Structure-Reactivity relationship of olefins as Electrophiles and Nucleophiles: Factors Influencing

Jeetendra Panda,[a] Jigyansa Sahoo,[a] Gokarneswar Sahoo[a]*

National Institute of Technology Rourkela

a) Organocatalysis and Synthesis Laboratory, Department of Chemistry, National Institute of Technology Rourkela, Odisha, India, 769008

*Corresponding author, email: sahoog@nitrkl.ac.in

Abstract

This article depicts the reactivity study of olefins towards nucleophilic and electrophilic reactions. The real-time NMR kinetic experiments showcased how the reactivity of the olefins varies with varying electron density over the olefinic bond. Additionally, the SC-XRD study reveals not only the electron density over olefin makes the difference in reactivity but the planar arrangement also has an impact and could nullify these substitution effects.

1. Introduction

The soft π electron density present on the C=C double bond constitutes a reactive site on the hydrocarbon skeleton. Olefins are readily available and valuable building blocks in natural products, materials and pharmaceuticals. Therefore, many olefins have a tremendous demand in industry, such as ethylene (with a worldwide production over 225.52 million metric tons in 2022),[1] propene (with a worldwide production around 150.3 million metric tons in 2022),[2] and styrene (15.44 million metric tons in 2022).[3] Structurally, olefins contain at least one π bond, which can be either a good electrophile or nucleophile. The π-system represents the key step of many synthetically important reactions such as Sharpless dihydroxylation,[4] ozonolysis,[5] Diels-Alder reaction,[6] Wacker oxidation,[7] hydrogenation,[8] halohydrin synthesis,[9] Friedel-Crafts alkylations and acylations,[10] Prins reactions,[11] Hosomi-Sakurai allylations,[12] Mukaiyama aldol cross-couplings,[13] Nicholas propargylations,[14] Mannich aminoalkylations,[15] and Tsuji-Trost allylations[16].

In the case of unsubstituted alkenes, the two carbon atoms participating in the double bond are comparatively electron rich because of the higher electronegativity of the carbon atom relative to the hydrogen atom (***C*=*C***–H). The more electronegative character of the sp^2 carbon with respect to the sp^3 carbon is an additional source for the better stabilization of a negative charge

in the former case. Therefore, the usual reactivity pattern of the C=C functionality is the attack by electrophiles, E^+. However, this behavior can be reversed or modified by suitable substitutions. For instance, in presence of an electron donating group the olefinic bond is more reactive towards the electrophilic substitution reaction whereas in presence of an electron withdrawing group the probable reactivity of C=C functionality would be more towards the nucleophiles. Additionally, the alignment of the double bond with the substituents (EDG/EWG) also affects its reactivity. Previous literature studies[17] have reported that the reactivity of an olefin towards the electrophile or nucleophile depend upon the electron density of the C=C.

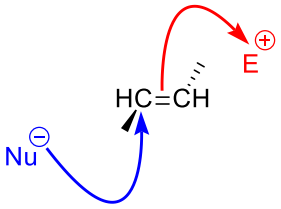


Figure 1. Functionalization of C=C using electrophile and nucleophile

2. Results and Discussion

various reactivity patterns were observed with different types of substrates towards the dibromination protocol: NBS-300 mol%, pyrrolidine-10 mol% (Figure 1).[18] The olefinic bond of substituted methyl (*E*)- cinnamates and *β*-nitrostyrenes reacted well with the established protocol whereas, substituted *β*-methyl-*β*-nitrostyrenes surprisingly did not provide the corresponding dibromo product except for 4-methoxy-*β*-methyl *β*-nitrostyrene. Thus a detailed investigation was carried out to find the reactivity pattern of C=C functionality in *β*-methyl-*β*-nitrostyrenes in comparison to substituted methyl (*E*)-cinnamates and *β*-nitrostyrenes.

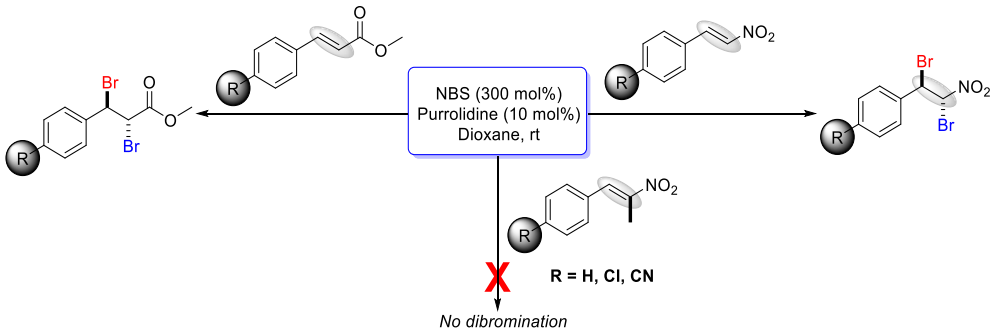


Figure 2. The reactivity difference of various C=C functionality

With the intent to study the reactivity of the differently substituted olefinic bonds, we have taken various electrophilic sources such as molecular bromine (Br_2, **1a**), N-bromosuccinimide

(NBS, **1b**), 2-bromotetrahydrocyclopentapyrrole-1,3-dione (**1c**) and N-bromophthalimide (**1d**) and pyrrolidine as the nucleophilic source **2**.

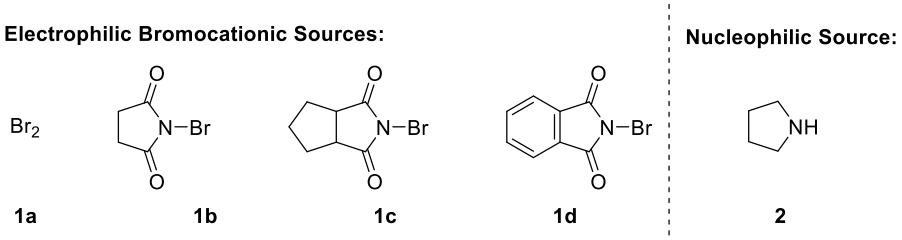
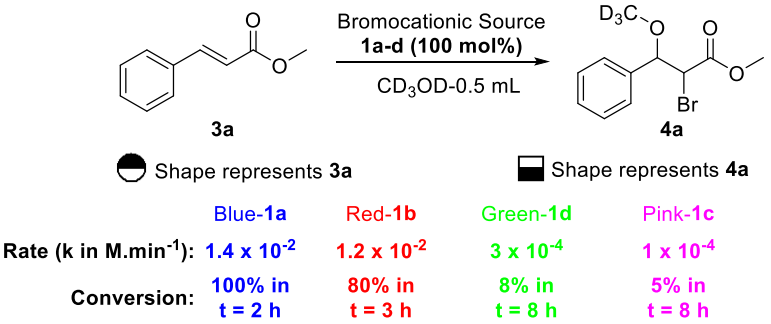


Figure 3. Various electrophilic and nucleophilic sources used to study C═C reactivity

Reactivity of olefin in presence of electrophiles: Initially, the nucleophilic character of the C═C bond was studied for all the olefinic substrates.

a) **Reactivity of methyl (*E*)-cinnamate (3a) in presence of electrophiles:** At first, upon reaction with methyl (*E*)-cinnamate (**3a**), Br_2 and NBS acted as reactive electrophilic reagents resulting in the co-halogenated product [**4a**]$t_{2\ h}$ **4a** = 100 and [**4a**]$t_{3\ h}$ = 80% respectively. Whereas 2-bromotetrahydrocyclopentapyrrole-1,3-dione (**1c**) and N-bromopthalimide (**1d**) acted as poor electrophilic sources resulting in co-halogenated product **4a** in 5% at t = 8 h and 8% at t = 8 h respectively. In comparison to Br_2 and NBS, 2-bromotetrahydrocyclopentapyrrole-1,3-dione and N-bromopthalimide showed slower reaction rates (Figure 4). The conjugation of the phenyl ring to the succinimide backbone in N-bromophthalimide (**1d**), might decrease the electrophilicity of the 'Br' atom, whereas for **1c** the reason is not very clear to us.



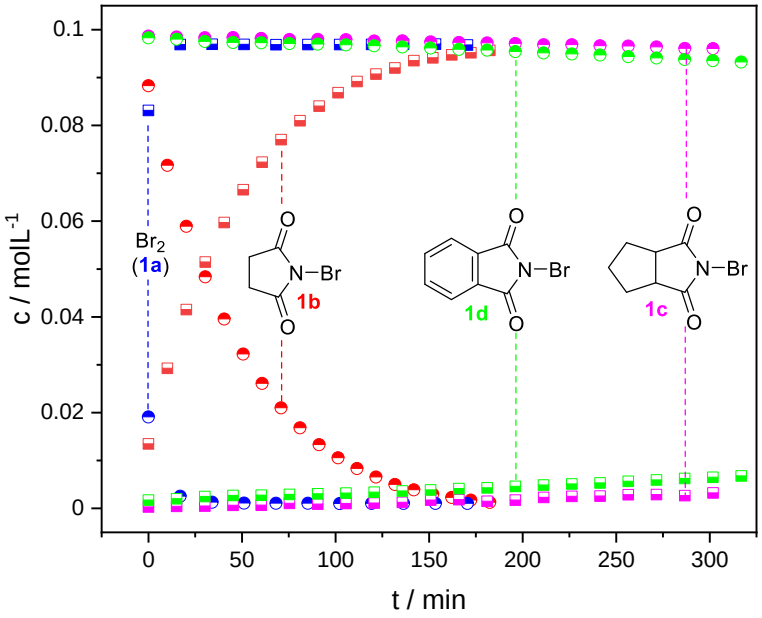
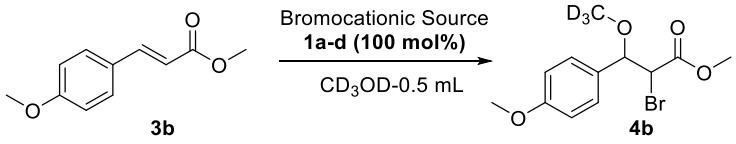


Figure 4. A plot for concentration vs. time for reaction of methyl (*E*)-cinnamate with various electrophilic bromine sources in CD_3OD; **Note**: In case of molecular bromine (Br_2, **1a**), there was a mixture of dibromo product and methoxy bromo product **4a** in the ratio of 20:80.

b) **Reactivity of methyl (*E*)-4-methoxycinnamate (3b) in presence of electrophiles:** In case of methyl (*E*)-4-methoxycinnamate (**3b**) all the electrophilic bromo reagents (**1a-d**) reacted relatively at a faster rate than methyl (*E*)-cinnamate (Figure 5). The conversion of methoxy-bromo product **4b** has been measured for various electrophilic bromo reagents are [**1a**]$t_{1.5\ h}$ = 74%, [**1b**]$t_{3\ h}$ = 100%, [**1c**]$t_{8\ h}$ = 56%, [**1d**]$t_{6\ h}$ = 60% respectively. The rate of the reaction is highest in Br_2 (**1a**) followed by **1b**, **1c** and **1d** correspondingly, in the similar sequence as of reaction with **3a**. This could be attributed to the electron donating effect of the methoxy substituent present at C-4 of the phenyl ring.



	Blue-**1a**	Red-**1b**	Green-**1d**	Pink-**1c**
Rate (k in $M.min^{-1}$):	Fast Reaction	1.06×10^{-2}	3.9×10^{-3}	1.6×10^{-3}
Conversion:	74% in t = 1.5 h	100% in t = 2.5 h	60% in t = 6 h	56% in t = 8 h

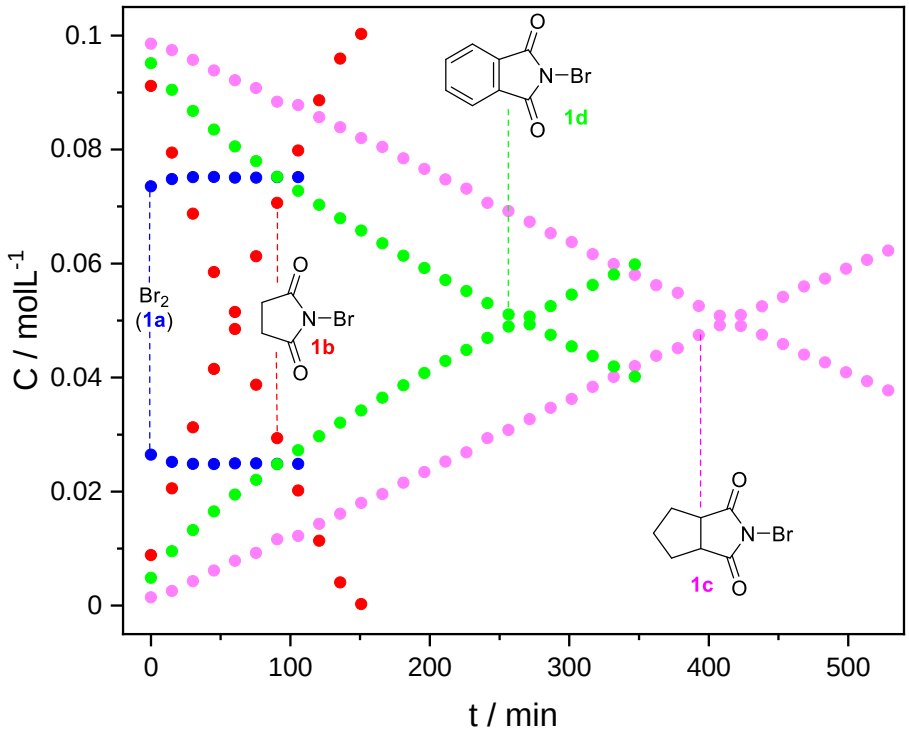
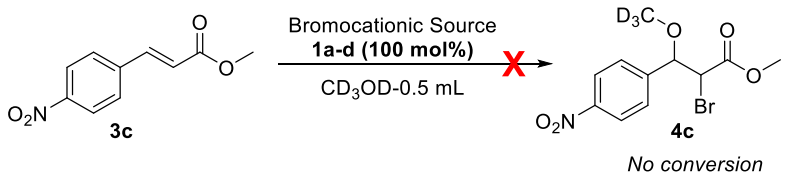


Figure 5. A plot for concentration vs. time for reaction of methyl-4-methoxy-(*E*)-cinnamate with various electrophilic sources in CD_3OD

c) Reactivity of methyl (*E*)-4-nitrocinnamate (3c) in presence of electrophiles: In a similar way, when the same electrophilic bromo reagents (**1a-d**) were reacted with methyl (*E*)-4-nitrocinnamate (**1c**), no product formation was observed. In this case, the presence of the electron withdrawing substituent ($-NO_2$) at C-4 of the phenyl ring might be the reason for lowering the electron density of the olefin making it unreactive (Scheme 1).



Scheme 1. Reactivity of C=C of methyl-(*E*)-4-nitrocinnmates (**3c**) in presence of various electrophilic bromocationic sources (**1a-d**)

By comparing the above results it was found that, in case of *(E)*-cinnamates, the nucleophilicity of the olefinic bond is substantially affected by the nature of the substituents on the phenyl ring. The electron donating groups present on the phenyl ring increases the nucleophilic activity of the olefinic bond by pushing the electron flow towards the C=C whereas the electron

withdrawing groups decreases the nucleophilic activity of the same by pulling the electron density. Subsequently, when the reactivity order of the various electrophilic bromo reagents is compared (**3a-d**), it was found that Br_2 reacts at a faster rate than the NBS followed by 2-bromotetrahydrocyclopentapyrrole-1,3-dione (**3c**) and N-bromopthalimide (**3d**) (Figure 5 and Figure 6).

In a similar way, a comparison study presenting the reactivity of substituted methyl cinnamates showed the electrophilic reaction is faster in case of –***OCH₃*** substitution on the phenyl ring whereas the –***NO₂*** substituted methyl (*E*)-cinnamate remained unreactive (Figure 6).

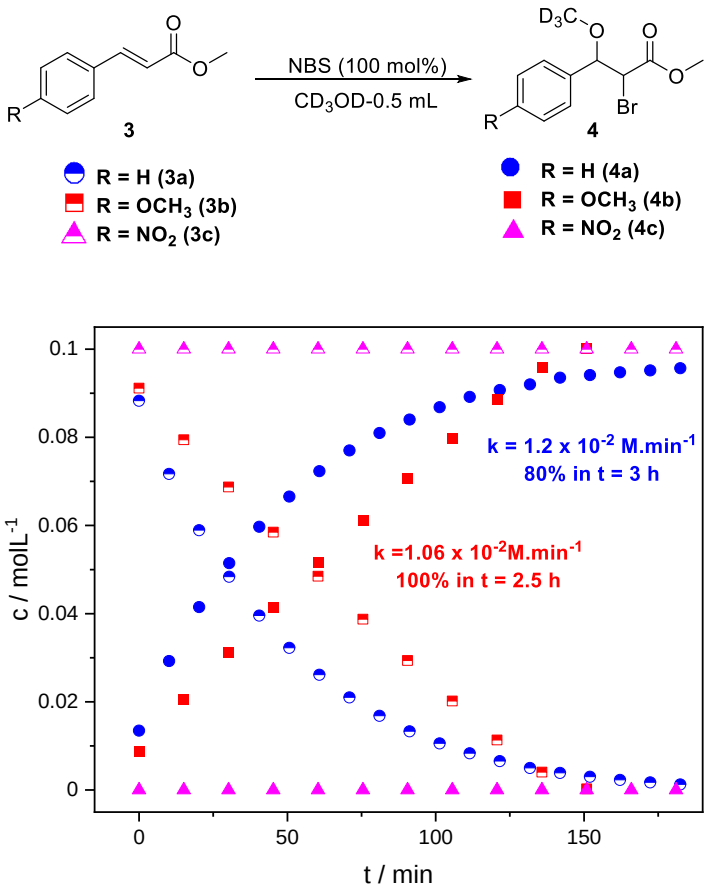
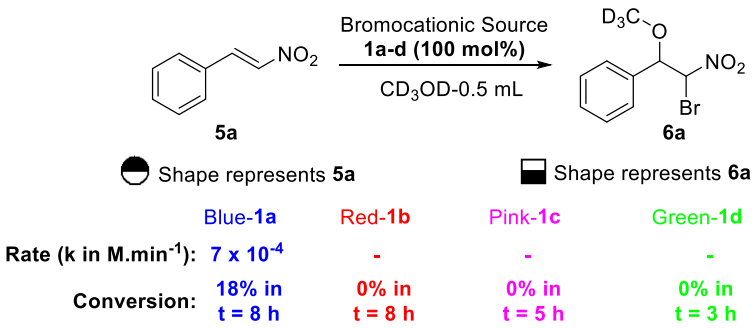


Figure 6. A comparison study of substituent effect on the electrophilic substitution reaction of methyl (*E*)-cinnamates (**3a-c**)

Further, the nucleophilic reactivity of the C=C functionality of various substituted *β*-nitrostyrenes were studied with the above mentioned bromo-electrophiles (**1a-d**). Similar to methyl (*E*)-cinnamates (**4.3**), it was observed that the rate of the reaction is influenced depending upon the substituents present on the phenyl ring.

d) **Reactivity of *β*-nitrostyrene (5a) in presence of electrophiles:** Although *β*-nitrostyrene (**5a**) follows the similar trend to that of methyl (*E*)-cinnamates as a nucleophile but the reaction rate is relatively slower. In case of *β*-nitrostyrene (**5a**), the co-halogenated product **6a** forms with molecular bromine (Br_2), but with only 18% conversion in 8 h, whereas all others electrophiles (**1b-d**) remain unreacted (Figure 7).



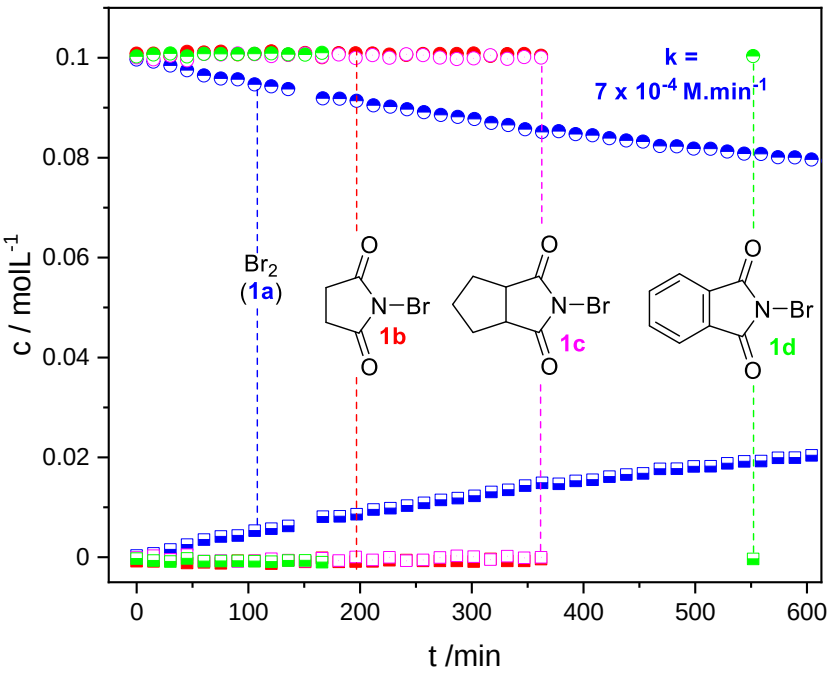


Figure 7. A plot for concentration vs. time for reaction of *β*-nitrostyrenes with various electrophilic sources in CD_3OD; **Note**: In case of molecular bromine (Br_2, **1a**), there is a mixture of dibromo *β*-nitrostyrene and methoxy bromo *β*-nitrostyrene (**6a**) in the ratio of 30:70.

e) **Reactivity of 4-methoxy *β*-nitrostyrene (5b) in presence of electrophiles:** In case of 4-methoxy-*β*-nitrostyrene (**5b**) all the electrophilic bromo reagents (**1a-d**) reacted swiftly which could be due to the increased electron density over the olefinic bond owing to the presence of

electron donating substituent on the phenyl ring (Figure 8). The conversion of methoxy-bromo 4-methoxy-*β*-nitrostyrene **(5b)** has been measured for various electrophilic bromo reagents is [**1a**]$t_{2\ h}$ = 100%, [**1b**]$t_{4\ h}$ = 100%, [**1c**]$t_{8\ h}$ = 100%, [**1d**]$t_{6\ h}$ = 100% respectively. Additionally, the rate of the reaction is highest in Br_2 (**1a**) followed by **1b**, **1c** and **1d** correspondingly.

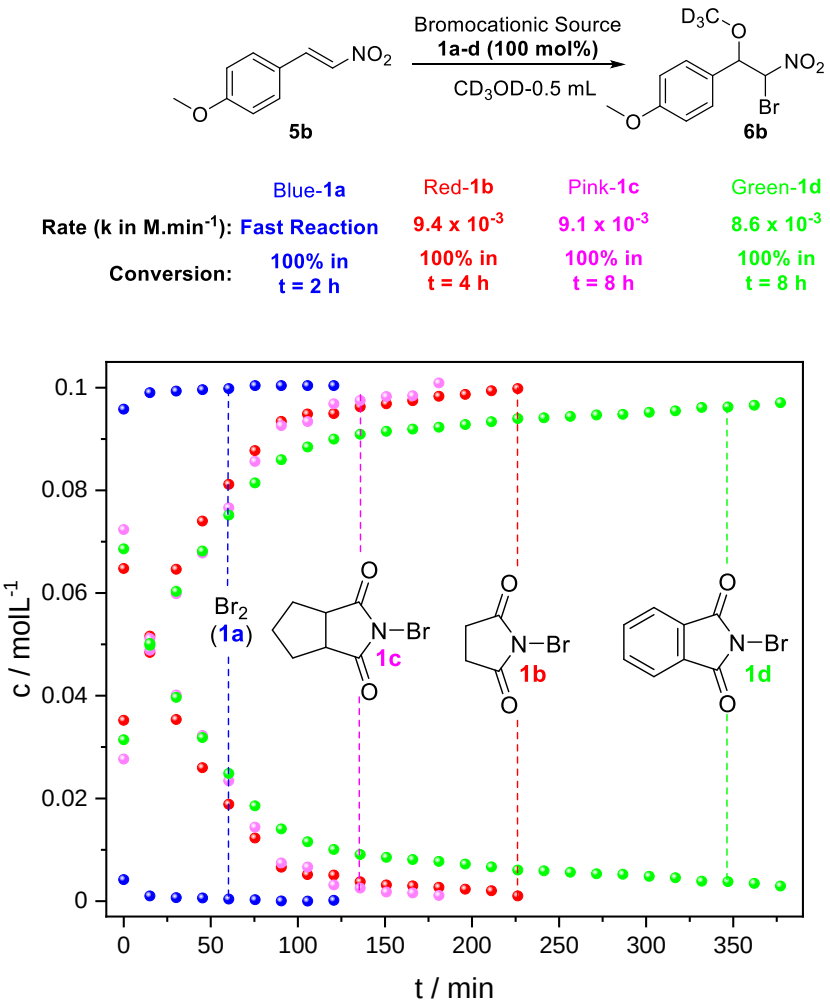
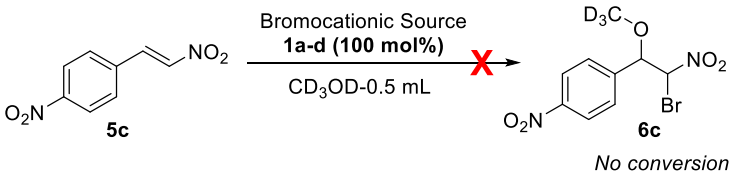


Figure 8. A plot for concentration vs. time for reaction of 4-methoxy-*β*-nitrostyrene (**5b**) with various electrophilic sources in CD_3OD

f) **Reactivity of 4-nitro-*β*-nitrostyrene (5c) in presence of electrophiles:** 4-nitro-*β*-nitrostyrene (**5c**) remained unreactive towards all the electrophilic reagents as seen in previous experiments (Scheme 2).



Scheme 2. Reactivity of C=C 4-nitro-*β*-nitrostyrene (**5c**) in presence of various electrophilic bromocationic sources (**1a-d**)

Therefore, by comparing the reactivity of substituted *β*-nitrostyrenes **5**, it was found that, the co-halogenated product **6** resulted with only 4-methoxy-*β*-nitrostyrene (**5b**) with 100 % conversion in 4 h and the rate of the reaction was measured to be k = 9.4 x 10^{-3} min^{-1}. However, *β*-nitrostyrene (**5a**) and 4-nitro-*β*-nitrostyrene (**5c**) remained unreactive (Figure 9).

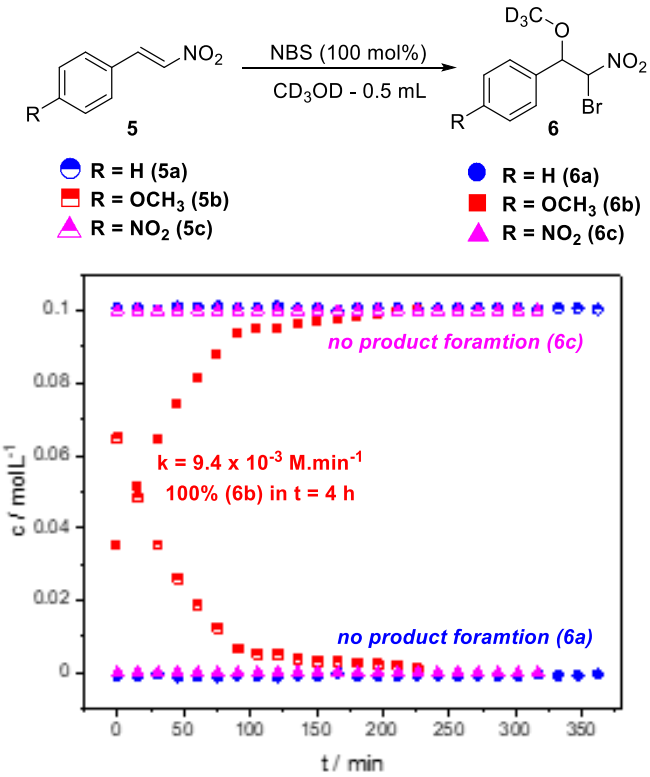
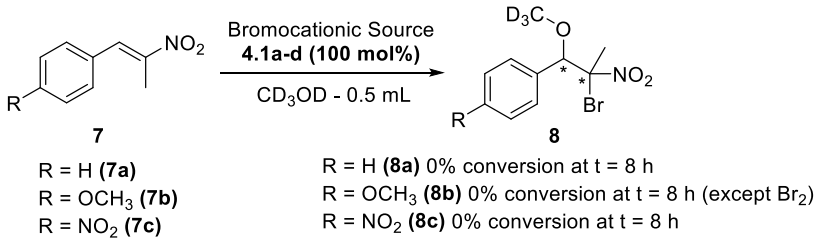


Figure 9. A comparison study of substituent effect on the electrophilic substitution reaction of *β*-nitrostyrenes **5**

Unlike substituted *β*-nitrostyrenes **5**, substituted *β*-methyl-*β*-nitrostyrenes **7** did not react with the electrophilic bromo reagents (**1a-d**). The only exception being the reaction of 4-methoxy-*β*-methyl-*β*-nitrostyrene (**7b**) with molecular bromine (Br_2, **1a**) which resulted in the co-halogenated product **8b** with 51% conversion at t = 4 h.



Scheme 3. Reactivity of C=C of *β*-methyl-*β*-nitrostyrenes **7** in presence of various electrophilic bromocationic sources (**1a-d**)

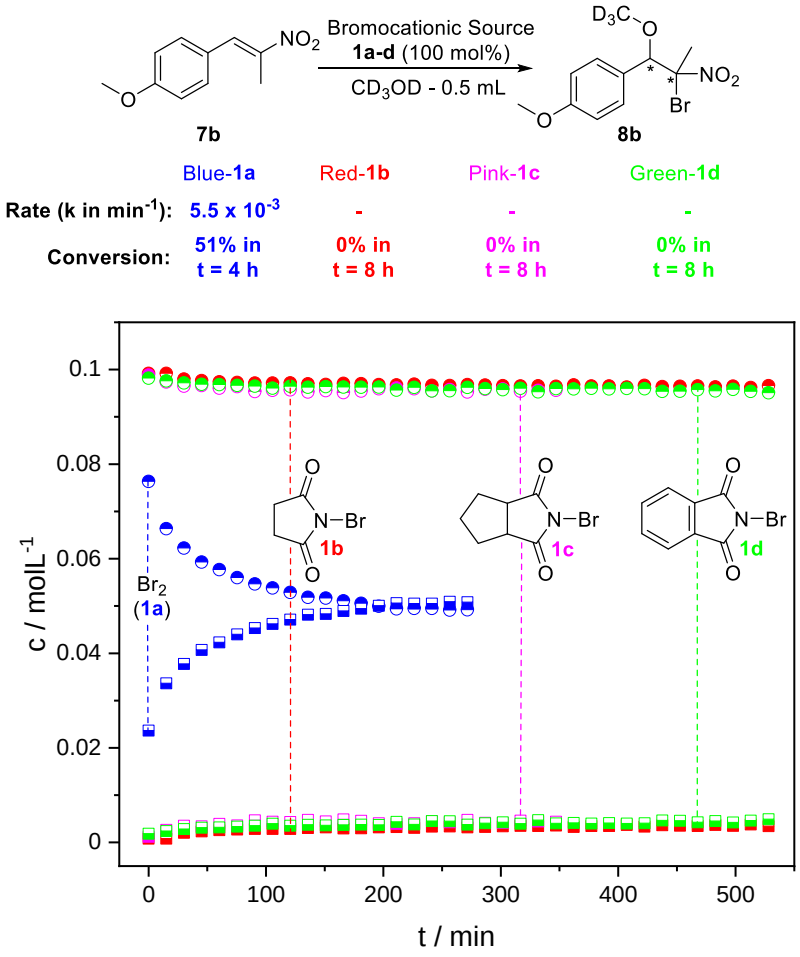


Figure 10. A plot for concentration vs. time for reaction of 4-methoxy-*β*-methyl-*β*-nitrostyrene (**7b**) with various electrophilic sources in CD_3OD

When substituted *β*-methyl-*β*-nitrostyrenes **7** were compared for reactivity towards N-bromosuccinimide (**1b**), it was found that none of the nitrostyrenes **7** gave the co-halogenated product **8** unlike methyl-(*E*)-4-cinnmates **3** and *β*-nitrostyrenes **5** (Figure 11).

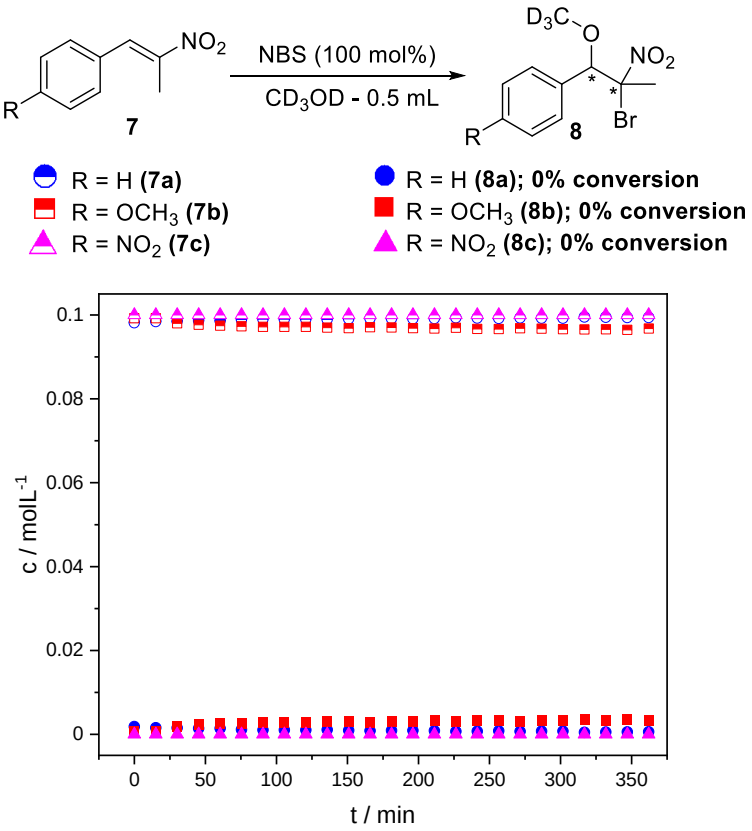
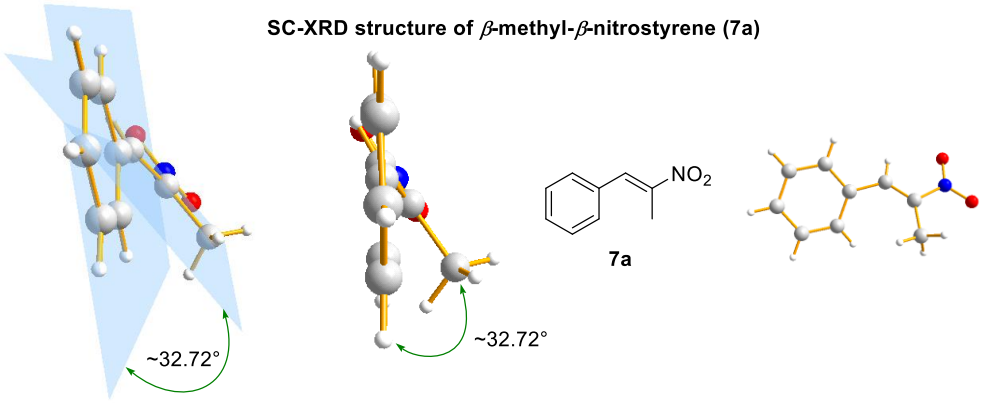
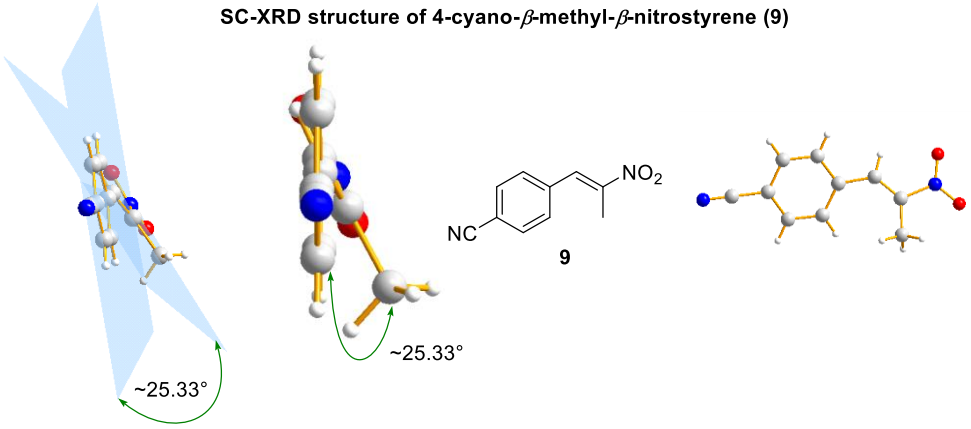


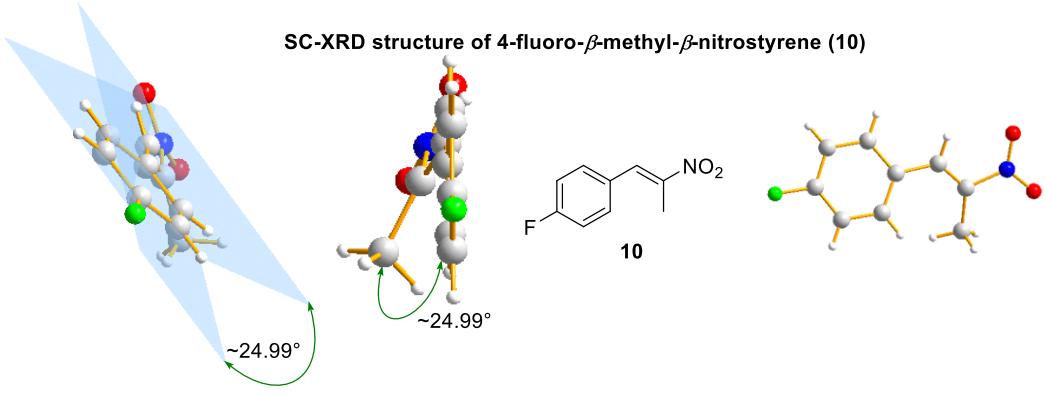
Figure 11. A comparison study of substituent effect on the electrophilic substitution reaction of *β*-methyl-*β*-nitrostyrenes

The discrepancy in the reactivity of *β*-methyl-*β*-nitrostyrenes **7** in presence a methyl substituent only, was quite intriguing. Presence of methyl substituent at the olefin, is expected to increase the nucleophilicity of the olefinic bond. But the sluggishness of the reactions was observed. Primarily, the decrease in reactivity of the C=C in the presence of an extra substituent at *β*-carbon could be either due to the steric hindrance at the olefin bond or disruption of the conjugation of the olefinic bond with the phenyl ring. Thus we continued our study to examine the structure of *β*-methyl-*β*–nitrostyrene derivatives through the SC-XRD crystal structures (Figure 12). Although we were not successful to get appropriate crystals of **7b**, and **7c**, for SC-XRD studies, we did get the single crystal structures of three *β*-methyl-*β*–nitrostyrenes **7a** (R = H),[17] **9** (R = CN) and **10** (R = F) as well as *β*–nitrostyrene (**5a**)[17]. In the Figure 4.13, it can clearly be seen that the phenyl ring and the olefin are in different planes.[17] This could cause a disruption of conjugation as a result of which the nature of the phenyl ring could be inconsequential in determining the electron density over the double bond. However, this makes the electron withdrawing nature of the nitro group dominant lowering the electron density over the olefin making the *β*-methyl-*β*–nitrostyrenes unsuitable for nucleophilic attack. We believe

that the structures of **7b**, and **7c** would be similar to that of **7**, **9** and **10** with the phenyl ring out-of-conjugation with the olefin.







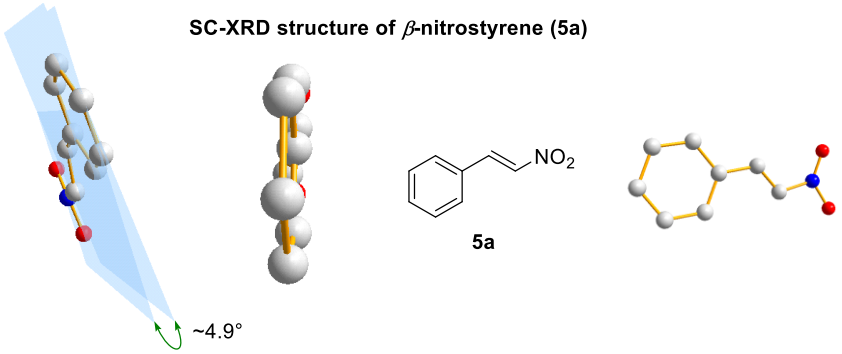
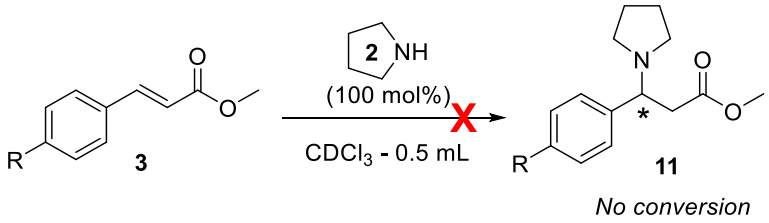


Figure 12. Single Crystal-XRD structure of *β*-methyl *β*-nitrostyrenes (**7a**, **9**, **10**) and *β*-nitrostyrene (**5a**)

Reactivity of olefin in presence of nucleophile: After being able to find the structure-reactivity relationship of the olefins towards electrophilic addition reaction, we intended to examine the same for nucleophilic addition reaction with an assumption of a reverse structure-activity relationship. The nucleophilic substitution reaction of the C=C functionality was then accessed to compare the reactivity of the olefins. In contrast to electrophilic substitution reaction, the rate of reaction of substituted methyl (*E*)-cinnamates towards nucleophiles showed no product formation. This could be due to the poor electrophilic nature of the olefinic bond owing to the presence of ester group.



R = -H (**3a**)
R = -OCH_3 (**3b**)
R = -NO_2 (**3c**)

R = -H (**11a**), t = 14 h
R = -OCH_3 (**11b**), t = 11 h
R = -NO_2 (**11c**), t = 10 h

Scheme 4. Reaction of substituted methyl (*E*)-cinnamate with pyrrolidine in $CDCl_3$

In order to investigate the nucleophilic substitution reactions similar control experiments were performed with various *β*-nitrostyrenes **5** and *β*-methyl-*β*-nitrostyrenes **7** using pyrrolidine as the nucleophile. As a result, with *β*-nitrostyrenes **5a** and **5c**, the product aldamine **12** formation was observed immediately after the addition of pyrrolidine. However, with 4-methoxy-*β*-nitrostyrene (**5b**), the aldamine product **12** was obtained correspondingly at a slower rate.

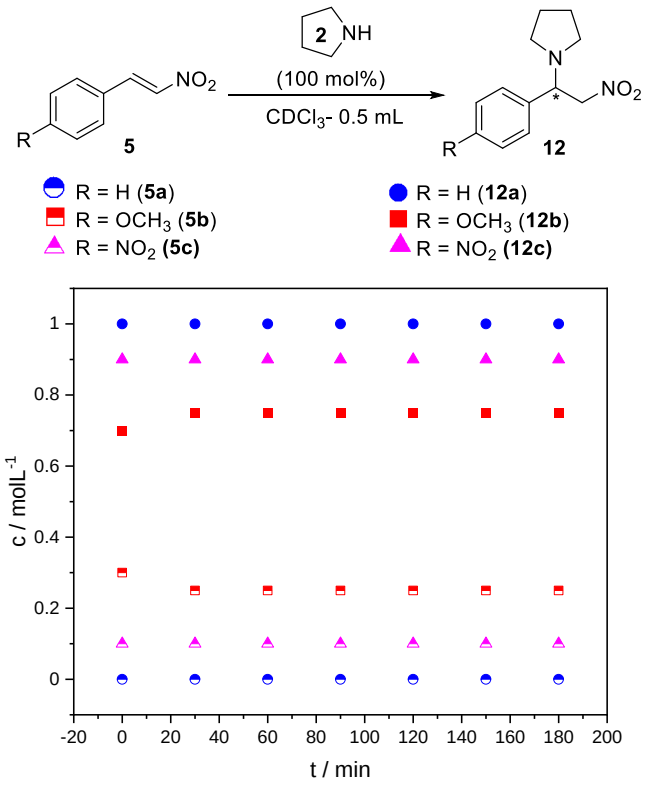


Figure 13. A plot for concentration vs. time showing the comparative study of substituent effect on the nucleophilic substitution reaction of *β*-nitrostyrenes **5**

However, as seen in the reaction profile diagrams, the quick formation of the aldamine product was observed in *β*-nitrostyrenes **4**, whereas in case of *β*-methyl*β*-nitrostyrene **6** a gradual increase in concentration of the product was obtained. *β*-methyl *β*-nitrostyrenes having electron withdrawing groups on the aromatic ring showed faster reversal to the aldamine intermediate **13** as compared to those having electron donating groups. With *β*-methyl *β*-nitroalkene (4-H, **7a**) the aldamine intermediate formation at [**13a**]t_0 = 0.05, whereas with groups having electron donating groups such as (4-OMe, **7b**) the aldamine concentration is [**13b**]t_0 = 0.02 (Figure 4.13). With electron withdrawing group (4-NO_2, **7c**), the aldamine concentration was relatively higher, [**13c**]t_0 = 0.09 (Figure 14).

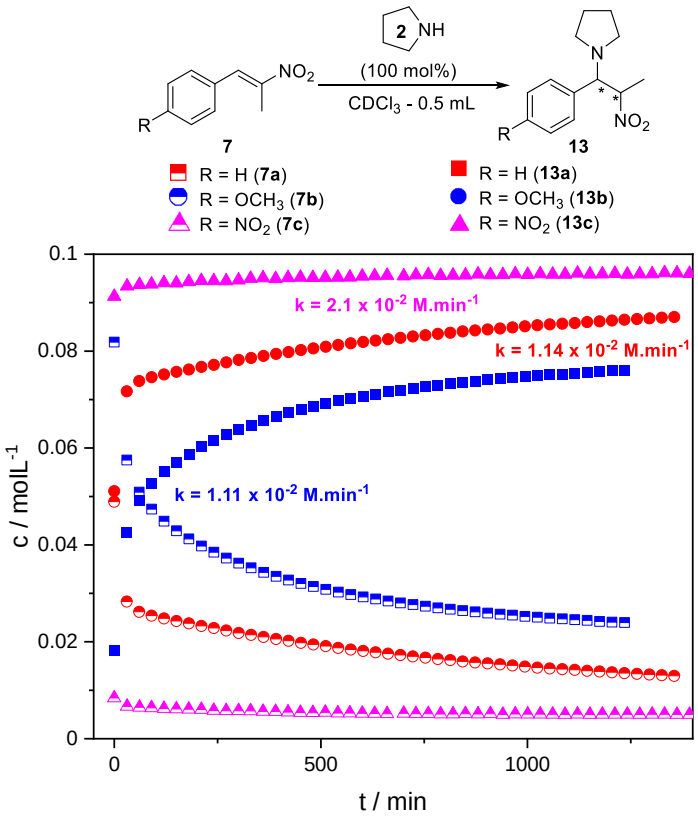


Figure 14. A plot for concentration vs. time showing the comparative study of substituent effect on the nucleophilic substitution reaction of *β*-methyl-*β*-nitrostyrene

3. Conclusion

In conclusion, rate of electrophilic substitution reaction of various types of olefins were studied and it was observed that the C=C functionality present in methyl (*E*)-cinnamate has the highest rate of reaction towards the electrophilic sources. Comparing the *β*-methyl-*β*-nitrostyrenes, *β*-nitrostyrenes reacted well with the electrophiles but due to the missing conjugation with the aromatic ring owing to the extra methyl group at *β*-carbon, *β*-methyl-*β*-nitrostyrenes remained unreactive towards electrophilic substitution reaction. However, the reactivity of the olefinic bond towards nucleophile showed just the opposite order. The presence of the $-CH_3$ group at *β*-carbon of the *β*-methyl-*β*-nitrostyrene interrupts the conjugation, due to which the C=C functionality facilitates the nucleophilic attack of the pyrrolidine. Thereby, in this short study we have shown real-time experiments of how the reactivity of the olefins vary when the electron density over the olefinic bond is varied due to substituents.

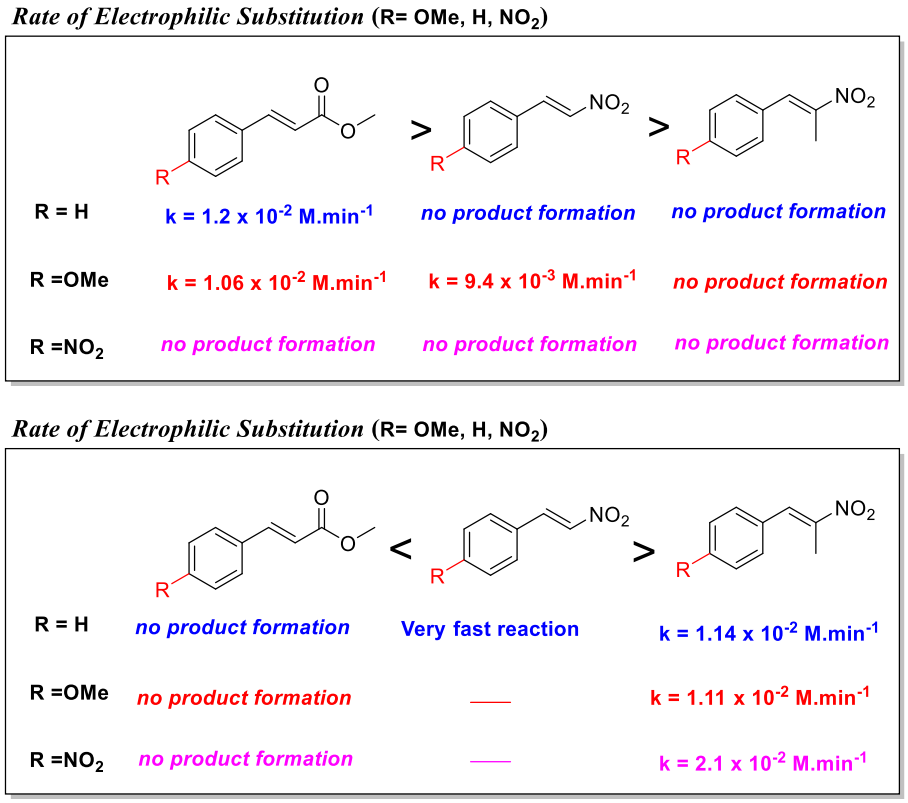


Figure 15. Comparative study of electrophilic and nucleophilic reactivity of olefinic bond

References:

1) Garside, M. Global production capacity of ethylene 2014-2024 *GlobalData* **2022**, *https://www.statista.com/statistics/1067372/global-ethylene-production-capacity/*.

2. Garside, M. Global production capacity of propylene 2018-2030 *GlobalData* **2022**, *https://www.statista.com/statistics/1065879/global-propylene-production-capacity/*

3) Garside, M. Global price of styrene 2017-2021 *Krungsri Research* **2022**, *https://www.statista.com/statistics/1171073/price-styrene-forecast-globally/*

4) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. *Chem*. *Rev*. **1994**, *94*, 2483-2547.

5) Fisher, T. J.; Dussault, P. H. Alkene ozonolysis. *Tetrahedron*, **2017**, *73*, 4233-4258.

6. Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. Mechanism of the Diels-Alder reaction: reactions of butadiene with ethylene and cyanoethylenes. *J. Am. Chem. Soc.* **1986**, *108*, 5771-5779.

7) Fernandes, R. A.; Jha, A. K.; Kumar, P. Recent advances in Wacker oxidation: from conventional to modern variants and applications. *Catal. Sci. Technol*. **2020**, *10*, 7448-7470.

8) Jacobs, T. L. The Chemistry of Alkenes. *J. Am. Chem. Soc*. **1966**, *88*, 2350-2351.

9) Tang, S.; Liu, K.; Liu, C.; Lei, A. Olefinic C-H functionalization through radical alkenylation. *Chem. Soc. Rev*. **2015**, *44*, 1070-1082.

10) (a) Roberts, R. M.; Khalaf, A. A. Friedel-Crafts Alkylation Chemistry: A Century of Discovery; Marcel Dekker: New York, **1984**. (b) Olah, G. A. Friedel-Crafts Chemistry; Wiley-Interscience: New York, **1973**. (c) Olah, G. A. Friedel-Crafts and Related Reactions; Wiley-Interscience: New York, **1963-1965**; Vols. I-IV.

11) Snider, B. B. In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: Oxford, **1991**, *2*, 527-561.

12) (a) Hosomi, A. Characteristics in the Reactions of Allylsilanes and Their Applications to Versatile Synthetic Equivalents. *Acc. Chem. Res*. **1988**, *21*, 200-206. (b) Fleming, I.; Dunogue`s, J.; Smithers, R. The Electrophilic Substitution of Allylsilanes and Vinylsilanes. In Organic Reactions; Kende, A. S., Ed.; Wiley: New York, **1989**, *37*, 57-575.

13) (a) Mukaiyama, T.; Murakami, M. Cross-coupling reactions based on acetals. *Synthesis* **1987**, 1043-1054. (b) Mahrwald, R. Diastereoselection in Lewis-Acid-Mediated Aldol Additions. *Chem. Rev.* **1999**, *99*, 1095-1120.

14) Green, J. R. Chemistry of Propargyldicobalt Cations: Recent Developments in the Nicholas and Related Reactions. *Curr. Org. Chem.* **2001**, *5*, 809-826.

15) Arend, M.; Westermann, B.; Risch, N. Modern Variants of the Mannich Reaction. *Angew. Chem., Int. Ed.* **1998**, *37*, 1044-1070.

16) Godleski, S. In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon: Oxford, **1991**, *4*, 585-661.

17) Duschmalé, J.; Wennemers, H. Adapting to substrate challenges: peptides as catalysts for conjugate addition reactions of aldehydes to α, β-disubstituted nitroolefins. ***Chem. Eur. J.*** **2012,** ***18***, 1111-1120**.**

18) Panda, J.; Sahoo, J.; Dutta, J.; Biswal, H. S.; Sahoo, G.* Spectroscopic and Computational Study of Organocatalytic Umpolung of Bromocations: An Accelerated Stereoselective Dibromination Protocol. *Chem. Eur. J.* **2023**, *29*, e202300675.