Triazolinedione bearing gels

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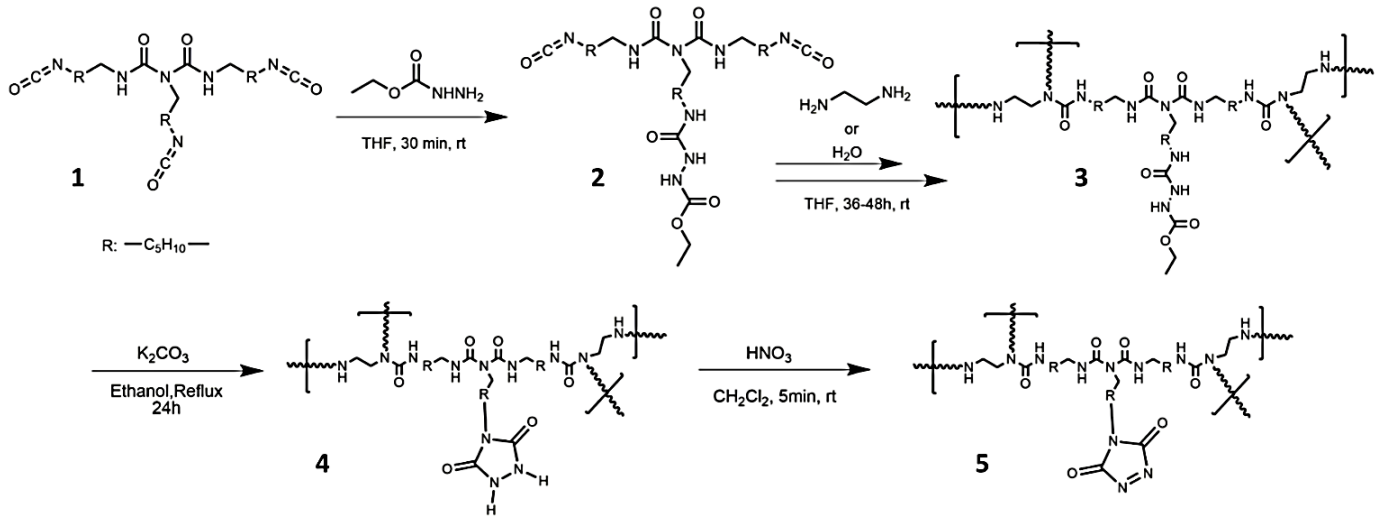
ABSTRACT: Triazolinediones (TADs) have been extensively used for the modification and crosslinking of polymers. However, no TAD-bearing gels have been reported thus far, except an inorganic silica gel on which TAD is immobilized via ionic bonding. Here, I report a simple, scalable, and general strategy to synthesize TAD containing gels from commercially available poly(hexamethylene diisocyanate). The covalently bonded TAD-gel platform could find many different applications such as the fabrication of hybrid materials, chemo-sensing, and scavenging excess reagents. In this study, potential scavenging applications for TAD-gels were demonstrated with three different compounds: furan, aniline, and limonene. Moreover, 1-naphthol was selectively and completely removed from its mixture with 2-naphthol. The proposed strategy enables the preparation of poly(urea)- and poly(urethane)-based novel materials via ultrafast modification at TAD moieties.

Triazolinediones (TADs) are exceptionally reactive compounds with varying degrees of stability—of the order of minutes to months—depending on their substructure. Recently, they have become very popular among polymer chemists owing to their ultrafast reactions that do not require UV, heat, or a chemical initiator. The simple mixing of the reagents at ambient temperature is generally sufficient for TAD reactions.

To date, TADs have been used in many different areas such as Diels-Alder reactions,[1] homopolymerization,[2] step-growth polymerization,[3] modification of polydienes,[4] protection and deprotection of indole's π-bond,[5] fluorescent labeling of vitamin D,[6] scavenging dienes,[7,8] ultrafast preparation of multilayer films,[9] modification of amino acids—furyl-alanine,[10] tyrosine,[11–17] and tryptophan,[18] and fabrication of poly(amino acid)-based hybrid gels.[19] Moreover, some TAD reactions are reversible, and this property has been exploited to create self-healing dynamic materials,[20] light-responsive compounds,[21] and light-stabilized materials.[22] Many other uses of TADs and TAD-related materials have been reported in literature.[23] However, TAD-bearing gels have not yet been reported. TAD-gels could be extremely advantageous because a variety of functional groups can be attached to these gels in an ultrafast and "click-like" manner. Therefore, these TAD-gels can find use in many different applications such as purifying and separating mixtures, sensing analytes, fabricating polyurethane-poly(amino acid) platforms, and designing hybrid materials with self-healing capability. In this study, I report a simple preparation method to obtain TAD-bearing gels from commonly available reagents. Moreover, I demonstrate their potential as possible scavengers for Diels-Alder, electrophilic aromatic substitution (EAS), and Alder-ene reactions.

Previously, Keana et al. reported the synthesis of silica-gel-bound TAD by a reaction between custom synthesized sulfonated 4-Aryl-TADs and amine-bearing silica gels.[7] In this system, 0.4 mmol active TAD was present for 1 g of silica-TAD as quantified by titration. They showed that the silica-TAD material can be used to separate diene-containing ergosterol from a cholesterol mixture. Werner and Curran demonstrated the scavenging potential of TAD in a solution, rather than as a solid-supported TAD, by synthesizing several fluorous dienophiles and thereby removing excess dienes in the Diels-Alder reaction.[8] The reacted fluorous dienophiles were removed by filtering over fluorous silica gel. Among all tested dienophiles, TAD derivatives showed superior reactivity. Inspired by these

Scheme 1. Synthesis of triazolinedione bearing gel



studies, I demonstrated the practicality of TAD-gels reported here to simplify the scavenging process. In terms of practicality, TAD-gels are easy to synthesize, unlike silica-TAD, and do not require a special fluorous column for filtration, unlike fluorous TAD scavengers. Additionally, the TAD content of the gels reported herein was relatively higher—up to 0.62 mmol of TAD per gram gel—compared to that of silica-TAD.

A trifunctional isocyanate (**1**) poly(hexamethylene diisocyanate) was chosen as the starting material (Scheme 1). Then, either 1 or 1.5 mol of isocyanate groups were reacted with equimolar ethyl carbazate to form isocyanate-semicarbazide containing intermediate (**2**). In the same reaction flask, this intermediate was indirectly polymerized via the addition of water. Eventually, the polymerization of poly(urea) was accompanied with gelation (**3**). Semicarbazide containing poly(urea) gel (**3**) was cyclized into a urazole-containing gel (**4**) under basic conditions. Finally, the oxidation of the urazole-containing gel by HNO_3 resulted in the TAD-bearing gel (**5**). The synthetic procedure and a video summarizing all steps are available as Supporting Information.

Results and Discussion

TAD formation can be monitored by the naked eye owing to the characteristic red/pink color of TAD compounds (Figure 1 a-b). Moreover, FTIR analysis revealed the occurrence of a new carbonyl mode at 1765 cm^{-1} and an increase in the C-N mode at 1360 cm^{-1} induced in the structure owing to N=N formation. An unknown mode appeared at 729 cm^{-1}; however, it might be related to the gel backbone-HNO_3 interaction as it did not change after the TAD reaction or decomposition. The scavenging experiments discussed below further verify the TAD origin of these gels.

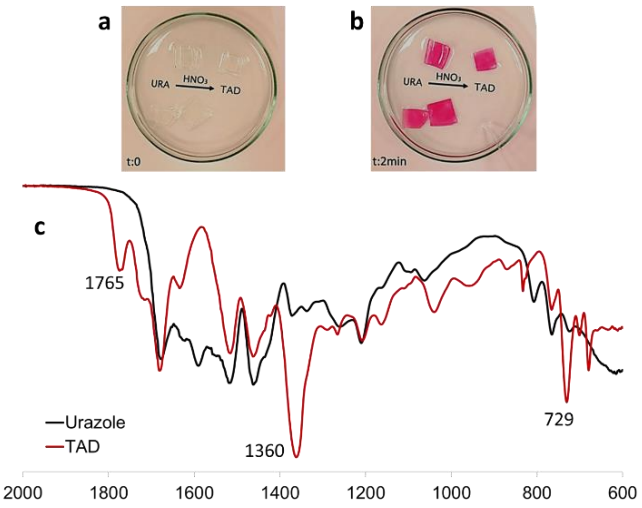


Figure 1. a) Urazole-bearing gels placed in a dichloromethane-containing glass petri dish. **b)** 2 min after 100 µl of HNO_3 was added to urazole gel. **c)** FT-IR spectrum of urazole-bearing gel (neat) and its oxidized form, the TAD-bearing gel (neat).

The stabilities of the synthesized TAD gels were tested in different solvents (Figure 2). Approximately 100 mg of TAD-bearing gel was placed into 1.5 mL of solvent in the test tubes. Then, the tubes were shaken for 20–30 seconds, and the gel stabilities were monitored through discoloration. For most solvents, the TAD-gels were active for up to 40 min, which is much longer than the duration of typical TAD reactions. Trifluoroacetic acid was found to be incompatible with TAD-gel. After 2–3 min, popping sounds and turbidity were observed. The gels were quite stable in ethyl acetate, acetonitrile, and tetrahydrofuran. In other solvents, TADs barely survived for 1 h. DMSO and DMF caused deformation in the gels after 24 h. In other solvents, no deformation was observed. When the TAD-gel was kept as a solid under ambient conditions, its pink color disappeared in 5-6 hours at room temperature. On the other hand, the TAD activity remained for intact at least a week at -20°C.

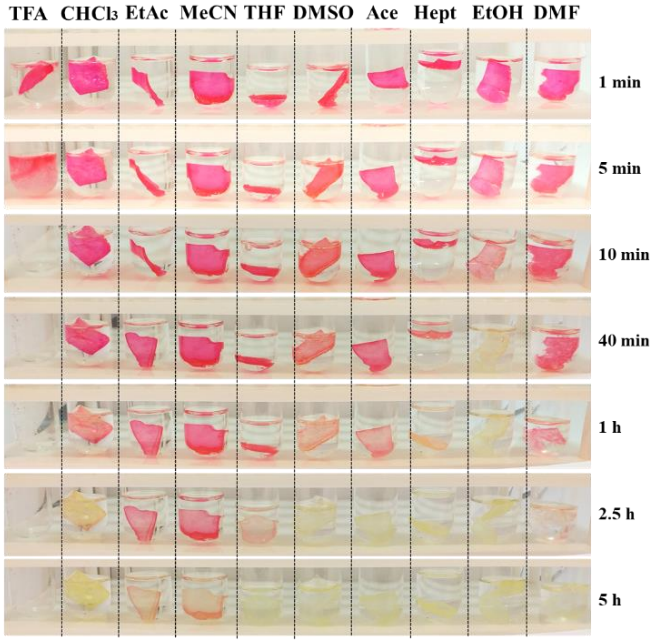


Figure 2. Stability of TAD-gels in different solvents. Detailed information about the solvents is listed in the experimental section. Solvents left to right: trifluoroacetic acid, chloroform, ethyl acetate, acetonitrile, tetrahydrofuran, dimethyl sulfoxide, acetone, heptane, ethanol, and N,N-dimethylformamide. TFA stability test was stopped after 5 min owing to incompatibility.

The decomposition mechanism was attributed to the water content of the solvents because it is well known that water decomposes TAD moieties gradually over time. However, gels in solvent-grade heptane and heptane dried by molecular sieves showed very similar decomposition times. This observation indicates that gel decomposition was either dominated by other factors or by the absorbed water coming from HNO_3. As for other possible decomposition mechanisms, free amines, biuret groups, or TAD self-dimerization may decompose TAD groups over time. Further studies can be conducted to elucidate the underlying mechanism, such as exploring different oxidation methods and changing synthesis pathway to obtain poly(urethane), rather than poly(urea).

The scavenging capabilities of TAD gels were tested with different compounds: aniline, limonene, and furan. Aniline reacts with TAD via (EAS) and limonene, via the Alder-ene reaction. On the other hand, Furan derivates react commonly via Diels-Alder but also via EAS.[10] For the experiments, the gels were cut into smaller pieces to increase the surface area and to decrease the diffusion time of the reactants into the gel. In equimolar concentrations, Furan was observed to react the fastest, whereas aniline and limonene reacted at nearly the same rate. After ~20 min, the red color of TADs completely disappeared in all reactions, whereas no change was observed in the control group (Figure 3). The gels were characterized by FTIR

analysis. For all compounds, the C=C-H bending mode appeared at 907 cm^{-1} and for aniline, the C-NH2 stretching mode appeared at 1300 cm^{-1} (Figure S2-4).

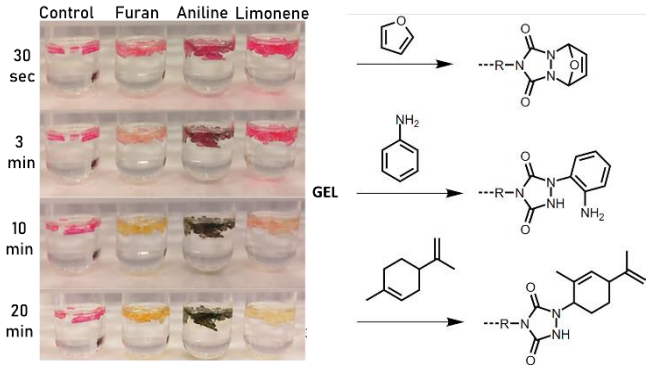


Figure 3. Reaction of TAD-gels with furan, aniline, and limonene in dichloromethane. Characteristic red color of TAD disappeared after the reaction.

Active TAD groups on the gels can be quantified by titration against one of the reactants. However, the titration method for this gel is prone to human error as the reactants take some extra time to diffuse deeper into the gel. By contrast, nuclear magnetic resonance (NMR) analysis may be used to quantify TADs more reliably. To perform NMR quantification, a standard solution was prepared in $CDCl_3$ (6 mL) using furan (50 µl) as a reactant and acetonitrile (50 µl) as a reference peak for NMR integration. This solution was kept closed at all times to prevent the loss of furan as it has a low boiling point. First, 200 mg of TAD gel was added to $CDCl_3$ and the NMR spectrum was obtained after 10 and 30 min. Then, another 200 mg of TAD-gel was added. After 60 min, the red color disappeared completely. The NMR analysis showed a decrease of 36% for furan peaks. This means that 50 µl (×36%) furan (18 µl - 16.8mg - 0.283 mmol) reacted with 400 mg of gel. Therefore, 1 g of TAD gels contains at least 0.62 mmol of TAD. It should also be noted that some active TADs decomposed without reacting with furan, which results in a smaller value.

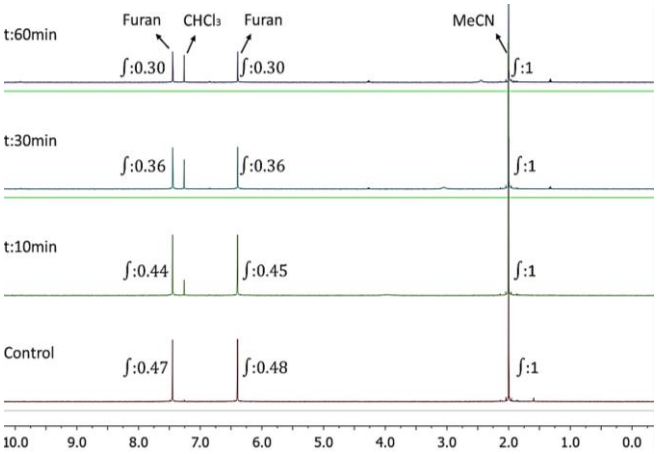


Figure 4. ^{1}H-NMR spectrum of TAD-gel scavenged furan and acetonitrile-containing $CDCl_3$ stock solution over time. Acetonitrile was added as a reference for integration to quantify the furan loss.

Theoretically, a maximum of 1.65 mmol of TAD can exist if equimolar ethyl carbazate and triisocyanate are used at the beginning. Triisocyanate:ethyl carbazate in 1:1.5 ratio was also observed to form crosslinked gels. Therefore, there is still space to optimize oxidation conditions and explore different formulations to obtain higher active TAD content.

After demonstrating the scavenging potential with individual molecules, a more realistic and challenging scavenging test was performed. Here, an equimolar mixture of 1-naphtol and 2-naphtol was treated with TAD-gel. 1-naphtol could react with the TAD-gel via electrophilic aromatic substitution or 5-8 adduct formation. By contrast, 2-naphtol could also react via 1-4 adduct formation in addition to these reaction pathways. NMR studies indicated that TAD-gel selectively reacted with 1-naphtol (Figure 5). After 15 min, 1-naphtol was almost completely removed from the solution; however, almost no change was observed in the 2-naphtol peak. The 2-naphtol peak was observed to decrease 1 h after the treatment, indicating a reaction between the TAD-gel and 2-naphtol. These results demonstrate that the TAD-gel can potentially be used as a selective scavenger for mixtures.

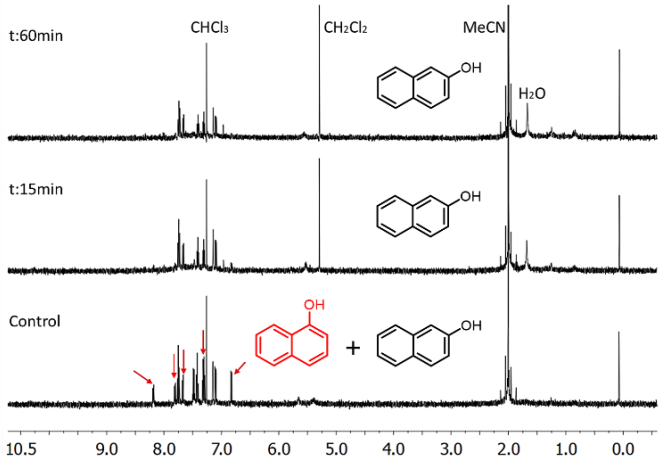


Figure 5. ^{1}H-NMR spectrum of TAD-gel scavenged 1-naphthol and 2-naphthol mixture. Peaks at 8.18, 7.82, 7.49, 7.47, 7.43, and 6.83 ppm disappeared after soaking TAD-gel into the solution.

TAD-gels can easily be synthesized at a large scale from commonly available and low-cost reagents. As an alternative to the route described here with trifunctional isocyanates, difunctional isocyanates could also be used together with water or multiamine linkers to synthesize similar TAD gels by tuning the stoichiometric ratios of ethyl carbazate/diisocyanate and multiamine containing linkers. Moreover, rigid or elastomeric isocyanates could also be used as comonomers by just adding them after the first step of the synthesis.

The decomposition of TAD-gels might seem to be a limitation at first glance; however, the ultrafast reactivity of TADs ensures that the reactions proceed much faster than the decomposition. In general, TAD reactions finish within seconds or several minutes. Therefore, the relatively slow nature of the decomposition renders decomposition-related problems insignificant for practical purposes. By contrast, the precursor of the TAD gel—urazole gel—is very stable. The urazole gel can be stored for months and can be readily oxidized into TAD-gels whenever desired. As mentioned before, poly(urethane)-based TAD gels can also be synthesized, and their stability is expected to be even better because amine formation in poly(urea) is thought to be one factor in TAD decomposition. To change the route, polyols—instead of water—could be used in the second step of the synthesis.

The oxidation of urazole to TAD could be carried out in many alternative ways. Here, HNO_3 is used as an oxidizer as it is readily available and can be washed away easily. However, care must be taken with HNO_3 incompatibilities such as with aniline. Therefore, gels have to be washed well to remove HNO_3. Additionally, water from HNO_3 will gradually decompose TAD. Interestingly, some oxidation methods such as electrooxidation or photooxidation could be used to create patterned TAD-gels from urazole gels. Alternatively, an oxidizer solution could also be used to create patterns via inkjet printing.

In conclusion, I have reported an easy way to prepare TAD-containing gels. These new gels can be used to prepare poly(urea)- or poly(urethane)-based novel materials. Among many possible application areas, scavenging excess reagents was tested. TAD-gel was found to be usable as a scavenger for different reactions and a variety of functional groups.

ASSOCIATED CONTENT

Electronic Supporting Information and gel synthesis video are available.

AUTHOR INFORMATION

Author Contributions

All work was done by Saltuk B. Hanay.

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