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METHOXY AS A REMOVABLE ACTIVATING GROUP IN THE TRIAZOLINEDIONE REARRANGEMENT ROUTE TO AZO COMPOUNDS

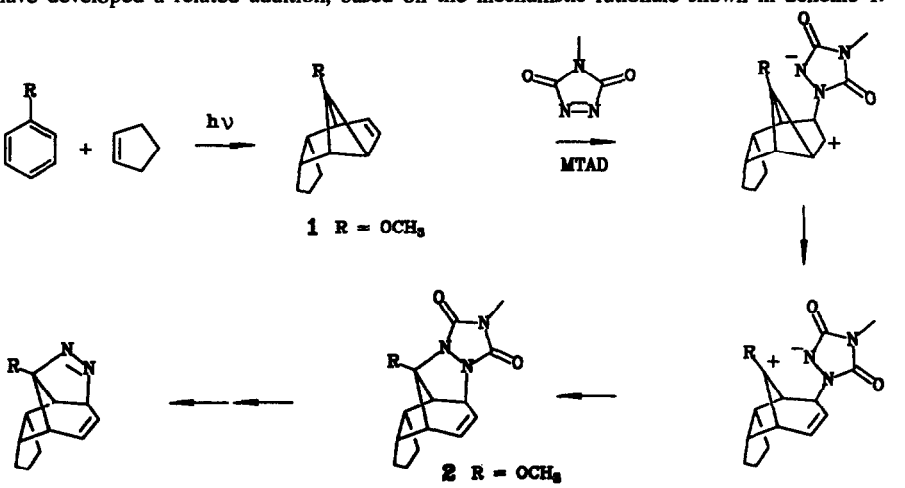
John Dover and Robert S. Sheridan*[1]
University of Nevada, Reno, Nevada 89557

Summary: *A methoxy group dramatically increases the yield of stepwise homo-Diels-Alder additions of N-methyltriazolinedione to aromatic meta-photoadducts, and can conveniently be subsequently replaced by other substituents.*

Triazolinediones (TADs) add to a diverse range of organic compounds to give polycyclic urazoles.[2] TADs undergo, for example, Diels-Alder additions, homo-Diels-Alder additions, ene reactions, and [2+2] additions to olefins and strained σ-bonds. The adducts, in turn, have been converted to a wide variety of interesting azo compounds. One very versatile extension of this approach is the dipolar cycloaddition route elegantly developed by Adam and coworkers,[2b,3] which has led to a number of polycyclic azo compounds not available by other means. The general mechanism of this rearrangement route, at least formally, involves electrophilic TAD addition to strained olefins, followed by carbocationic migrations and finally cyclization.

Seeking independent routes to biradicals proposed to be intermediates in aromatic meta-photoadditions to olefins, we have developed a related addition, based on the mechanistic rationale shown in Scheme 1.[4]

SCHEME 1



Homo-Diels-Alder additions to vinylcyclopropanes are extremely rare,[5] but these MTAD reactions, although inefficient, provided enough materials for our initial surveys. Through investigations of the corresponding azo compounds, we not only found direct evidence for the intermediacy of the putative biradicals,[4b] but we also observed a novel retro homo-Diels-Alder cycloreversion.[4a] Moreover, we obtained direct evidence for stepwise thermal and photochemical denitrogenation in certain cases.[4c] To facilitate our further exploration of the complex chemistry of these azo compounds, we needed both more efficient routes to the urazoles and a broader range of substituents. There are a number of obstacles that presented themselves to

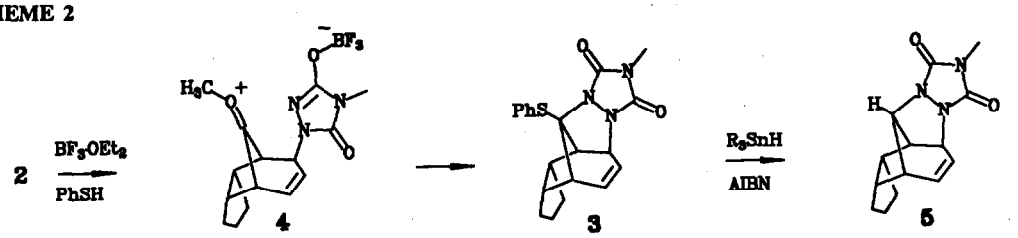
thwart this approach, however: (1) The range of aromatic substituents for which intermolecular meta-photoadditions are preparatively efficient is very limited;[6] (2) In photoadditions of multiply substituted aromatics, the best electron donor invariably ends up at the apical position as shown above, further limiting the possible substitution patterns;[6] (3) When R = H we get only very poor yields for the TAD additions,[5] probably due to difficulties in cyclopropane opening; (4) When R = alkyl, elimination (homo-ene reaction) competes with cyclization.[4]

To skirt some of these difficulties, we have developed a modified route to the desired urazoles that not only gives considerable increases in yield, but also affords the opportunity for introduction of a variety of substituents. This approach capitalizes on both the well-known meta-photoaddition directing effect[6] and the powerful carbocation stabilizing effect of the methoxy group.

Scheme 2 shows one application of this approach. The anisole and cyclopentene combination is known as one of the most efficient intermolecular meta-photoadditions.[6] Yields as high as 85 % have been reported,[7] and it is easy to generate ca. 4 g quantities of **1** as needed. We have found that the apical methoxy group also facilitates MTAD addition; the yield of formation of **2** is typically 75 - 85 %. For comparison, the corresponding MTAD additions to the benzene-cyclopentene photoadduct (R = H), and the toluene-cyclopentene (R = CH_3) adducts give only ca. 14 % and 6 % yields respectively.[8]

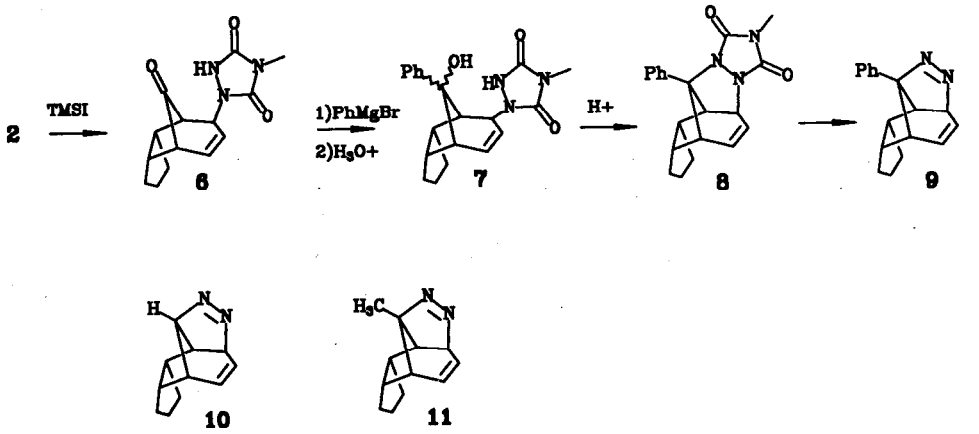
We reasoned that the apical functionality in urazoles such as **2** might make it possible to easily replace the methoxy group with other nucleophiles. This has turned out to be the case. For example, treatment of **2** with thiophenol and $BF_3{\cdot}OEt_2$ gave good yields of **3** (92 %), likely formed through the intermediacy of **4**. The thiophenoxy group can then be conveniently replaced by hydrogen through free radical tin hydride reduction. The overall yield of **2** to **5** was 74 %, which is a considerable improvement on the direct addition of MTAD to the benzene-cyclopentene adduct (vide supra).

SCHEME 2



It is also possible to replace the apical methoxy group with a substituent not available from meta photoaddition. It would be of interest, for example, to probe the effect of phenyl substitution on this azo framework, but biphenyl does not appear to undergo meta photoaddition to olefins.[6] A phenyl group can be easily introduced as shown in Scheme 3, however. Although acid-catalyzed hydrolysis cleaves **2** to ketone **6** in poor yield, we have found that TMSI effects this conversion nicely (80 % yield). Reaction of **6** with two equivalents of phenylmagnesiumbromide gives alcohol **7**, as an undetermined mixture of stereoisomers (80 % yield). Azeotropic dehydration with TsOH gave the cyclized urazole **8** in 52 % overall from **2**. The azo compound **9** can be generated by the usual KOH deprotection, $CuCl_2$ oxidation procedure.

SCHEME 3



Azo compound **9** is considerably more labile ($t_{1/2}$ = 0.5 h at 24 °C, cyclohexane) than other azo compounds of this type we have studied. For example, **10** and **11** have $t_{1/2}$ of 964, and 54 h at 24 °C, respectively.[8] The cumulative destabilizing effect of the allylic and phenyl groups in **9** is interesting. We[2a] and others[9] have presented evidence for concerted thermal [$_{\pi}2_s+_{\sigma}2_s+_{\sigma}2_s$] cycloreversion in these azo compounds. Apical stabilizing groups as in **9** may accelerate this retro homo-Diels-Alder reaction. On the other hand, Engel and coworkers[10] have suggested mechanisms by which both substituents in unsymmetric azo compounds may together lower the barrier to stepwise denitrogenation. We hope that with study of appropriately substituted azo compounds, now available via this approach, we may be able to address these questions.

The above results suggest that alkoxy substituents may be generally useful in facilitating and directing the regiochemistry of dipolar cycloadditions of TADs. The resultant products can provide substituted azo compounds and biradicals previously unavailable.[11,12]

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1. Fellow of the A. P. Sloan Foundation, 1986 - 1990.

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11. All new compounds exhibited appropriate spectra, consistent with our previous investigations in this area,[4] and satisfactory elemental analysis (stability permitting).

12. For previous use of alkoxy substituents as cyclopropane activating groups, see for example Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27.

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