisen fragmentation of hemiketals provides a direct route to these compounds. Efficient and selective synthesis of γ-nitro ketones can significantly enhance the efficiency of synthetic routes, reducing the number of steps required to obtain target molecules.[11] Several research groups have advanced the field of cascade Michael addition/hemiketalization/retro-Claisen fragmentation. For example, Pan and co-workers used a cinchona alkaloid-derived bifunctional thiourea catalyst for reactions between 2-hydroxy-*trans*-β-nitrostyrene and acetylacetone in mesitylene, yielding γ-nitro ketones efficiently.[16] Similarly, Singh and co-workers employed a bifunctional organocatalyst for the cascade reaction between monofluorinated β-diketones and 2-hydroxy-*trans*-β-nitrostyrene in THF, also resulting in γ-nitro ketones in good yields.[17] Andres and co-workers reported a squaramide-based organocatalysis, focusing on retro-Claisen fragmentation in hemiketal intermediates from reactions between 2-hydroxy-trans-β-nitrostyrene and dibenzoyl methane under neat conditions to provide γ-nitro ketones in good yields.[10] Wang and co-workers presented a triethylamine-catalyzed cascade reaction in CH_3CN, synthesizing γ-nitro ketones from active methylene carbonyls and 2-hydroxy-*trans*-β-nitrostyrene, achieving yields up to 80%.[18]

Traditional synthesis of 4*H*-chromenes and γ-nitro ketones are often performed in organic solvents (CH_2Cl_2, $CHCl_3$, CH_3CN, and THF), which pose environmental and safety concerns. The

development of more sustainable synthetic methods, such as those employing nanoreactors in water, is therefore highly desirable. The integration of nanoreactors in these catalytic systems offers a promising strategy for further enhancing reaction efficiency and selectivity. By providing a confined and controlled environment, nanoreactors can stabilize reactive intermediates, control local concentrations of reactants, and facilitate multi-step reactions under milder conditions. [4]

Recently our research group reported the synthesis of a salt-free CatAnionic amphiphile of *N*,*N*-didodecylammonium *N*,*N*-didodecyldithiocarbamate (**AmDTC-$C_{12}C_{12}$**). [19] This amphiphile was synthesized *via* a straightforward one-step condensation reaction between a secondary amine and carbon disulfide (**Scheme 1B**). The **AmDTC-$C_{12}C_{12}$** possesses a unique structure due to its inclusion of double-chain cationic (dialkylammonium) and double-chain anionic (dithiocarbamate) amphiphile within the structure. The **AmDTC-$C_{12}C_{12}$** dispersed in water to create salt-free CatAnionic vesicles, which spontaneously formed without the need for external force. The **AmDTC-$C_{12}C_{12}$** vesicle showed high stability in water and was applied as a nanoreactor for the Michael addition between nitroolefins and 1,3-dicarbonyls. This resulted in the formation of Michael adducts with yields ranging from 65–92%.

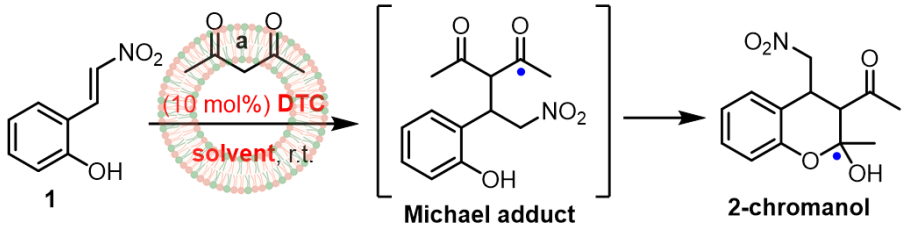
In this study, we investigate the application of dithiocarbamate amphiphiles, particularly **AmDTC-$C_{12}C_{12}$**, in aqueous cascade synthesis, focusing on its ability to catalyze the 2-step cascade Michael addition/hemiketalization for the synthesis of 4*H*-chromenes and the 3-step cascade Michael addition/hemiketalization/retro-Claisen fragmentation for the synthesis of γ-nitro ketones. The aim is to develop a more sustainable and efficient methodology for the synthesis of both 4*H*-chromenes and γ-nitro ketones, leveraging the unique properties of the CatAnionic vesicular nanoreactor formed by dithiocarbamate amphiphiles. The study also seeks to expand the substrate scope for these cascade reactions, exploring various Michael donors and acceptors to understand the versatility and limitations of the nanoreactor system.

Results and Discussion

Cascade Michael Addition/Hemiketalization Catalyzed by Dithiocarbamate Vesicular Nanoreactor: Dithiocarbamate Optimization

From the ongoing work in our laboratory, dithiocarbamate amphiphiles have been characterized as vesicular nanoreactors when dispersed in water. [19] For example, dispersion of **AmDTC-$C_{12}C_{12}$** in water generated vesicle with a particle diameter of 397 nm and zeta potential of -40.6 mv. Expanding upon understanding the DTC nanoreactor, we initiated a study on the catalytic activities of dithiocarbamate as an organocatalyst for the cascade Michael addition/hemiketalization in water. Our objective was to identify an appropriate DTC organocatalyst and reaction conditions for the synthesis of the 2-chromanol intermediate. The optimization process involved using 2-hydroxy-*trans*-β-nitrostyrene (**1**) and acetylacetone (**a**) as model substrates, resulting in the synthesis of 2-chromanol (**Table 1**). The reaction took place in water at ambient temperature, employing 10 mol% of the DTC catalyst, in which the concentration exceeded the critical vesicular concentration (CVC; if applicable) of amphiphiles.

Table 1. Cascade Michael addition/hemiketalization catalyzed by dithiocarbamate amphiphile



Entry[a]	DTC Catalyst	Solvent	Time (h)	Conversion[b] (%)
1	NaDTC-C_2C_2	H_2O	48	30
2	NaDTC-$C_{12}C_{12}$	H_2O	6	100
3	AmDTC-C_2C_2	H_2O	48	35
4	**AmDTC-$C_{12}C_{12}$**	**H_2O**	**6**	**100**
5	AmDTC-$C_{12}C_{12}$	toluene	48	45
6	AmDTC-$C_{12}C_{12}$	CH_2Cl_2	48	30
7	AmDTC-$C_{12}C_{12}$	CH_3CN	48	35

[a]Standard conditions: DTC catalyst (10 mol%), Michael acceptor **1** (0.3 mmol), acetylacetone (**a**) (1.2 equiv.), solvent 1.5 mL, 3 h, r.t.. [b]Conversion was monitored by ^{1}H NMR of crude mixture.

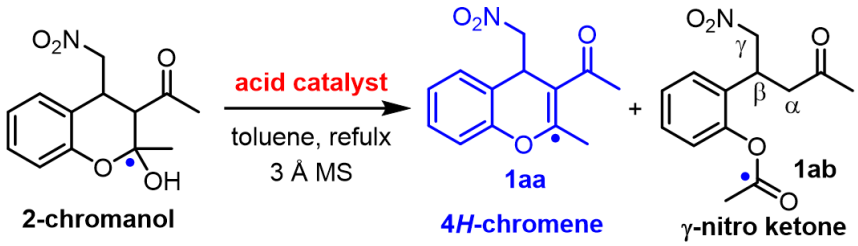
Among the anionic amphiphiles of NaDTCs, [20-23] **NaDTC-C_2C_2**, which has the shortest hydrocarbon chain length, showed good solubility in water and did not form vesicles in the aqueous solution. Therefore, the heterogeneous reaction between Michael donor **a** and acceptor **1** extended for 48 hours, resulting in a 30% conversion of the Michael acceptor **1** (**Table 1**, entry 1). Next, we engaged **NaDTC-$C_{12}C_{12}$** with a long hydrocarbon chain, thereby forming an anionic vesicular system. The reaction mixture was cloudy with partially solubilized precursors, and the

reaction reached completion within 6 hours, with a 100% conversion (entry 2). We then moved to the AmDTCs, **AmDTC-C_2C_2**, which possesses the shortest hydrocarbon chain. As expected, the resulting mixture developed heterogeneity, resulting in only 35% conversion over 48 hours (entry 3). Next, we utilized **AmDTC-$C_{12}C_{12}$**, which underwent spontaneous self-assembly to form the CatAnionic vesicle. The reaction proceeded smoothly, and the conversion of the starting material was observed to be 100% within 6 hours (entry 4). Subsequently, we engaged petroleum-based organic solvents, such as toluene, CH_2Cl_2, and CH_3CN, with the **AmDTC-$C_{12}C_{12}$** catalyst. It was hypothesized that the active dithiocarbamoyl head of the DTC catalyst could still catalyze the Michael addition but not as effectively as when the long hydrophobic components also form the vesicles. After 48 hours, the conversion of the reaction in toluene was only 45% (entry 5), whereas the conversion in CH_2Cl_2 was 30% (entry 6), and the conversion in CH_3CN was 35% (entry 7). The high conversion observed when using water as reaction media can be attributed to the formation of a vesicular nanoreactor. This nanoreactor acts as a lipophilic pocket, thereby enhancing the catalytic activity of the hydrophilic head of dithiocarbamate. This characteristic of the DTC vesicular nanoreactor did not exist when the reactions were carried out in organic media, leading to the poor performance of the **AmDTC-$C_{12}C_{12}$** as an organocatalyst in organic solvents (entries 5–7).

Synthesis of 4*H*-Chromene by Dehydration of 2-Chromanol: Acid Optimization

The intermediate 2-chromanol generated from the cascade Michael addition/hemiketalization was subjected to acid-catalyzed dehydration to yield the desired 4*H*-chromene **1aa**. In total, we tested three different Bronsted acids such as *para*-toluene sulfonic acid (*p*-TsOH), camphor sulfonic acid (CSA), and phenol sulfonic acid–formaldehyde resin–I (**PAFR–I**), [24] to carry out the dehydration in toluene at refluxing temperature. Among the acids evaluated, *p*-TsOH gave the best result, achieving completion within 1 hour and yielding the desired 4*H*-chromene **1aa** in good yield (60%) (**Table 2**, entry 1). The dehydration catalyzed by CSA produced just a 22% yield of **1aa** (entry 2), whereas the reaction catalyzed by **PAFR–I** produced a 15% yield of **1aa** (entry 3). Using *p*-TsOH under refluxing conditions in CH_3CN gave an inferior result with a 36% yield of **1aa** (entry 4), requiring a longer reaction time (5 h) than using toluene as the solvent (entry 1).

Table 2. Synthesis of 4*H*-chromene by dehydration of 2-chromanol



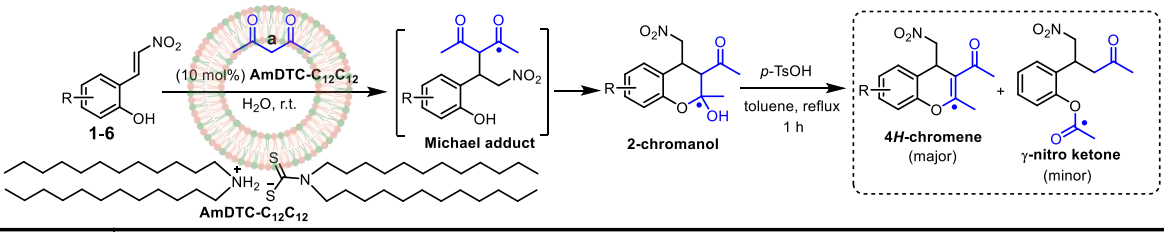
Entry[a]	Catalyst	Time (h)	Yield[b] (%)
1	***p*-TsOH**	**1**	**1aa (60), 1ab (20)**
2	CSA	1	**1aa** (22), **1ab** (20)
3	PAFR-I	4	**1aa** (15) , **1ab**(47)
4[c]	*p*-TsOH	5	**1aa** (36)

[a]Standard conditions: acidic catalyst (10 mol%), toulene 1.5 mL, reflux. [b]Isolated yields. [c]Reaction was carried out in acetonitrile at reflux temperature.

However, in addition to the desired 4*H*-chromene **1aa**, we detected a side product identified as phenylacetate of γ-nitro ketone **1ab** derived from the retro-Claisen fragmentation of the 2-chromanol. The selectivity towards **1ab** among the various catalysts tested was also noted. Fragmentation with *p*-TsOH produced a 20% yield of γ-nitro ketone **1ab** (entry 1). CSA gave almost the same yield of **1ab** in 20% (entry 2). When using heterogeneous **PAFR-I**, the selectivity towards **1ab** is 47% yield (entry 3), significantly higher than the desired **1aa** (15% yield). Furthermore, the formation of γ-nitro ketone **1ab** was not detected when using *p*-TsOH in CH_3CN for dehydration, but an unidentifiable mixture was observed (entry 4).

Cascade Synthesis of 4*H*-Chromene: Michael Addition/Hemiketalization and Dehydration

With the optimal conditions available, we broadened the scope of the Michael acceptors, specifically 2-hydroxy-trans-β-nitrostyrenes (**1**–**6**). Firstly, the Michael addition/hemiketalization was carried out using a catalytic amount (10 mol%) of **AmDTC-$C_{12}C_{12}$** in water at room temperature, resulting in the 2-chromanol intermediates. Secondly, the dehydration with *p*-TsOH in refluxing toluene was performed to generate the desired 4*H*-chromenes (**1aa**–**6aa**). The findings of the investigations were summarized in **Scheme 2**.



	Michael Acceptor					
	1	**2**	**3**	**4**	**5**	**6**
Michael Donor	6 h (**1aa**:**1ab** = 3:1)	12 h (**2aa**:**2ab** = 1.5:1)	48 h (**3aa**:**3ab** = 1.3:1)	12 h (**4aa**:**4ab** = 2.7:1)	5 h (**5aa**:**5ab** = 4.6:1)	24 h (**6aa**:**6ab** = 1:0)
a	**1aa**, 60%	**2aa**, 47%	**3aa**, 34%	**4aa**, 46%	**5aa**, 60%	**6aa**, 45%
	1ab, 20%	**2ab**, 31%	**3ab**, 27%	**4ab**, 17%	**5ab,** 13%	**6ab**, not observed
	column 1	*column 2*	*column 3*	*column 4*	*column 5*	*column 6*

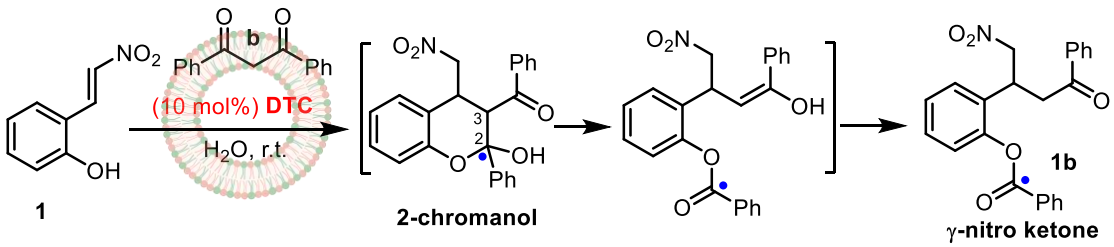
Scheme 2. Cascade synthesis of 4*H*-chromene with various Michael acceptors

The reaction of 2-hydroxy-*trans*-β-nitrosyrene (**1**) and acetylacetone (**a**) generated 2-chromanol within 6 hours, followed by the acid-dehydration to produce the desired 4*H*-chromene **1aa** as the major product in 60% yield accompanied by γ-nitro ketone side product **1ab** in 20% yield (**Scheme 2**, column 1). Following the same operation, treatment of nitrostyrene **2**, **3**, **4**, **5**, and **6** with acetylacetone (**a**) yielded the corresponding 2-chromanol as expected with different reaction times. It is noted that the reaction rates were found to be correlated with the nucleophilicity of the olefinic bond on the nitrosyrenes. The parent and unsubstituted nitrostyrene **1** showed the highest rate (6 h) among nitrostyrene derivatives. Slower rates were observed when the aromatic groups of nitrostyrene were substituted with the methoxy electron donating group, particularly at the *para*-position of nitrostyrene **3** or the naphthyl group on nitrostyrene **6**. In these cases, the reaction time increased significantly from 6 to 48 hours and 24 hours, respectively. This observation was likely a result of the destabilization at the olefinic bond during the addition of the nucleophilic DTC catalyst or acetylacetone (**a**). Next, the acid-dehydration was performed on 2-chromanol, leading to the formation of 4*H*-chromenes **2aa** (47% yield), **3aa** (34% yield), **4aa** (46% yield), **5aa** (60% yield), and **6aa** (45% yield) over 2 steps. Additionally, the side products of γ-nitro ketones, derived from retro-Claisen fragmentation, were obtained as **2ab** (31% yield), **3ab** (27% yield), **4ab** (17% yield), and **5ab** (13% yield). The formation of **6ab** was not observed after the acidic dehydration, but an unidentifiable mixture was observed (*column 6*). Although both 4*H*-chromene and γ-nitro ketone were produced, the dehydration was still dominant over the C-C bond cleavage, as evidenced by the ratio between 4*H*-chromene: γ-nitro ketone ranging from 1.3:1 to 4.6:1.

Cascade Michael Addition/Hemiketalization/Retro-Claisen Fragmentation Catalyzed by Dithiocarbamate Vesicular Nanoreactor: Dithiocarbamate Optimization

During the process of retro-Claisen fragmentation, we hypothesized that the presence of an aryl ketone at the C-3 position of 2-chromanol would enhance the stability of the intermediate formed following the C-C bond cleavage through the conjugated enol/enolate system (**Table 3**). This would influence the formation of γ-nitro ketones over the 4*H*-chromenes during acidic dehydration. The use of dibenzoyl methane (**b**) as the Michael donor would have generated such 2-chromanol equipped with aryl ketone. Surprisingly, treatment of 2-hydroxy-*trans*-β-nitrostyrene (**1**) with dibenzoyl methane (**b**) under **AmDTC-$C_{12}C_{12}$** catalysis in water produced γ-nitro ketones **1ab** directly in 75% yield. This reaction proceeded smoothly without requiring acidic dehydration at high temperatures (**Table 3**, entry 9). Moreover, the 2-chromanol was not detected in the crude mixture. This finding nicely demonstrated energy differences that facilitate the cascade transformation from the Michael adduct to 2-chromanol and ultimately to the γ-nitro ketone final product inside a vesicular nanoreactor environment.

Table 3. Cascade Michael addition/hemiketalization/retro-Claisen fragmentation catalyzed by dithiocarbamate amphiphile



Entry[a]	DTC Catalyst	Time (h)	Conversion[b] (%)	Yield[c] (%)
1	NaDTC-C_2C_2	14	100	9
2	NaDTC-C_6C_6	6	100	28
3	NaDTC-C_8C_8	6	100	31
4	NaDTC-$C_{12}C_{12}$	3	100	23
5	KDTC-$C_{12}C_{12}$	3	100	16
6	AmDTC-C_2C_2	14	100	18
7	AmDTC-C_6C_6	6	100	56
8	AmDTC-C_8C_8	6	100	54
9	**AmDTC-$C_{12}C_{12}$**	**5**	**100**	**75**
10	no catalyst	24	0	0

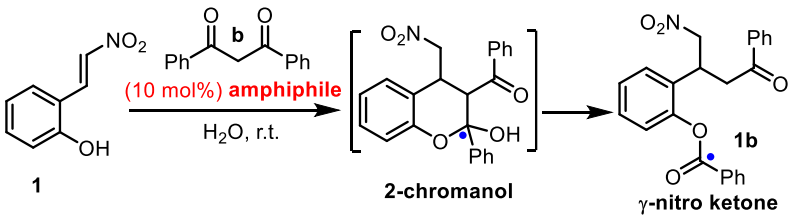
[a]Standard conditions: DTC catalyst (10 mol%), Michael acceptor **1** (0.3 mmol), dibenzoylmethane (**b**) (1.2 equiv.), H_2O 1.5 mL, 3 h, r.t. [b]Conversion was monitored by crude ^1H NM analysis. [c]Isolated yield.

The investigation for other DTCs as catalysts were carried out for the 3-step cascade Michael addition/hemiketalization/retro-Claisen fragmentation. Five different variants of 10 mol% sodium and potassium DTCs, namely **NaDTC-C_2C_2**, **NaDTC-C_6C_6**, **NaDTC-C_8C_8**, **NaDTC-$C_{12}C_{12}$**, and **KDTC-$C_{12}C_{12}$** were examined for the catalysis (entries 1–5). Full conversions of nitrostyrene (**1**) were observed in all cases, but the yields of γ-nitro ketone **1b** were very low (9–31%). ^{1}H NMR analysis revealed several unidentifiable unknowns in the crude mixture. Subsequently, catalysis under dialkylammonium DTCs with different hydrocarbon chain lengths was explored. Applying **AmDTC-C_2C_2**, **AmDTC-C_6C_6**, and **AmDTC-C_8C_8** (entries 6–8) provided the desired product in low to moderate yields (18–56%) despite the complete consumption of Michael acceptor **1**. As expected, the absence of a DTC catalyst resulted in no consumption of nitrostyrene (**1**) within 24 hours, resulting in complete recovery of the precursor (entry 10). Finally, the **AmDTC-$C_{12}C_{12}$** was selected as the optimum catalyst for the 3-step cascade Michael addition/ hemiketalization/retro-Claisen fragmentation (entry 9).

Influence of Amphiphiles on Cascade Michael Addition/Hemiketalization/Retro-Claisen Fragmentation

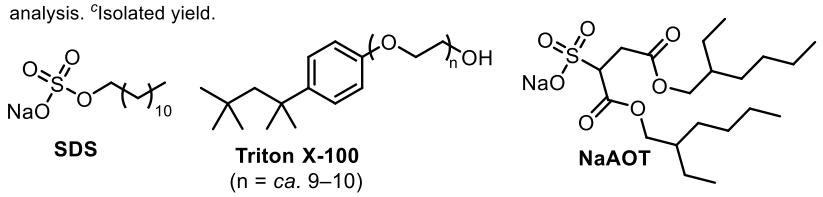
Typically, the hydrophilic head of amphiphiles was designed to maximize the hydration of amphiphiles with an aqueous environment surrounding the micelle or vesicle. [25] Meanwhile, the hydrophobic tail provided a hydrophobic environment to contain organic molecules. In this work, we proposed that the success of **AmDTC-$C_{12}C_{12}$** in the cascade synthesis of γ-nitro ketone arises from the dual functioning of the hydrophilic head in **AmDTC-$C_{12}C_{12}$** vesicular nanoreactor. The hydrophilic dithiocarbamoyl group provided both hydration ability and catalytic activity for the cascade synthesis, while the dodecyl hydrocarbon chains encapsulated the Michael donor and acceptor within the vesicle. To gain more understanding, we examined additional anionic and non-ionic amphiphiles that are commercially accessible. This was done in order to showcase the significance of the dithiocarbamate moiety in catalysis. The single-chain amphiphile of sodium dodecyl sulfate (SDS) and non-ionic Triton-X100 amphiphile were selected as a micelle-forming amphiphile. A double-chain amphiphile of sodium bis(2-ethylhexyl) sulfosuccinate (NaAOT) was chosen as an anionic vesicle-forming vesicle. All of these amphiphiles possessed either a sulfate, sulfonate, or alcoholic head group, none of which were expected to participate in the catalysis in this study (**Table 4**).

Table 4. The influence of amphiphiles on cascade Michael addition/hemiketalization/retro-Claisen fragmentation



Entry[a]	Amphiphile	Time (h)	Conversion[b] (%)	Yield[c] (%)
1	**AmDTC-$C_{12}C_{12}$**	**5**	**100**	**75**
2	SDS	72	0	0
3	Triton X-100	72	0	0
4	NaAOT	72	0	0
5	SDS + NaDTC-C_2C_2	18	100	13
6	Triton X-100 + NaDTC-C_2C_2	18	100	31
7	NaAOT + NaDTC-C_2C_2	18	100	13

[a]Standard conditions: amphiphile (10 mol%), Michael acceptor **1** (0.3 mmol), Michael donor **b** (1.2 equiv.), H_2O 1.5 mL, 3 h, r.t. [b]Conversion was monitored by crude ^1H NMR analysis. [c]Isolated yield.

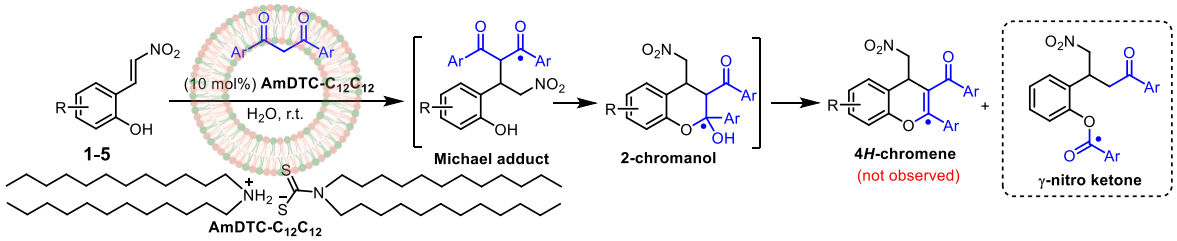


Under the standard conditions, using 10 mol% of amphiphiles (at a concentration higher than the critical micelle concentration (CMC) or critical vesicle concentration (CVC) of amphiphiles), the micelle-forming SDS and Triton-X100, as well as the vesicle-forming NaAOT did not catalyze the cascade reaction between nitrostyrene (**1**) and dibenzoyl methane (**b**). As a result, there was no conversion of Michael acceptor **1** even after 72 hours (**Table 4**, entries 2–4). We envisaged that adding **NaDTC-C_2C_2** to the amphiphiles would enhance the conversion, as the reaction medium would then contain both the catalyst and amphiphile. The reaction mixture containing SDS + **NaDTC-C_2C_2**, Trition X-100 + **NaDTC-C_2C_2**, and NaAOT + **NaDTC-C_2C_2** showed full consumption of the nitrostyrene (**1**) within 18 hours. Nevertheless, the production of γ-nitro ketone remained low (13–31%; entries 5–7) in comparison to the optimal **AmDTC-$C_{12}C_{12}$** catalyst (75%; entry 1).

Cascade Synthesis of γ-Nitro Ketone with Symmetrical 1,3-Dicarbonyls in Water

To explore the scope of the cascade Michael addition/hemiketalization/retro-Claisen fragmentation in water, we initiated this study by focusing on the reactions between 2-hydroxy-*trans*-β-nitrostyrenes (**1**–**5**) featuring electron-donating groups at different positions on the aromatic rings, and symmetrical aromatic containing 1,3-dicarbonyls (**b**, **d**, **f**) with various electronic nature. The **AmDTC-$C_{12}C_{12}$** (10 mol% or 14.7 mg/mL) was used as a vesicular nanoreactor. The findings of the investigations are presented in **Table 5**

Table 5. Cascade synthesis of γ-nitro ketone with symmetrical 1,3-dicarbonyls in water



	Symmetrical Michael Donor		
	b	**d**	**f**
Michael Acceptor			
entry 1 **1**	**1b**, 75% (5 h)	**1d**, 24% (16 h)	**1f**, 84% (4 h)
entry 2 **2**	**2b**, 72% (18 h)	**2d**, 27% (72 h)	N.A.
entry 3 **3**	**3b**, 64% (18 h)	**3d**, 70% (68 h)	N.A.
entry 4 **4**	**4b**, 54% (18 h)	**4d**, 31% (16 h)	N.A.
entry 5 **5**	**5b**, 84% (18 h)	**5d**, 78% (72 h)	**5f**, 77% (16 h)

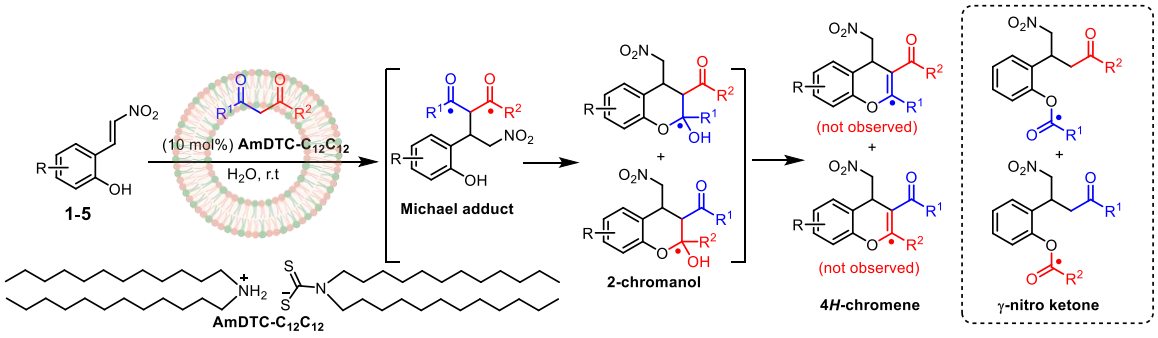
The cascade synthesis of γ-nitro ketone between the parent nitrostyrene (**1**) and 1,3-dicarbonyl **b**, electron-rich 1,3-dicarbonyl **d**, and electron-poor 1,3-dicarbonyl **f** revealed the correlation between reaction time and product yields when considering the electronic nature of the 1,3-dicarbonyls (**Table 5**, entry 1). The yields of γ-nitro ketone **1f**, **1b**, and **1d** were obtained in 84% (4 h), 75% (5 h), and 24% (16 h), respectively. Moreover, the cascade reaction between nitrostyrene (**5**) and 1,3-dicarbonyl **b**, **d**, and **f** also showed a similar relationship, where the formation of γ-nitro ketone **5f** (77%, 16 h) and **5b** (84%, 18 h) occurred at a significantly faster rate compared to the production of γ-nitro ketone **5d** from the electron-rich 1,3-dicarbonyl **d**, which took 72 hours to complete with a yield of 78% (entry 5). This finding suggested that a high reaction rate was observed when the electron-deficient 1,3-dicarbonyl, *i.e.* Michael donor **f**, was used. This could be explained by the rapid cyclization of the phenol and activated carbonyl at the hemiketalization of the Michael adduct leads to the formation of 2-chromanol.

Next, the electronic nature of the nitrostyrenes **1**–**5** was considered to gain more insight. The reaction between the unsubstituted dibenzoyl methane (**b**) and nitrostyrene **2**–**5** bearing electron-donating methoxy group took 18 hours to produce **2b** (72%), **3b** (64%), **4b** (54%), and **5b** (84%). In contrast, the synthesis of **1b** was completed in just 5 hours. In addition, the reaction between the *p*-methoxy substituted dibenzoyl methane **d** and electron-rich nitrostyrene **2**–**5** needed a much longer time to finish. The synthesis of γ-nitro ketone **2d**, **3d**, and **5d** required 68 to 72 hours for completion. Nevertheless, the synthesis of **4d** required 16 hours for completion, albeit with a low yield of 31%. The slow reaction rate observed when using electron-rich nitrostyrene **2**–**5** as the Michael acceptor can be attributed to the low reactivity of the olefinic bond towards nucleophilic addition. In summary, the use of electron-rich precursors for both Michael donor and acceptor led to a decreased reaction rate for the cascade Michael addition/hemiketalization/retro-Claisen fragmentation in water, particularly the production of **2d**, **3d**, and **5d**.

Cascade Synthesis of γ-Nitro Ketone with Unsymmetrical 1,3-Dicarbonyls in Water

Next, the cascade synthesis of γ-nitro ketone from unsymmetrical 1,3-dicarbonyls in water was carried out. The Michael addition/hemiketalization/retro-Claisen fragmentation between 2-hydroxy-*trans*-β-nitrostyrenes (**1**–**5**) and unsymmetrical 1,3-dicarbonyls of benzoyl acetone (**c**) and avobenzone (**e**) with **AmDTC-$C_{12}C_{12}$** (10 mol%) was performed. The results of the investigations are presented in **Table 6**.

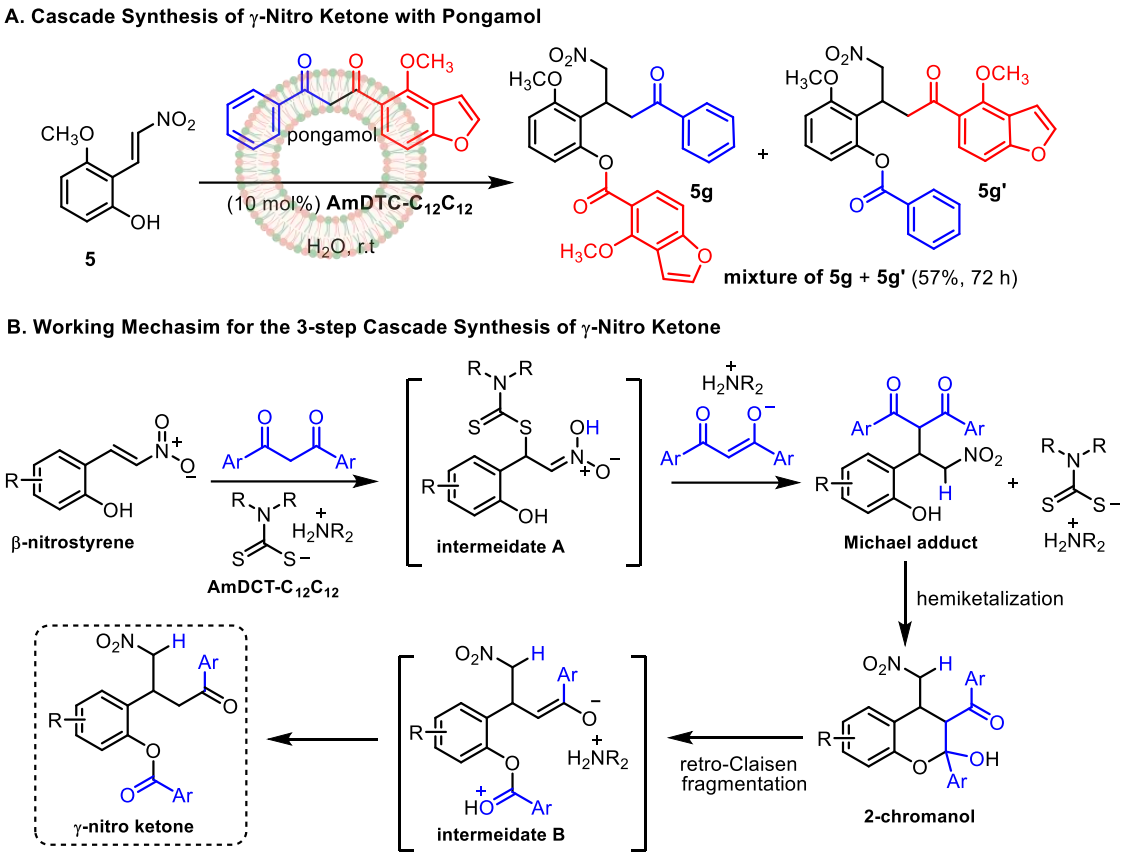
Table 6. Cascade synthesis of γ-nitro ketone with unsymmetrical 1,3-dicarbonyls in water



	Unsymmetrical Michael Donor	
	c	**e**
Michael Acceptor		
entry 1 **1**	97% (3 h) (**1c**:**1c'** = 3.8:1) **1c**, 77% **1c'**, 20%	80% (16 h) (**1e**:**1e'** = 1.1:1) **1e**, 41% **1e'**, 39%
entry 2 **2**	90% (3 h) (**2c**:**2c'** = 4.3:1) **2c**, 73% **2c'**, 17%	81% (16 h) (**2e**:**2e'** = 0.8:1) **2e**, 35% **2e'**, 46%
entry 3 **3**	84% (18 h) (**3c**:**3c'** = 3.4:1) **3c**, 65% **3c'**, 19%	81% (68 h) (**3e**:**3e'** = 0.8:1) **3e**, 35% **3e'**, 46%
entry 4 **4**	91% (4 h) (**4c**:**4c'** = 3.6:1) **4c**, 71% **4c'**, 20%	73% (48 h) (**4e**:**4e'** = 0.6:1) **4e**, 28% **4e'**, 45%
entry 5 **5**	93% (3 h) (**5c**:**5c'** = 4.8:1) **5c**, 77% **5c'**, 16%	78% (16 h) (**5e**:**5e'** = 1.6:1) **5e**, 48% **5e'**, 30%

When using an unsymmetrical Michael donor, two possible isomers of γ-nitro ketone were produced. The cascade reaction between benzoyl methane (**c**) and nitrostyrenes **1**–**5** produced a mixture of phenyl acetate **1c**–**5c** and phenyl benzoate **1c'**–**5c'** of the γ-nitro ketone in high yields (84–97%; entries **1**–**5**). Both isomeric γ-nitro ketones were successfully separated using column chromatography. The molar ratios between phenyl acetate **1c**–**5c** and phenyl benzoate **1c'**–**5c'** indicated the preference for the formation of phenyl acetate over the phenyl benzoate, with ratios ranging from 3.4:1 to 4.8:1. The observed chemoselectivity of the acetyl group transfer over the benzoyl group was attributed to the stabilization of the intermediate, which is formed after the C-C bond cleavage, by the conjugated enol/enolate. This stabilization was most pronounced when the aryl ketone group was substituted at the C-3 position on 2-chromanol and led to the production of phenyl acetate **1c**–**5c**, which is a product of acetyl group transfer. On the other hand, the isomeric mixture obtained from the cascade reaction with avobenzone (**e**) exhibited less preference between the isomeric mixture of γ-nitro ketone **1e**–**5e** over γ-nitro ketone **1e'**–**5e'**. The isomeric mixtures were separatable by column chromatography, and the molar ratios of isomer **e**:**e'** were determined to range from 0.6:1 to 1.6:1. The similarity in electric nature between the *p*-methoxy phenyl and *p*-*tert*-butyl phenyl groups of the 1,3-dicarbonyl could account for this observation. Nevertheless, the combination of isolated yields of γ-nitro ketone **1e**+**1e'** to **5e**+**5e'** showed high yields (73–81%) but required longer reaction time due to the electron-rich character of avobenzone (**e**) compared to using the benzoyl methane (**c**) as Michael donor.

Finally, the naturally occurring 1,3-dicarbonyl, namely pongamol, was subjected to the **AmDTC-$C_{12}C_{12}$** catalyzed cascade synthesis using nitrostyrenes **5** as Michael acceptor (**Scheme 3A**). As anticipated, the reaction took over 72 hours to reach completion since both precursors were electron-rich Michael donor and acceptor. An isomeric mixture of γ-nitro ketone **5g** and **5g'** was obtained as an inseparable mixture in 57% yield. In this work, we mainly focused on the synthesis of electron-rich 4*H*-chromene or γ-nitro ketone, which possesses significant bioactivity, particularly as an antioxidant.



386

387 **Scheme 3.** (A) cascade synthesis of γ-nitro ketone with pongamol. (B) Working mechanism for
388 cascade synthesis catalyzed by vesicular nanoreactor from dithiocarbamate.

389

390 Based on these results, the success of **AmDTC-$C_{12}C_{12}$** in the catalysis in water can be
391 attributed to three factors (**Scheme 3B**); 1) the hydrophobic nature of the didodecyl hydrocarbon
392 chains, 2) the catalytic activity of the dithiocarbamoyl group, 3) the presence of
393 didodecylammonium ion as a cation. Herein, we present a working mechanism for the **AmDTC-**
394 **$C_{12}C_{12}$** catalyzed cascade synthesis of γ-nitro ketone in water. Firstly, the **AmDTC-$C_{12}C_{12}$**
395 undergoes nucleophilic addition to the α position of nitrostyrene, followed by protonation of the
396 nitro group to form the nitronic acid by 1,3-dicarbonyl. This leads to the formation of **intermediate**
397 **A** and enolate. Nucleophilic substitution by the enolate at the α position, accompanied by proton
398 transfer from the nitronic acid to the β position, yields the Michael adduct and releases **AmDTC-**
399 **$C_{12}C_{12}$** for the next catalytic cycle. Hemiketalization between phenolic hydroxyl and ketone
400 produces the 2-chromanol. Finally, the C-C bond cleavage during the retro-Claisen fragmentation
401 yields the enol/enolate **intermediate B,** which could be stabilized by the didodecylammonium
402 cation, and the proton transfer furnishes the γ-nitro ketone product. We proposed that these
403 transformations would occur at the interface between the surrounding water and the hydrophobic
404 bilayer of the vesicular nanoreactor.

405

406

Conclusion

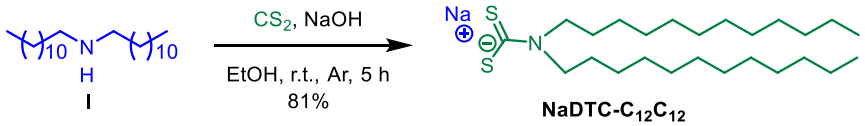
The study has demonstrated the successful application of *N*,*N*-didodecylammonium *N*,*N*-didodecyldithiocarbamate (**AmDTC-$C_{12}C_{12}$**) as a vesicular nanoreactor in water, showcasing its catalytic efficacy in the cascade synthesis of 4*H*-chromenes and γ-nitro ketone. **AmDTC-$C_{12}C_{12}$**, synthesized through the one-step condensation of *N*,*N*-didodecylamine, and carbon disulfide, self-assembled in water to form vesicular structures. This unique characteristic facilitates the cascade synthesis of 4*H*-chromenes and γ-nitro ketone, previously achievable only with petroleum-based organic solvents. Initial experiments identified that **AmDTC-$C_{12}C_{12}$** effectively catalyzed the synthesis of 4*H*-chromenes *via* a 2-step cascade Michael addition/hemiketalization in water at room temperature, yielding 2-chromanol intermediates. Subsequent acidic dehydration of these intermediates produced 4*H*-chromenes with moderate yields (34–60%) alongside γ-nitro ketone as a co-products (13–27%). Remarkably, the presence of aromatic moieties on 1,3-dicarbonyl Michael donors led to a spontaneous 3-step cascade process, Michael addition/hemiketalization/retro-Claisen fragmentation, eliminating the need for acidic dehydration and exclusively producing γ-nitro ketone with high efficiency (31–97%). The hydrophobic nature of the didodecyl hydrocarbon chains, the catalytic activity of the dithiocarbamoyl group, and the presence of didodecylammonium cation were proposed as key factors contributing to the nanoreactor's performance. By providing mechanistic insights and optimizing reaction conditions, we hope to establish a robust platform for future applications in complex molecule synthesis in water. Owing to the simplicity of the formation of dithiocarbamate, a large amount of the amine chiral pool could be examined. Our research group is currently investigating stereoselective synthesis employing chiral dithiocarbamate as an organocatalyst. Finally, this report highlights the potential of environmentally benign organocatalysts like **AmDTC-$C_{12}C_{12}$** for efficient chemical transformations in aqueous environments, paving the way for greener and more sustainable synthetic methodologies.

Experimental Section

All chemicals were purchased from Acros, Merck, Sigma-Aldrich, and TCI. Solvents were purchased from RCI Lab Scan. Reaction monitoring by TLC was performed on silica gel 60 F254 0.2 mm pre-coated aluminum plates purchased from Merck. Chemical spots on TLC were observed by visualization under 254 nm UV light, or by dipping in iodine (I2), or by staining with a ceric ammonium molybdate (CAM) staining solution. Silica gel 60 (70–230 mesh) from Merck was used for purification by column chromatography. Deuterated solvents for NMR experiments were purchased from Cambridge Isotope Laboratories. Chemical structure characterization was conducted by using a nuclear magnetic resonance (NMR) spectrometer on a Bruker Avance 400 NMR spectrometer operating at 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C{^{1}H} NMR or a JEOL JNM-ECZ500R/S1 spectrometer operating at 500 MHz for ^{1}H NMR, 126 MHz for ^{13}C{1H} NMR. The exact masses of all products were determined by high-resolution mass spectrometry (HRMS) on DART-QqTOF mass spectrometry, MALDI-TOF mass spectrometer: JEOL JMS-S3000 or ESI-QTOF: Bruker Daltonics micrOTOF-QII-ESI-QqTOF mass spectrometer.

Synthesis of Sodium *N*,*N*-Didodecyldithiocarbamate (NaDTC-$C_{12}C_{12}$)

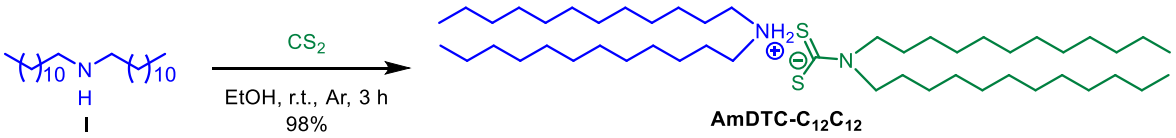
The synthesis of sodium *N*,*N*-didodecyldithiocarbamate (**NaDTC-$C_{12}C_{12}$**) was carried out through the following procedure. Sodium hydroxide (88 mg, 2.20 mmol, 1.1 equivalents) was added to a solution of *N*,*N*-didodecylamine (**I**) (707 mg, 2.00 mmol) and carbon disulfide (0.24 mL, 4.00 mmol, 2.0 equivalents) in ethanol (10 mL, $[c]_{rxn}$ = 0.2 M) at room temperature in a round-bottom flask under an argon atmosphere. After stirring for 5 hours, the solvent evaporated to dryness under reduced pressure. The crude mixture was purified by crystallization using ethyl acetate and hexanes. The **NaDTC-$C_{12}C_{12}$** was obtained as a white crystal (732 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.02–3.83 (m, 4H), 1.69 (dd, *J* = 9.7, 5.6 Hz, 4H), 1.27 (d, *J* = 13.6 Hz, 36H), 0.88 (t, *J* = 6.8 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 207.4, 54.9, 32.1, 30.0, 29.9, 29.7, 29.6, 27.3, 27.1, 22.8, 14.2. HRMS (ESI-QTOF): *m/z* calcd for $C_{25}H_{50}NS_2$ $[M]^+$ 428.33847, found 428.34004. The spectroscopic data of **NaDTC-$C_{12}C_{12}$** matched those reported in the literature (**Scheme S1**). [19, 26]



Scheme S1 Synthesis of Synthesis of **NaDTC-$C_{12}C_{12}$**

Synthesis of *N*,*N*-Didodecylammonium *N*,*N*-Didodecyldithiocarbamate (AmDTC-$C_{12}C_{12}$)

The synthesis of *N*,*N*-didodecylammonium *N*,*N*-didodecyldithiocarbamate (**AmDTC-$C_{12}C_{12}$**) was carried out through the following procedure. *N*,*N*-Didodecylamine (**I**) (707 mg, 2.00 mmol) and carbon disulfide (0.24 mL, 4.0 mmol), dissolved in ethanol (10 mL, $[c]_{rxn}$ = 0.2 M). at room temperature in a round-bottom flask under an argon atmosphere. After stirring for 3 hours, the solvent evaporated to dryness under reduced pressure. The crude mixture was purified by crystallization using acetone and water. The **AmDTC-$C_{12}C_{12}$** was obtained as a white solid (1.54 g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.01–3.88 (m, 4H), 3.10–2.97 (m, 4H), 1.85–1.63 (m, 8H), 1.42–1.17 (m, 73H), 0.87 (t, *J* = 6.9 Hz, 12H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 209.1, 54.1, 46.5, 329.3, 27.3 29.8, 29.7, 29.6, 29.5, 29.3, 27.3, 27.3, 27.3, 27.2, 25.9, 22.8, 14.2. HRMS (ESI-QTOF): *m/z* calcd for $C_{25}H_{50}NS_2$ [M]+ 428.33902, found 428.34021. HRMS (ESI-QTOF): *m/z* calcd for $C_{24}H_{52}N$ [M]+ 354.40943, found 354.41161 (**Scheme S2**). [19]



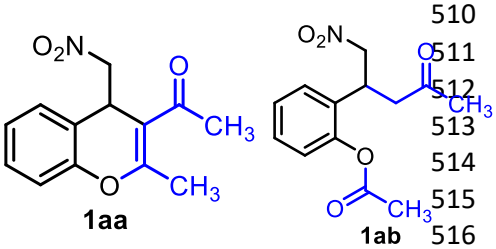
Scheme S2 Synthesis of **AmDTC-$C_{12}C_{12}$**

Synthesis of 4H-Chromenes (1aa–6aa) *via* Cascade Michael Addition/hemiketalization and Dehydration

General Procedure C: in a typical procedure, 0.1 equivalents (10 mol%) of **AmDTC-$C_{12}C_{12}$** were dissolved in 0.20–0.40 mL of isopropanol in a vial. Then, degassed deionized water ($[c]_{rxn}$ = 0.2 M) was added, and the mixture was stirred at room temperature for 3 hours. After this, 1.0 equivalent (0.30–1.00 mmol) of 2-hydroxy-*trans*-β-nitrostyrenes **1–6** and 1.2 equivalents (0.36–1.20 mmol) of acetylacetone (**a**) was added. The reaction progress was monitored by thin-

layer chromatography at 1-hour intervals until the total conversion of 2-hydroxy-*trans*-β-nitrostyrenes **1–6** was observed. The reaction was then quenched by adding 1.0 mL of saturated aqueous $NaHCO_3$, followed by extraction with ethyl acetate (3 × 10 mL) and washing with 10 mL of brine. The combined organic layers were dried over anhydrous Na_2SO_4, and solvents were removed under reduced pressure. The residue diastereomeric mixture of 2-chromanol intermediates was dissolved in toluene ($[c]_{rxn}$ = 0.1 M), 0.2 equivalents of *para*-toluene sulfonic acid were added, and the reaction was allowed to be stirred under reflux for 1 hour. In the setup for this reaction, an additional funnel equipped with a 3Å molecular sieve was attached to the reaction flask; this excludes water from the refluxing system. The reaction progress was monitored by thin-layer chromatography until the total conversion of the 2-chromanol intermediates. The reaction was then quenched with saturated aqueous $NaHCO_3$, followed by extraction with ethyl acetate (3 x 10 mL) and washed with 10 mL brine. The combined organic layers were dried over anhydrous Na_2SO_4, and solvents were removed under reduced pressure. The residues were purified by silica gel column chromatography through gradient elution using ethyl acetate and hexanes. However, the reaction could not give maximum yields of the expected 4H-chromenes due to retro-Claisen fragmentation leading to the formation of 2-phenylacetate of γ-nitro ketone side products.

*1-(2-Methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**1aa**) and 2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**1ab**)*

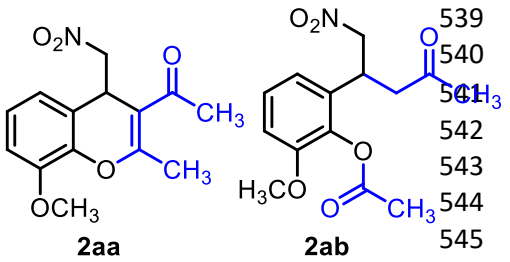


The cascade synthesis was carried out as described in **General Procedure C**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (50 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 6 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**1aa**) and 0.24 (**1ab**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(2-Methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**1aa**) was obtained as the major product in the form of a yellow syrup (45 mg, 60%), while 2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**1ab**) was obtained as minor product in the form of yellow syrup (16 mg, 20%).

1aa; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.29–7.24 (m, 1H), 7.17 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.11 (td, *J* = 7.4, 1.2 Hz, 1H), 7.05 (dd, *J* = 8.3, 1.2 Hz, 1H), 4.64 (dd, *J* = 8.0, 4.2 Hz, 1H), 4.48 (dd, *J* = 11.6, 4.2 Hz, 1H), 4.36 (dd, *J* = 11.7, 8.0 Hz, 1H), 2.45 (d, *J* = 3.3 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.9, 164.0, 150.6, 129.1, 128.2, 125.3, 120.7, 116.4, 111.5, 80.3, 35.2, 31.1, 21.1. HRMS (ESI-QTOF): m/z calcd for $C_{13}H_{13}NO_4Na$ [M + Na^+] 270.07368, found 270.07161. The spectroscopic data of methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**1aa**) matched those reported in the literature. [10]

1ab; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.33–7.25 (m, 1H), 7.20 (q, *J* = 2.4 Hz, 2H), 7.07 (dd, *J* = 8.1, 2.2 Hz, 1H), 4.60 (ddd, *J* = 6.6, 5.6, 2.4 Hz, 2H), 4.17 (td, *J* = 6.9, 2.3 Hz, 1H), 2.88 (dt, *J* = 5.8, 2.7 Hz, 2H), 2.37 (d, *J* = 2.3 Hz, 3H), 2.10 (d, *J* = 2.3 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 205.3, 169.7, 148.6, 131.0, 128.9, 127.7, 126.7, 1234, 78.4, 45.4, 32.7, 30.3, 21.1**.** HRMS (ESI-qTOF): $C_{13}H_{15}NO_5Na$ [M + Na^+] 288.08424, found 288.08354.

*1-(8-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**2aa**) and 2-methoxy-6-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**2ab**)*



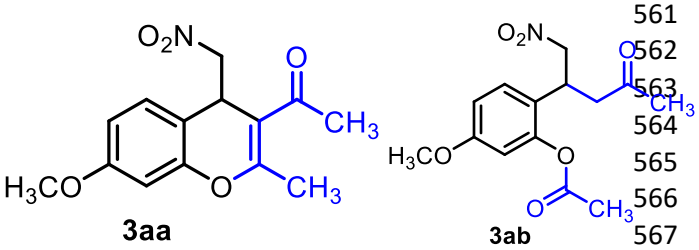
2aa **2ab**

The cascade synthesis was carried out as described in **General Procedure C**. Using 3-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**2**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 12 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**2aa**) and 0.24 (**2ab**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(8-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**2aa**) was obtained as the major product in the form of a yellow syrup (39 mg, 47%), while 2-methoxy-6-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**2ab**) was obtained as minor product in the form of yellow syrup (27 mg, 31%).

2aa; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.14–7.00 (m, 1H), 6.86 (dt, *J* = 8.2, 1.0 Hz, 1H), 6.75 (dt, *J* = 7.8, 0.8 Hz, 1H), 4.64 (dd, *J* = 8.1, 4.3 Hz, 1H), 4.47 (ddd, *J* = 11.6, 4.3, 0.8 Hz, 1H), 4.34 (ddd, *J* = 11.6, 8.1, 0.8 Hz, 1H), 3.89 (d, *J* = 0.8 Hz, 3H), 2.58–2.39 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.9, 163.9, 147.7, 140.6, 125.3, 121.8, 119.5, 111.5, 111.4, 80.2, 56.1, 35.3, 31.1, 21.1.

2ab; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.18 (t, *J* = 8.1 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.81–6.77 (m, 1H), 4.61 (d, *J* = 6.7 Hz, 2H), 4.19 (p, *J* = 6.9 Hz, 1H), 3.82 (s, 3H), 2.89 (dd, *J* = 6.9, 2.9 Hz, 2H), 2.40 (s, 3H), 2.12 (s, 3H).

*1-(7-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**3aa**) and 5-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**3ab**)*



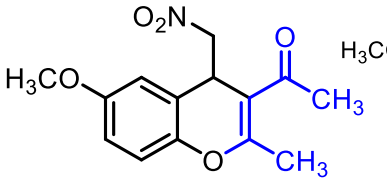
3aa **3ab**

The cascade synthesis was carried out as described in **General Procedure C**. Using 4-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**3**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 48 hours. The reaction was monitored by TLC (40% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**3aa**) and 0.24 (**3ab**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(7-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**3aa**) was obtained as the major product in the form of a yellow syrup (28 mg, 34%), while 5-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**3ab**) was obtained as minor product in the form of yellow syrup (23.6 mg, 27%).

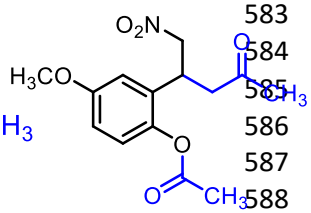
3aa; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.07 (d, *J* = 8.5 Hz, 1H), 6.69 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.60 (d, *J* = 2.6 Hz, 1H), 4.59 (dd, *J* = 8.0, 4.2 Hz, 1H), 4.47 (dd, *J* = 11.5, 4.2 Hz, 1H), 4.34 (dd, *J* = 11.5, 8.0 Hz, 1H), 3.79 (s, 3H), 2.45 (d, *J* = 9.0 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 197.1, 163.7, 160.2, 151.3, 128.7, 112.6, 111.8, 111.8, 101.7, 80.5, 55.6, 34.8, 31.1, 21.1.

3ab; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.11 (d, *J* = 8.6 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.63 (d, *J* = 2.6 Hz, 1H), 4.58 (dd, *J* = 7.1, 5.6 Hz, 2H), 4.09 (s, 1H), 3.77 (s, 3H), 2.87 (dd, *J* = 6.9, 5.3 Hz, 2H), 2.39 (s, 3H), 2.12 (s, 3H).

*1-(6-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**4aa**) and 4-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**4ab**)*



4aa



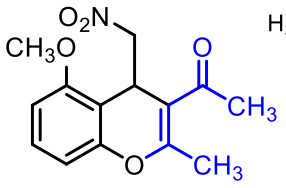
4ab

The cascade synthesis was carried out as described in **General Procedure C**. Using 5-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**4**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 12 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**4aa**) and 0.24 (**4ab**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(6-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**4aa**) was obtained as the major product in the form of a yellow syrup (38 mg, 46%), while 4-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**4ab**) was obtained as minor product in the form of yellow syrup (14.5 mg, 17%).

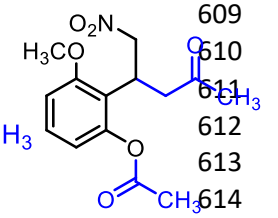
4aa; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 6.99 (d, *J* = 8.9 Hz, 1H), 6.81 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.68 (d, *J* = 2.9 Hz, 1H), 4.65–4.61 (m, 1H), 4.49 (dd, *J* = 11.7, 4.2 Hz, 1H), 4.38 (dd, *J* = 11.7, 8.0 Hz, 1H), 3.77 (s, 3H), 2.46 (d, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.9, 164.4, 156.9, 144.7, 121.5, 117.3, 115.1, 112.0, 110.7, 80.2, 55.8, 35.6, 31.1, 21.2.

4ab; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.01 (d, *J* = 8.9 Hz, 1H), 6.81 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.71 (d, *J* = 3.0 Hz, 1H), 4.60 (dd, *J* = 7.1, 3.8 Hz, 2H), 4.13 (s, 1H), 3.78 (d, *J* = 0.9 Hz, 3H), 2.88 (d, *J* = 6.9 Hz, 2H), 2.37 (s, 3H), 2.13 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 205.3, 170.2, 157.7, 141.9, 132.0, 124.1, 113.6, 113.2, 78.3, 55.7, 45.4, 32.8, 30.3, 21.1.

*1-(5-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**5aa**) and 3-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**5ab**)*



5aa



5ab

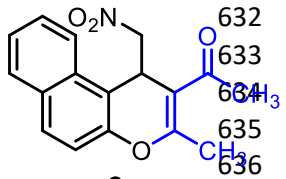
The cascade synthesis was carried out as described in **General Procedure C**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 5 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**5aa)** and 0.24 (**5ab**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(5-Methoxy-2-methyl-4-(nitromethyl)-4H-chromen-3-yl)ethan-1-one (**5aa**) was obtained as the major product in the form of a yellow syrup (50 mg, 60%), while 3-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenyl acetate (**5ab**) was obtained as minor product in the form of yellow syrup (12 mg, 13%).

5aa; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.22 (t, *J* = 8.3 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 2H), 4.75 (t, *J* = 4.4 Hz, 1H), 4.58 (dd, *J* = 12.0, 4.4 Hz, 2H), 3.86 (s, 3H), 2.47 (s, 3H), 2.43 (d, *J* = 0.7 Hz, 3H).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 197.3, 163.2, 156.8, 151.6, 129.1, 111.7, 109.0, 108.9, 106.1, 78.9, 55.8, 31.3, 31.2, 21.1.

5ab; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.24 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.71 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.73 (dd, *J* = 7.3, 3.0 Hz, 2H), 4.35 (dd, *J* = 7.4, 6.0 Hz, 1H), 3.87 (s, 3H), 2.97 (dd, *J* = 10.4, 6.6 Hz, 2H), 2.39 (s, 3H), 2.09 (s, 3H).

*1-(3-Methyl-1-(nitromethyl)-1H-benzo[f]chromen-2-yl)ethan-1-one (**6aa**)*



6aa

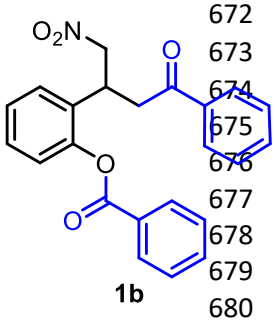
The cascade synthesis was carried out as described in **General Procedure C**. Using 1-naphthyl-2-hydroxy-*trans*-β-nitrostyrene (**6**) (68 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), acetylacetone (**a**) (0.37 µL, 0.36 mmol) and water (1.5 mL), reaction time was 24 hours. The reaction was monitored by TLC (40% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 1-(3-Methyl-1-(nitromethyl)-1H-benzo[f]chromen-2-yl)ethan-1-one (**6aa**) was obtained as the only product in the form of a brown syrup (42 mg, 45%).

6aa; ^1H NMR (500 MHz, $CDCl_3$) δ_H 8.00 (d, *J* = 8.4 Hz, 1H), 7.89–7.85 (m, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.62 (s, 1H), 7.52–7.47 (m, 1H), 7.27–7.22 (m, 1H), 5.33 (s, 1H), 4.64 (d, *J* = 4.5 Hz, 1H), 4.59 (d, *J* = 5.2 Hz, 1H), 2.53 (d, *J* = 4.2 Hz, 6H**).** $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 197.0, 163.5, 149.2, 131.5, 130.2, 129.8, 129.3, 127.9, 125.4, 121.6, 116.7, 112.6, 112.2, 79.2, 32.2, 31.3, 21.1.

6. General Procedure for the Cascade Michael Addition/Hemiketalization/Retro-Claisen Fragmentation

General Procedure D: in a typical procedure, 0.1 equivalents (10 mol%) of **AmDTC-$C_{12}C_{12}$** were dissolved in 0.20–0.4 mL of isopropanol in a vial. Then, degassed deionized water ($[c]_{rxn}$ = 0.2 M) was added, and the mixture was stirred at room temperature for 3 hours. After this, 1.0 equivalent (0.30–0.60 mmol) of 2-hydroxy-*trans*-β-nitrostyrenes **1**–**5** and 1.2 equivalents (0.36–0.72 mmol) of 1,3-dicarbonyl compounds **b**–**f** was added. The reaction progress was monitored by thin-layer chromatography at 1-hour intervals until the total conversion of 2-hydroxy-*trans*-β-nitrostyrenes **1**–**5** was observed. The reaction was then quenched by adding 1.0 mL of saturated aqueous $NaHCO_3$, followed by extraction with ethyl acetate (3 × 10 mL) and washing with 10 mL of brine. The combined organic layers were dried over anhydrous Na_2SO_4, and solvents were removed under reduced pressure. The residues were purified by silica gel column chromatography through gradient elution using ethyl acetate and hexanes.

*2-(1-Nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**1b**)*

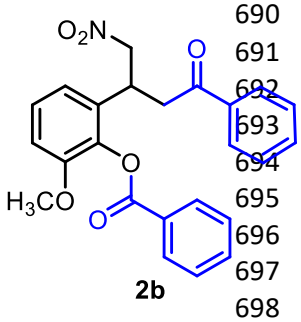


1b

The cascade synthesis was carried out as described in **General Procedure D**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (100 mg, 0.60 mmol), **AmDTC-$C_{12}C_{12}$** (47 mg, 0.06 mmol), dibenzoylmethane (**b**) (161 mg, 0.72 mmol) and water (3 mL), reaction time was 5 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-(1-Nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**1b**) was obtained as a yellow syrup (176 mg, 75%).

1b; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H ^{1}H NMR (500 MHz, CHLOROFORM-*D*) δ 8.22 (d, *J* = 6.9 Hz, 2H), 7.85 (d, *J* = 8.6 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 3H), 7.37 (dt, *J* = 21.2, 7.7 Hz, 4H), 7.29 – 7.19 (m, 2H), 4.83 – 4.72 (m, 2H), 4.50 – 4.42 (m, 1H), 3.52 – 3.36 (m, 2H) ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.9, 165.4, 149.0, 136.3, 134.2, 133.7, 131.4, 130.4, 129.1, 129.0, 128.9, 128.2, 126.8, 123.5, 78.5, 40.8, 33.5. The spectroscopic data of 2-(1-Nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**1b**) matched that reported in the literature. [15]

*2-Methoxy-6-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**2b**)*

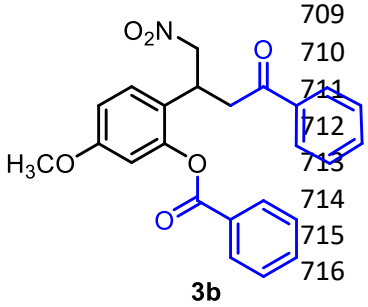


2b

The cascade synthesis was carried out as described in **General Procedure D**. Using 3-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**2**) (117 mg, 0.60 mmol), **AmDTC-$C_{12}C_{12}$** (47 mg, 0.06 mmol), dibenzoylmethane (**b**) (161 mg, 0.72 mmol) and water (3 mL), reaction time was 18 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-Methoxy-6-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**2b**) was obtained as white solid (182 mg, 72%).

2b; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.25 (d, *J* = 6.9 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.69–7.63 (m, 1H), 7.53 (t, *J* = 7.7 Hz, 3H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 2H), 4.94–4.69 (m, 2H), 4.50–4.42 (m, 1H), 3.77 (s, 3H), 3.54–3.35 (m, 2H). ^{13}C{^{1}H}NMR (126 MHz, $CDCl_3$) δ_C 197.0, 164.8, 151.8, 138.4, 136.3, 134.0, 133.6, 132.9, 130.6, 128.9, 128.9, 128.8, 128.2, 127.2, 111.8, 78.5, 56.1, 40.8. HRMS (DART-qTOF): m/z calcd for $C_{24}H_{22}NO_6$ [M + H]$^+$ 420.14471, found 420.14570

*5-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**3b**)*



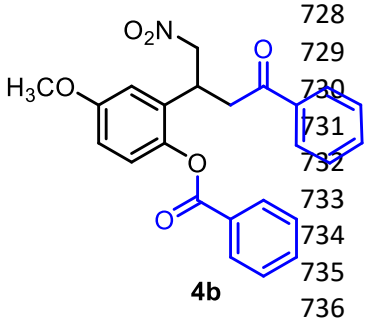
3b

The cascade synthesis was carried out as described in **General Procedure D.** Using 4-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**3**) (117 mg, 0.60 mmol), **AmDTC-$C_{12}C_{12}$** (47 mg, 0.06 mmol), dibenzoylmethane (**b**) (161 mg, 0.72 mmol) and water (3 mL), reaction time was 18 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent.

5-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**3b**) was obtained as a yellow syrup (161 mg, 64%).

3b; ^{1}H NMR 500 MHz, $CDCl_3$) δ_H 8.22 (d, *J* = 9.7 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.68–7.61 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 3H), 7.42–7.34 (m, 2H), 7.26 (s, 1H), 6.81 (d, *J* = 8.9 Hz, 1H), 6.76 (s, 1H), 4.79–4.67 (m, 2H), 4.38 (p, *J* = 7.6 Hz, 1H), 3.75 (s, 3H), 3.48–3.33 (m, 2H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 197.1, 165.3, 159.9, 149.7, 136.3, 134.2, 133.6, 130.4, 129.0, 128.8, 128.7, 128.2, 123.1, 113.0, 109.0, 78.8, 55.6, 41.0, 33.2. The spectroscopic data of 5-methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**3b**) matched those reported in the literature. [15]

*4-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**4b**)*

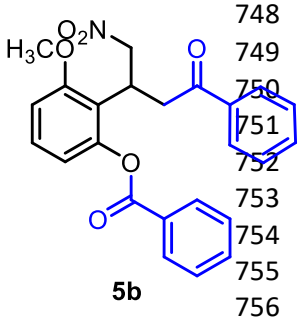


4b

The cascade synthesis was carried out as described in **General Procedure D**. Using 5-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**4**) (117 mg, 0.60 mmol), **AmDTC-$C_{12}C_{12}$** (47 mg, 0.06 mmol), dibenzoylmethane (**b**) (161 mg, 0.72 mmol) and water (3 mL), reaction time was 18 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 4-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**4b)** was obtained as a yellow oil (134.5 mg, 54%).

4b; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.21 (d, *J* = 8.3 Hz, 2H), 7.84 (d, *J* = 9.7 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 6.4 Hz, 3H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.13 (d, *J* = 8.9 Hz, 1H), 6.89–6.81 (m, 2H), 4.75 (qd, *J* = 12.7, 7.2 Hz, 2H), 4.41 (p, *J* = 7.2, 6.6 Hz, 1H), 3.76 (s, 3H), 3.47 (dd, *J* = 17.8, 6.0 Hz, 1H), 3.37 (dd, *J* = 17.6, 7.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 196.8, 165.8, 157.8, 142.3, 136.2, 134.1, 133.7, 132.4, 130.4, 129.1, 128.9, 128.8, 128.2, 124.2, 114.0, 113.4, 78.5, 55.7, 40.8, 33.7. The spectroscopic data of 4-methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**4b**) matched those reported in the literature. [27]

*3-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**5b**)*



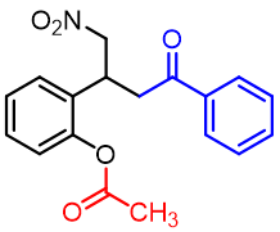
5b

The cascade synthesis was carried out as described in **General Procedure D**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), dibenzoylmethane (**b**) (161 mg, 0.36 mmol) and water (1.5 mL), reaction time was 18 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 3-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl benzoate (**5b**) was obtained as a white solid (106 mg, 84%).

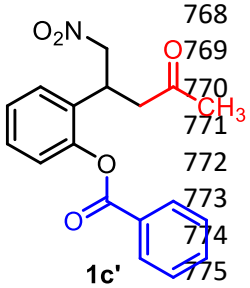
5b; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.20 (d, *J* = 4.9 Hz, 2H), 7.84 (d, *J* = 5.2 Hz, 2H), 7.66–7.60 (m, 1H), 7.53–7.47 (m, 3H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 2H), 4.93–4.82 (m, 2H), 4.62 (q, *J* = 7.2, 6.6 Hz, 1H), 3.90 (s, 3H), 3.58–3.47 (m, 2H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 197.8, 165.4, 158.9, 150.0, 136.4, 134.0, 133.4, 130.5, 129.2, 129.1, 128.9,

128.7, 128.2, 119.9, 115.8, 109.1, 55.9, 39.4, 31.2. HRMS (MALDI-TOF): m/z calcd for $C_{24}H_{21}NO_6Na$ [M+Na$^+$] 442.1261, found 442.1279.

*2-(1-Nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**1c**) and 2-(1-nitro-4-oxopentan-2-yl)phenyl benzoate(**1c'**)*



1c



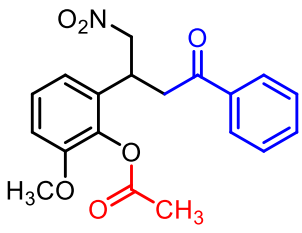
1c'

The cascade synthesis was carried out as described in **General Procedure D**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (50 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), benzoyl acetone (**c**) (58 mg, 0.36 mmol) and water (1.5 mL), reaction time was 3 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**1c**) and 0.28 (**1c'**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-(1-Nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**1c**) was obtained as the major product in the form of a yellow syrup (76 mg, 77%), while 2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**1c'**) was obtained as minor product in the form of yellow syrup (20 mg, 20%).

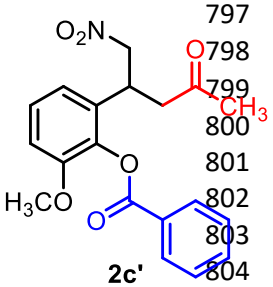
1c; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 8.5 Hz, 2H), 7.60–7.55 (m, 1H), 7.48–7.42 (m, 2H), 7.29 (d, *J* = 7.3 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 4.77 (dd, *J* = 12.7, 7.2 Hz, 1H), 4.69 (dd, *J* = 12.7, 7.0 Hz, 1H), 4.41 (p, *J* = 7.2 Hz, 1H), 3.44 (dd, *J* = 6.9, 4.0 Hz, 2H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.8, 169.8, 148.7, 136.3, 133.8, 131.3, 128.9, 128.9, 128.9, 128.2, 127.6, 126.8, 123.4, 78.5, 40.9, 32.9, 21.1. The spectroscopic data of (**1c**) matched that reported in the literature. [27]

1c'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.26 (d, *J* = 7.2 Hz, 2H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 5.8 Hz, 1H), 7.28 (d, *J* = 11.3 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 1H), 4.69 (d, *J* = 7.1 Hz, 2H), 4.25 (t, *J* = 7.0 Hz, 1H), 2.98–2.81 (m, 2H), 2.09 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 205.4, 165.4, 148.9, 134.2, 131.1, 130.4, 129.1, 129.0, 128.1, 126.8, 123.5, 78.4, 45.3, 33.2, 30.3. The spectroscopic data of (**1c'**) matched that reported in the literature. [16]

*2-Methoxy-6-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**2c**) and 2-methoxy-6-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**2c'**)*



2c



2c'

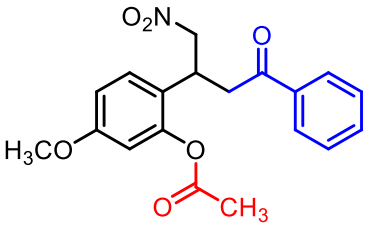
The cascade synthesis was carried out as described in **General Procedure D**. Using 3-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**2**) (59 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), benzoyl acetone (**c**) (58 mg, 0.36 mmol) and water (1.5 mL), reaction time was 3 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes: dipping in CAM, R_f = 0.30 (**2c**) and 0.29 (**2c'**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-Methoxy-6-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**2c**) was obtained as major product in the form of yellow syrup (78 mg, 73%), while 2-methoxy-6-(1-nitro-4-

oxopentan-2-yl)phenylbenzoate (**2c'**) was obtained as minor product in the form of yellow syrup (18 mg, 17%).

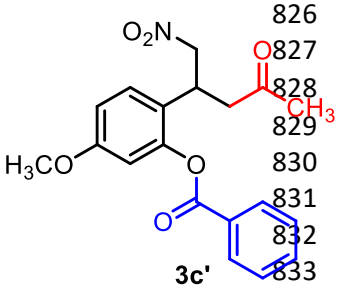
2c; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 9.9 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.48–7.40 (m, 2H), 7.18 (t, *J* = 8.1 Hz, 1H), 6.87 (dd, *J* = 16.7, 7.4 Hz, 2H), 4.75 (dd, *J* = 12.7, 7.1 Hz, 1H), 4.68 (dd, *J* = 12.6, 7.0 Hz, 1H), 4.44–4.37 (m, 1H), 3.81 (s, 3H), 3.51–3.36 (m, 2H), 2.38 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 196.9, 169.3, 151.6, 138.1, 136.3, 133.7, 132.7, 128.9, 128.2, 127.1, 118.8, 111.7, 78.4, 56.1, 40.8, 33.2, 20.7. HRMS (MALDI-TOF): m/z calcd for $C_{19}H_{19}NO_6Na$ [M+Na$^+$] 380.1110, found 380.1108.

2c'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.25 (d, *J* = 9.7 Hz, 2H), 7.72–7.65 (m, 1H), 7.55 (t, *J* = 7.9 Hz, 2H), 7.22 (t, *J* = 8.1 Hz, 1H), 6.93 (d, *J* = 6.9 Hz, 1H), 6.86 (d, *J* = 6.5 Hz, 1H), 4.68 (t, *J* = 8.5 Hz, 2H), 4.21 (t, *J* = 7.0 Hz, 1H), 3.78 (s, 3H), 2.90 (d, *J* = 6.5 Hz, 2H), 2.09 (s, 3H). HRMS (MALDI-TOF): m/z calcd for $C_{19}H_{19}NO_6Na$ [M +Na$^+$] 380.1110, found 380.1139.

*5-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**3c**) and 5-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**3c'**)*



3c



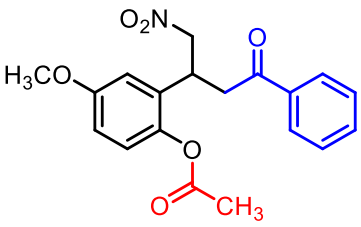
3c'

The cascade synthesis was carried out as described in **General Procedure D**. Using 4-methoxy-2-hydroxy-*trans*-β-nitrostyre- ne (**3**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), benzoyl acetone (**c**) (58 mg, 0.36 mmol) and water (1.5 mL), reaction time was 18 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25 (**3c**) and 0.23 (**3c'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 5-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**3c**) was obtained as the major product in form of yellow solid (69.6 mg, 65%) while 5-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**3c'**) was obtained as the minor product in the form of yellow solid (19.8 mg, 19%).

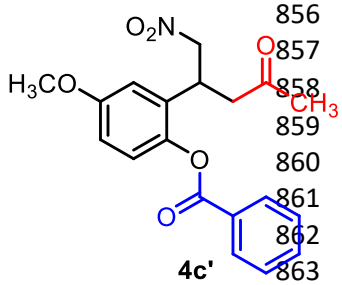
3c; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.90 (d, *J* = 6.9 Hz, 2H), 7.59–7.53 (m, 1H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 1H), 6.76 (d, *J* = 8.9 Hz, 1H), 6.64 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 12.6, 7.2 Hz, 1H), 4.63 (dd, *J* = 12.5, 7.0 Hz, 1H), 4.33–4.25 (m, 1H), 3.75 (s, 3H), 3.39 (d, *J* = 8.6 Hz, 2H), 2.36 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 197.0, 169.7, 159.7, 149.4, 136.3, 133.7, 128.9, 128.2, 128.1, 123.0, 112.8, 108.9, 78.7, 55.6, 41.0, 32.6, 21.1.

3c'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.25 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.69 (s, 1H), 7.56 (dd, *J* = 8.5, 7.1 Hz, 2H), 7.18 (d, *J* = 8.7 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.74 (d, *J* = 2.6 Hz, 1H), 4.65 (dd, *J* = 7.1, 0.7 Hz, 2H), 4.19–4.11 (m, 1H), 3.79 (s, 3H), 2.88 (d, *J* = 0.9 Hz, 2H), 2.08 (s, 3H). HRMS (MALDI-TOF): m/z calcd for $C_{19}H_{19}NO_6Na$ [M +Na$^+$] 380.1110, found 380.1143. The spectroscopic data of (**3c'**) matched that reported in the literature. [16]

*4-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**4c**) and 4-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**4c'**)*



4c



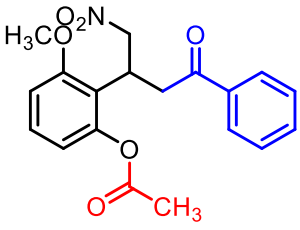
4c'

The cascade synthesis was carried out as described in **General Procedure D**. Using 5-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**4**) (59 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), benzoyl acetone (**c**) (58 mg, 0.36 mmol) and water (1.5 mL), reaction time was 4 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**4c**) and 0.25 (**4c'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 4-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**4c**) was obtained the major product in the form of yellow solid (76 mg, 71%) while 4-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**4c'**) was obtained as the minor product in form of yellow solid (21 mg, 20%).

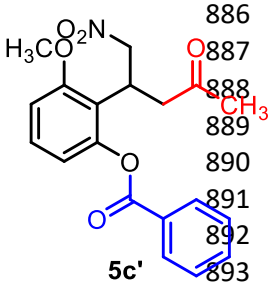
4c; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 8.2 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 1H), 6.83–6.76 (m, 2H), 4.75 (dd, *J* = 12.7, 7.2 Hz, 1H), 4.67 (dd, *J* = 12.7, 7.0 Hz, 1H), 4.38–4.31 (m, 1H), 3.77 (s, 3H), 3.50–3.36 (m, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.7, 170.2, 157.7, 142.0, 136.2, 133.8, 132.3, 128.9, 128.2, 124.1, 113.6, 113.1, 78.4, 55.7, 40.8, 33.1, 21.0.

4c'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.24 (d, *J* = 7.1 Hz, 2H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 1H), 6.86 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.78 (d, *J* = 3.0 Hz, 1H), 4.67 (d, *J* = 7.0 Hz, 2H), 4.17 (p, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 2.95–2.82 (m, 2H), 2.09 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 205.4, 165.8, 157.8, 142.2, 134.1, 132.1, 130.4, 129.0, 128.9, 124.2, 113.9, 113.5, 78.4, 55.7, 45.3, 33.4, 30.3. The spectroscopic data of 4-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**4c'**) matched that reported in the literature. [16]

*3-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**5c**) and 3-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**5c'**)*



5c



5c'

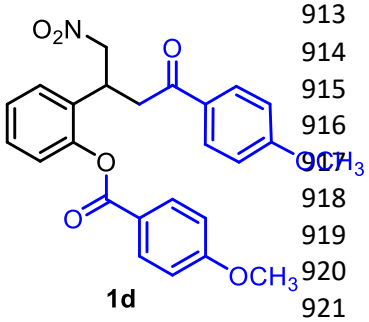
The cascade synthesis was carried out as described in **General Procedure D**. Using 6-Methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), benzoyl acetone (**c**) (58 mg, 0.36 mmol) and water (1.5 mL), reaction time was 3 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**5c**) and 0.25 (**5c'**)). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 3-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl acetate (**5c**) was obtained as the major product in the form of yellow solid (97 mg, 77%), while 3-methoxy-2-(1-nitro-4-oxopentan-2-yl)phenylbenzoate (**5c'**) was obtained as the minor product in the form of yellow solid (21 mg, 16%).

5c; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.27 (d, *J* = 7.1 Hz, 2H), 7.69–7.64 (m, 1H), 7.53 (s, 2H), 7.33–7.25 (m, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.84–4.71 (m, 2H), 4.48–4.40 (m, 1H), 3.05–2.93 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 197.8, 169.8, 158.8, 149.7, 136.5, 133.4, 129.1, 128.7, 128.2,

119.9, 115.7, 109.0, 77.2, 55.9, 39.5, 30.9, 21.0. HRMS (DART-TOF): m/z calcd for $C_{19}H_{19}NO_6$ $[M+H]^+$ 358.1291, found 358.1252.

5c'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.30–8.24 (m, 2H), 7.69–7.64 (m, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 17.5 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 2H), 4.78 (dd, *J* = 18.4, 7.4 Hz, 2H), 4.45 (d, *J* = 7.1 Hz, 1H), 3.90 (s, 3H), 2.99 (dd, *J* = 10.3, 6.8 Hz, 2H), 2.06 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 206.1, 165.4, 158.8, 149.9, 134.0, 130.5, 129.1, 128.9, 119.8, 115.8, 109.0, 77.1, 55.9, 44.2, 30.6, 30.0. HRMS (MALDI-TOF): m/z calcd for $C_{19}H_{19}NO_6Na$ $[M+Na^+]$ 380.1110, found 380.1140.

*2-(4-(4-Methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-methoxybenzoate (**1d**)*

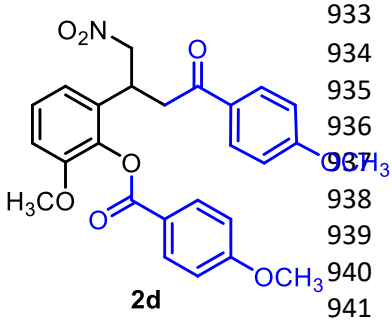


1d

The cascade synthesis was carried out as described in **General Procedure D**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (50 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), 1,3-bis(4-methoxyphenyl)-1,3-propanedione (**d**) (102 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**1d**) was obtained as a yellow solid (32 mg, 24%).

1d; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.17 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.26 (s, 2H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.85–4.74 (m, 2H), 4.48–4.39 (m, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 3.37 (dd, *J* = 24.5, 7.0 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 195.5, 165.1, 164.3, 163.9, 149.0, 132.6, 131.5, 130.5, 129.4, 128.9, 128.2, 127.6, 126.7, 126.1, 123.6, 121.2, 113.9, 78.6, 55.7, 55.6, 40.5, 33.9, 32.0. The spectroscopic data of *2*-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**1d**) matched that reported in the literature. [27]

*2-Methoxy-6-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**2d**)*

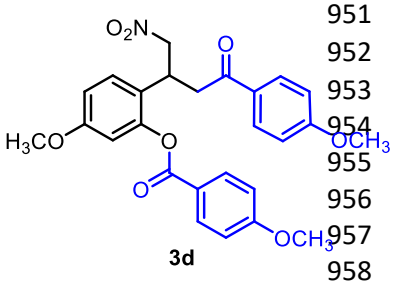


2d

The cascade synthesis was carried out as described in **General Procedure D**. Using 3-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**2**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), 1,3-bis(4-methoxyphenyl)-1,3-propanedione (**d**) (102 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 72 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 2-Methoxy-6-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**2d**) was obtained as a yellow solid (39 mg, 27%).

2d; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.18 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.26–7.17 (m, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.89–6.80 (m, 4H), 4.82–4.70 (m, 2H), 4.40 (d, *J* = 2.1 Hz, 1H), 3.95–3.75 (m, 13H), 3.51–3.26 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 164.5, 164.2, 163.9, 151.9, 132.7, 130.5, 127.0, 121.2, 114.1, 113.9, 111.5, 78.4, 56.1, 55.7, 55.6, 29.8, 22.8.

*5-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**3d**)*

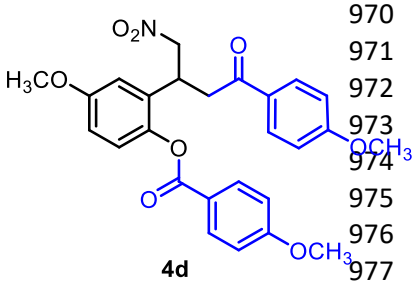


3d

The cascade synthesis was carried out as described in **General Procedure D**. Using 4-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**3**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), 1,3-bis(4-methoxyphenyl)-1,3-propanedione (**d**) (102 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 68 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.20). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 5-methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**3d**) was obtained as a yellow solid (100 mg, 70%).

3d; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.14 (d, *J* = 9.2 Hz, 2H), 7.82 (d, *J* = 8.9 Hz, 2H), 7.26–7.20 (m, 1H), 6.98 (d, *J* = 9.2 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.80–6.77 (m, 1H), 6.72 (s, 1H), 4.75 (dd, *J* = 12.6, 6.9 Hz, 1H), 4.69 (dd, *J* = 12.5, 7.6 Hz, 1H), 4.34 (d, *J* = 13.7 Hz, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H), 3.39–3.26 (m, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 195.7, 165.1, 164.3, 163.9, 159.8, 149.8, 132.6, 130.5, 129.4, 128.7, 123.2, 121.1, 114.2, 113.9, 112.9, 109.0, 78.8, 55.7, 55.6, 40.7, 33.5.

*4-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**4d**)*

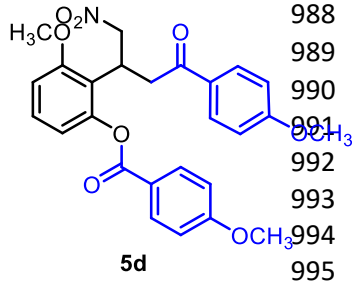


4d

The cascade synthesis was carried out as described in **General Procedure D**. Using 5-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**4**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), 1,3-bis(4-methoxyphenyl)-1,3-propanedione (**d**) (102 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 4-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**4d**) was obtained as a yellow solid (45 mg, 31%).

4d; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.16 (d, *J* = 8.9 Hz, 2H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.16–7.08 (m, 3H), 6.99 (d, *J* = 9.2 Hz, 3H), 6.86 (d, *J* = 8.9 Hz, 5H), 4.82–4.71 (m, 2H), 4.39–4.32 (m, 1H), 4.20 (q, *J* = 7.6 Hz, 1H), 3.90 (s, 4H), 3.84 (s, 3H), 3.80 (s, 3H), 3.40 (dd, *J* = 17.2, 5.7 Hz, 1H), 3.30 (dd, *J* = 17.2, 8.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 195.4, 165.5, 164.3, 163.9, 157.6, 142.4, 132.5, 130.5, 124.3, 114.2, 113.9, 113.4, 78.4, 55.7, 55.7, 55.6, 40.5, 34.1.

*3-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**5d**)*

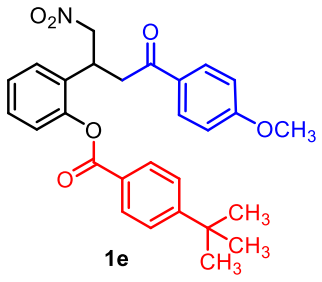


5d

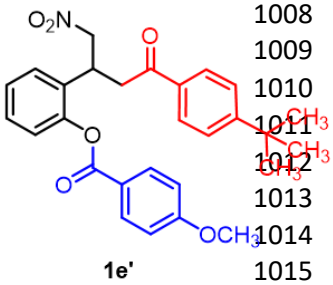
The cascade synthesis was carried out as described in **General Procedure D**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), 1,3-bis(4-methoxyphenyl)-1,3-propanedione (**d**) (102 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 72 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 5–20% ethyl acetate in hexanes as the eluent. 3-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)4-methoxybenzoate (**5d**) was obtained as a yellow solid (112 mg, 78%).

5d; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.14 (d, *J* = 8.9 Hz, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 7.29 (t, *J* = 8.3 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.85–6.79 (m, 4H), 4.89 (dd, *J* = 7.3, 2.5 Hz, 2H), 4.59 (t, *J* = 7.2 Hz, 1H), 3.90 (d, *J* = 1.3 Hz, 6H), 3.83 (s, 3H), 3.45 (d, *J* = 7.1 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.4, 165.1, 164.2, 163.7, 158.9, 150.0, 132.6, 130.5, 129.5, 129.0, 121.4, 120.0, 115.9, 114.1, 113.8, 108.9, 77.3, 55.9, 55.6, 55.5, 39.1, 31.5. HRMS (MALDI-TOF): m/z calcd for $C_{26}H_{25}NO_8Na$ [M+Na$^+$] 502.1472, found 502.1491.

*2-(4-(4-Methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(tert-butyl)benzoate (**1e**) and 2-(4-(4-(tert-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-methoxylbenzoate (**1e'**)*



1e



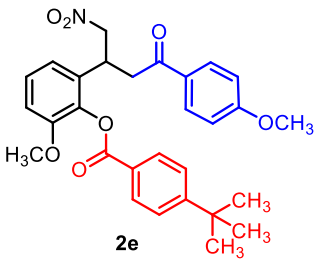
1e'

The cascade synthesis was carried out as described in **General Procedure D**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (50 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), avobenzone (**e**) (112 mg, 0.36 mmol and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25 (**1e**) and 0.23 (**1e'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 2-(4-(4-Methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(*tert*-butyl)benzoate (**1e**) was obtained as the major product in the form of yellow solid (58 mg, 41%), while 2-(4-(4-(*tert*-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-methoxylbenzoate (**1e'**) was obtained as the minor product in form of a yellow solid (56 mg, 39%).

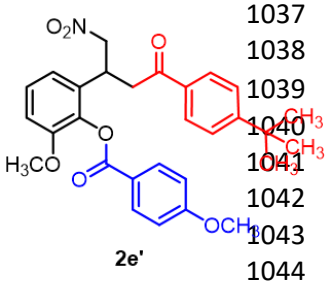
1e; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.20 (d, *J* = 8.9 Hz, 2H), 7.80 (d, *J* = 8.7 Hz, 2H), 7.44–7.31 (m, 3H), 7.27 (d, *J* = 7.1 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.01 (d, *J* = 9.0 Hz, 2H), 4.89–4.68 (m, 2H), 4.48–4.39 (m, 1H), 3.90 (s, 3H), 3.48 (dd, *J* = 17.4, 5.7 Hz, 1H), 3.34 (dd, *J* = 17.4, 8.4 Hz, 1H), 1.31 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 196.6, 165.2, 164.3, 157.5, 149.1, 133.7, 132.6, 131.5, 129.0, 128.2, 128.1, 126.7, 125.7, 123.6, 121.3, 114.2, 78.4, 55.7, 40.7, 35.2, 33.8, 31.1.

1e'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.15 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.39–7.30 (m, 2H), 7.28–7.23 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 2H), 4.85–4.73 (m, 2H), 4.44 (p, *J* = 7.3 Hz, 1H), 3.84 (s, 3H), 3.46–3.31 (m, 2H), 1.38 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 195.6, 165.5, 163.9, 158.0, 149.0, 131.5, 130.5, 130.4, 129.4, 129.0, 128.3, 126.7, 126.1, 126.0, 123.5, 114.0, 78.6, 55.6, 40.5, 35.4, 33.9, 31.2.

*2-Methoxy-6-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(tert-butyl)benzoate (**2e**) and 2-(4-(4-(tert-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-6-methoxyphenyl 4-methoxybenzoate (**2e'**)*



2e



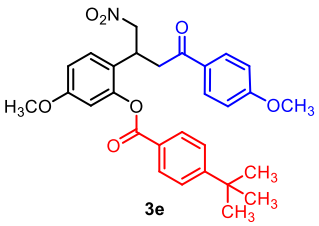
2e'

The cascade synthesis was carried out as described in **General Procedure D**. Using 3-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**2**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), avobenzone (**e**) (112 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (20% ethyl acetate in hexanes; dipping in CAM, R_f = 0.23 (**2e**) and 0.20 (**2e'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 2-(4-(4-(*Tert*-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-6-methoxyphenyl 4-methoxybenzoate (**2e'**) was obtained as the major product in the form of yellow solid (70.4 mg, 46%) while 2-methoxy-6-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(*tert*-butyl)benzoate (**2e**) was obtained as the minor product in form of yellow solid (52.5 mg, 35%).

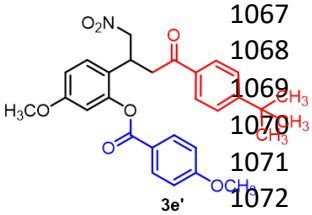
2e; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.21 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.40 (s, 2H), 7.21 (s, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 4.76 (s, 2H), 4.41 (dd, *J* = 8.2, 5.9 Hz, 1H), 3.90 (s, 3H), 3.78 (s, 3H), 3.47 (dd, *J* = 17.3, 5.4 Hz, 1H), 3.31 (dd, *J* = 17.4, 8.6 Hz, 1H), 1.31 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ_C 164.4, 164.1, 157.3, 151.9, 132.6, 128.1, 126.9, 125.6, 114.0, 111.7, 78.3, 56.0, 55.5, 35.1, 31.0.

2e'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.16 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.21 (ddt, *J* = 1.7, 1.1, 0.6 Hz, 1H), 6.92 (dd, *J* = 8.3, 1.0 Hz, 4H), 4.76 (s, 2H), 4.43–4.35 (m, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.39 (d, *J* = 5.5 Hz, 1H), 3.33 (d, *J* = 8.4 Hz, 1H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ_C 164.8, 163.8, 157.6, 151.8, 130.4, 130.4, 129.4, 126.9, 126.1, 125.7, 113.8, 111.7, 78.3, 56.0, 55.5, 40.4, 35.2, 31.1.

*5-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(tert-butyl)benzoate (**3e**) and 2-(4-(4-(tert-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-5-methoxyphenyl 4-methoxylbenzoate (**3e'**)*



3e



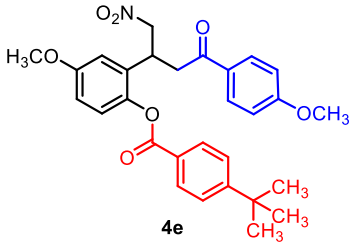
3e'

The cascade synthesis was carried out as described in **General Procedure D**. Using 4-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**3**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), avobenzone (**e**) (112 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 68 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**3e**) and 0.28 (**3e'**)) for 68 hours. The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 5-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(*tert*-butyl)benzoate (**3e**) was obtained as the minor product in the form of yellow solid (53 mg, 35%), while 2-(4-(4-(*tert*-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-5-methoxyphenyl 4-methoxylbenzoate (**3e'**) was obtained as the major product in the form of yellow solid (70 mg, 46%).

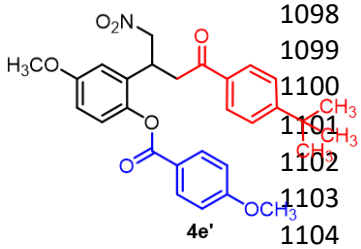
3e; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.19 (d, *J* = 8.9 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.28–7.21 (m, 1H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.81 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.74 (d, *J* = 2.5 Hz, 1H), 4.80–4.68 (m, 2H), 4.38–4.30 (m, 1H), 3.91 (s, 3H), 3.78 (s, 3H), 3.44 (dd, *J* = 17.3, 5.8 Hz, 1H), 3.32 (dd, *J* = 17.2, 8.3 Hz, 1H), 1.31 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ_C 196.6, 164.3, 159.6, 157.3, 149.8, 132.5, 128.6, 128.1, 125.6, 123.2, 121.2, 114.1, 112.8, 109.0, 78.6, 55.6, 55.5, 40.8, 35.1, 33.4, 31.0.

3e'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.07 (d, *J* = 8.6 Hz, 2H), 7.77 (d, *J* = 8.9 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.18 (d, *J* = 11.2 Hz, 1H), 6.79 (d, *J* = 9.2 Hz, 2H), 6.74 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.66 (d, *J* = 2.6 Hz, 1H), 4.71 (dd, *J* = 12.5, 6.7 Hz, 1H), 4.68–4.62 (m, 1H), 4.30–4.21 (m, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.34–3.21 (m, 2H), 1.31 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ_C 195.5, 165.2, 163.8, 159.8, 157.9, 149.7, 130.4, 130.2, 129.4, 128.7, 126.1, 125.8, 123.2, 113.8, 112.8, 108.9, 78.7, 55.5, 55.5, 40.5, 35.3, 33.6, 31.1.

*4-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(tert-butyl)benzoate (**4e**) and 2-(4-(4-(tert-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-4-methoxyphenyl 4-methoxylbenzoate (**4e'**)*



4e



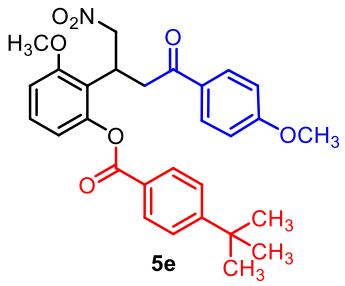
4e'

The cascade synthesis was carried out as described in **General Procedure D**. Using 5-Methoxy-2-hydroxy-*trans*-β-nitrostyrene (**4**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), avobenzone (**e**) (112 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 48 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**4e**) and 0.25 (**4e'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 4-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(*tert*-butyl)benzoate (**4e**) was obtained as the major product in the form of yellow syrup (41 mg, 28%) while, 2-(4-(4-(*tert*-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-4-methoxyphenyl 4-methoxylbenzoate (**4e'**) was obtained as the minor product in form of yellow syrup (68.4 mg, 45%).

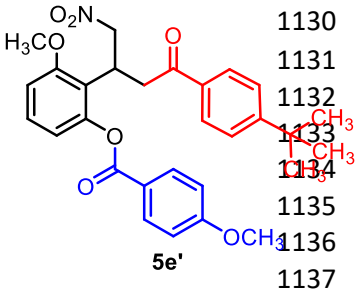
4e; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.17 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 9.2 Hz, 1H), 6.99 (d, *J* = 6.9 Hz, 2H), 6.84 (d, *J* = 6.9 Hz, 2H), 4.80–4.69 (m, 2H), 4.40–4.32 (m, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 3.45 (dd, *J* = 17.3, 5.6 Hz, 1H), 3.32 (d, *J* = 8.6 Hz, 1H), 1.30 (s, 9H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ_C 196.5, 165.5, 164.3, 157.7, 157.5, 142.4, 133.7, 132.6, 132.5, 128.2, 125.8, 124.3, 121.4, 114.2, 113.9, 113.4, 78.4, 55.7, 55.7, 40.7, 35.2, 34.0, 31.1.

4e'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.12 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 9.5 Hz, 1H), 6.85 (d, *J* = 9.2 Hz, 4H), 4.82–4.70 (m, 2H), 4.38–4.26 (m, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.39 (dd, *J* = 17.2, 5.7 Hz, 1H), 3.30 (dd, *J* = 17.2, 8.3 Hz, 1H), 1.36 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ_C 195.4, 163.9, 157.7, 142.3, 132.5, 130.5, 130.3, 129.1, 126.2, 125.9, 124.2, 114.0, 113.9, 113.4, 78.5, 55.7, 55.6, 40.4, 35.4, 34.1, 31.2.

*3-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(tert-butyl)benzoate (**5e**) and 2-(4-(4-(tert-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-3-methoxyphenyl 4-methoxylbenzoate (**5e'**)*



5e



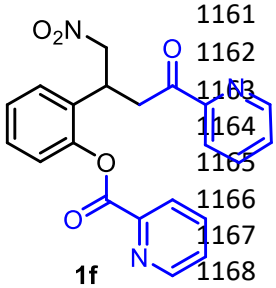
5e'

The cascade synthesis was carried out as described in **General Procedure D**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), avobenzone (**e**) (112 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.30 (**5e**) and 0.28 (**5e'**)). The crude mixture was purified by column chromatography using gradient elution with 5–30% ethyl acetate in hexanes as the eluent. 3-Methoxy-2-(4-(4-methoxyphenyl)-1-nitro-4-oxobutan-2-yl)phenyl 4-(*tert*-butyl)benzoate (**5e**) was obtained as the major product in the form of yellow solid (73 mg, 48%), while 2-(4-(4-(*tert*-butyl)phenyl)-1-nitro-4-oxobutan-2-yl)-3-methoxyphenyl 4-methoxylbenzoate (**5e'**) was obtained as the minor product in the form of yellow solid (45.4 mg, 30%).

5e; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.19 (d, *J* = 8.9 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.29 (s, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 6.82 (d, *J* = 8.3 Hz, 2H), 4.88 (dd, *J* = 22.5, 7.3 Hz, 2H), 4.64–4.57 (m, 1H), 3.90 (d, *J* = 1.5 Hz, 7H), 3.49 (dd, *J* = 7.2, 5.9 Hz, 2H), 1.30 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 197.3, 165.0, 164.1, 158.8, 157.0, 150.0, 133.9, 132.6, 128.9, 128.1, 125.5, 121.4, 120.1, 115.8, 114.1, 108.8, 77.1, 55.8, 55.5, 39.3, 35.1, 31.2, 31.0. HRMS (MALDI-TOF): m/z calcd for $C_{29}H_{31}NO_7Na$ [M+Na$^+$] 528.1993, found 528.2029.

5e'; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.13–8.07 (m, 3H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.29 (t, *J* = 8.3 Hz, 1H), 7.24 (s, 1H), 6.87–6.78 (m, 4H), 6.48 (dd, *J* = 28.6, 7.3 Hz, 1H), 4.89 (dd, *J* = 7.3, 1.6 Hz, 2H), 4.60 (t, *J* = 7.2 Hz, 1H), 3.91 (d, *J* = 7.4 Hz, 6H), 3.83 (s, 3H), 3.46 (d, *J* = 7.1 Hz, 2H), 1.37 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 196.4, 165.4, 163.7, 158.9, 157.7, 150.0, 133.8, 130.9, 130.5, 130.4, 129.5, 129.1, 127.8, 126.2, 126.1, 125.8, 120.0, 115.8, 113.8, 109.3, 109.0, 102.1, 77.3, 55.9, 55.5, 39.1, 35.3, 31.2, 29.7, 22.8. HRMS (ESI-QTOF): m/z calcd for $C_{29}H_{31}NO_7Na$ [M+Na$^+$] 528.19927, found 528.20063.

*2-(1-Nitro-4-oxo-4-(pyridin-2-yl)butan-2-yl)phenyl picolinate (**1f**)*

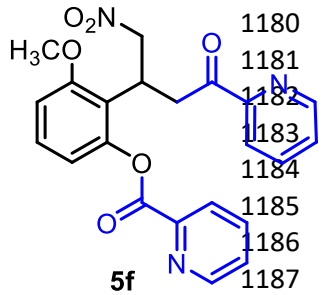


1f

The cascade synthesis was carried out as described in **General Procedure D**. Using 2-hydroxy-*trans*-β-nitrostyrene (**1**) (50 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), 1,3-di(2-pyridyl)1,3-propanedione (**f**) (81 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 4 hours. The reaction was monitored by TLC (40% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 10–50% ethyl acetate in hexanes as the eluent. 2-(1-Nitro-4-oxo-4-(pyridin-2-yl)butan-2-yl)phenyl picolinate (**1f**) was obtained as a yellow solid (98 mg, 84%).

1f; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.80 (d, *J* = 4.7 Hz, 1H), 8.51 (d, *J* = 2.7 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 7.95–7.84 (m, 2H), 7.73 (d, *J* = 6.0 Hz, 1H), 7.56–7.49 (m, 1H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.32–7.18 (m, 3H), 4.80 (d, *J* = 7.4 Hz, 2H), 4.53–4.45 (m, 1H), 3.83 (dd, *J* = 18.2, 6.8 Hz, 1H), 3.69–3.62 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 198.6, 163.5, 152.7, 150.3, 149.0, 147.2, 137.4, 137.0, 131.4, 128.9, 128.6, 127.6, 127.5, 126.8, 126.0, 123.1, 121.9, 78.7, 40.2, 33.9.

*3-Methoxy-2-(1-nitro-4-oxo-4-(pyridin-2-yl)butan-2-yl)phenyl picolinate (**5f**)*

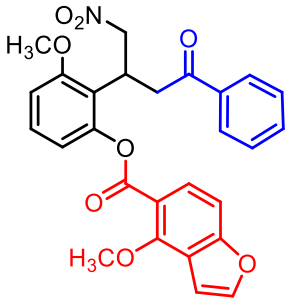


5f

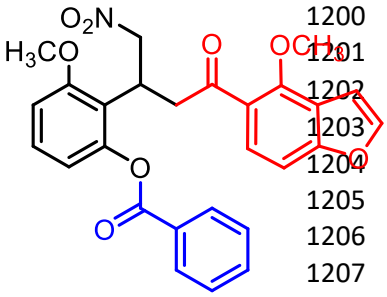
The cascade synthesis was carried out as described in **General Procedure D**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-C$_{12}$C$_{12}$** (24 mg, 0.03 mmol), 1,3-di(2-pyridyl)1,3-propanedione (**f**) (81 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 16 hours. The reaction was monitored by TLC (40% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25). The crude mixture was purified by column chromatography using gradient elution with 10–50% ethyl acetate in hexanes as the eluent. 3-Methoxy-2-(1-nitro-4-oxo-4-(pyridin-2-yl)butan-2-yl)phenyl picolinate (**5f**) was obtained as a yellow solid (97 mg, 77%).

5f; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.88–8.83 (m, 1H), 8.55–8.51 (m, 1H), 8.40 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.98–7.91 (m, 2H), 7.77 (d, *J* = 1.7 Hz, 1H), 7.57 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.42–7.38 (m, 1H), 7.28 (d, *J* = 13.6 Hz, 1H), 6.93–6.81 (m, 2H), 4.92 (d, *J* = 1.3 Hz, 2H), 4.77–4.70 (m, 1H), 3.91 (s, 3H), 3.90–3.84 (m, 1H), 3.78 (dd, *J* = 18.3, 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 199.1, 163.3, 159.0, 152.8, 150.2, 149.7, 148.8, 147.2, 137.6, 137.1, 129.0, 127.6, 127.4, 126.2, 120.1, 115.5, 109.2, 77.4, 56.0, 39.3, 30.8. HRMS (MALDI-TOF): m/z calcd for $C_{22}H_{19}N_3O_6Na$ [M +Na$^+$] 444.111661, found 444.12180.

*3-Methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl 7-methoxybenzofuran-6-carboxylate (**5g**) and 3-methoxy-2-(4-(4-methoxybenzofuran-5-yl)-1-nitro-4-oxobutan-2-yl)phenyl benzoate (**5g'**)*



5g



5g'

The cascade synthesis was carried out as described in **General Procedure D**. Using 6-methoxy-2-hydroxy-*trans*-β-nitrostyrene (**5**) (59 mg, 0.30 mmol), **AmDTC-$C_{12}C_{12}$** (24 mg, 0.03 mmol), pongamol (**g**) (106 mg, 0.36 mmol) and water (1.5 mL), the reaction time was 72 hours. The reaction was monitored by TLC (30% ethyl acetate in hexanes; dipping in CAM, R_f = 0.25 (**5g** and **5g'**)). The crude mixture was purified by column chromatography using gradient elution with 5–40% ethyl acetate in hexanes as the eluent. An inseparable mixture of 3-methoxy-2-(1-nitro-4-oxo-4-phenylbutan-2-yl)phenyl 7-methoxybenzofuran-6-carboxylate (**5g**) and 3-methoxy-2-(4-(4-methoxybenzofuran-5-yl)-1-nitro-4-oxobutan-2-yl)phenyl benzoate (**5g'**) was obtained as white solid (82 mg, 57%).

5g and **5g'**; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.14 – 8.09 (m, 3H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.56 (d, *J* = 2.3 Hz, 4H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 7.9 Hz, 3H), 7.28 (s, 3H), 7.12 (d, *J* = 8.7 Hz, 1H), 6.90 – 6.78 (m, 6H), 4.99 – 4.78 (m, 4H), 4.68 (dt, *J* = 33.6, 7.1 Hz, 2H), 4.15 (s, 2H), 4.01 (s, 4H), 3.89 (d, *J* = 5.0 Hz, 6H), 3.56 (d, *J* = 7.2 Hz, 4H), 3.48 (d, *J* = 7.0 Hz, 2H). HRMS (ESI-QTOF): m/z calcd for $C_{27}H_{23}NO_8Na$ [M+Na^+] 528.19927, found 528.20063.

Conflicts of interest

There are no conflicts to declare.

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