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LETTERS

Diels-Alder Reactions of *N*-Acetyl-2-azetine

Paritosh R. Dave,[a*] Rajagopal Duddu,[a] Rao Surapaneni,[b] and Richard Gilardi[c]

[a]*GEO-CENTERS, INC. at ARDEC, Building 3028, Picatinny Arsenal, NJ 07806-5000*
[b]*US Army ARDEC, Building 3022, Picatinny Arsenal, NJ 07806-5000*
[c]*Laboratory for the Structure of Matter, NRL, Washington, DC 20375*

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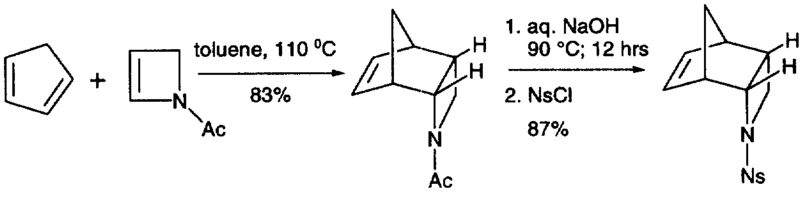
Abstract:

N-acetyl-2-azetine has been found to undergo facile [4+2] cycloadditions with various dienes to give products of endo addition exclusively.

Although the utility of enamides as dienophiles in intramolecular Diels-Alder reactions has been exploited in the syntheses of alkaloids,[1] and enediamides[2] and enamides activated by additional activating group in conjugation with the double bond[3] have been shown to undergo Diels-Alder reaction, the corresponding intermolecular [4+2] cycloadditons of simple enamides have not been reported to our knowledge. *N*-acetyl-2-azetine, (**1**),[4] represents a special case of enamide incorporating a highly strained reactive double bond that we have recently utilized in a photodimerization reaction.[5] We now report facile Diels-Alder reactions of **1** with various cyclic dienes.

The reaction of **1** with cyclopentadiene was carried out in toluene in a sealed tube to afford the adduct **2** as a yellow oil in 83% yield (Scheme 1).[6] The ^{1}H and ^{13}C NMR spectra of the product indicated the presence of a mixture of amide rotomers in a 2:3 ratio.

Scheme 1



1 **2** **3**

In order to ascertain the stereochemistry of the [4+2] addition, the product was transformed via base hydrolysis of the acetyl function to the secondary amine that was not isolated but converted directly to the corresponding p-nitrobenzenesulfonamide **3**. Spectral data[7] was consistent with the formation of a single product and x-ray crystallographic structure determination showed the addition to be endo (Figure 1).

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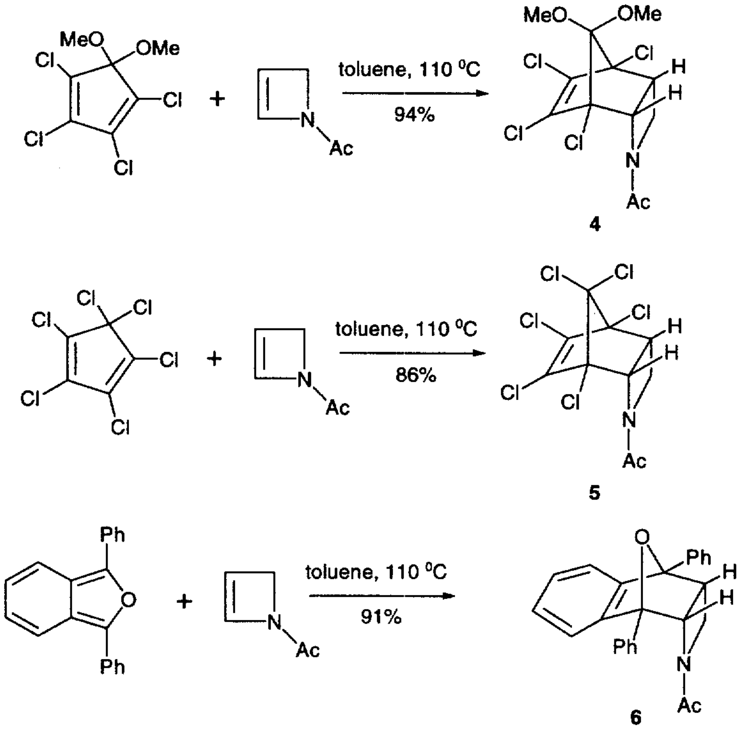
The Diels-Alder reaction of **1** was carried out similarly with other dienes and the adducts obtained in high yields as shown in Scheme 2.

Scheme 2



In the reaction of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene with **1**, a single product with the structure **4** was isolated in 94% yield. X-ray diffraction studies conclusively proved the product to have endo ring junction. The corresponding reaction of **1** with hexachlorocyclopentadiene was also facile producing the product **5** as an oil in 86% isolated yield. Based on comparision of the spectral data of **5** with that of **4**, and consistent with the other reactions shown herein, endo geometry is proposed. In yet another example, the thermal reaction of **1** with diphenylisobenzofuran proceeded to afford the adduct **6** as a crystalline solid in 91% isolated yield. The structure of **6** was unequivocally confirmed via single crystal x-ray diffraction, shown in Figure 1.

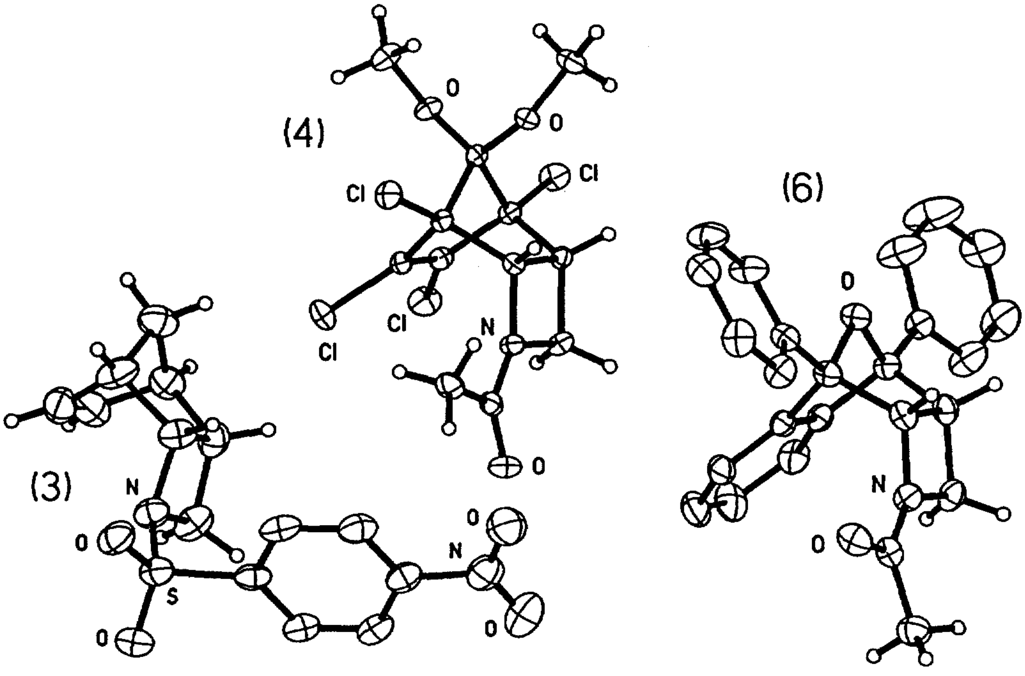


Fig. 1 Ortep view of compounds **3**, **4**, and **6**.

In conclusion, N-acetyl-2-azetine participates readily as a dienophile in Diel's-Alder reactions with various dienes to give exclusively products with endo configuration. Compound **4** possesses the requisite geometry and functionality for conversion to the homoazacubane system and ultimately to the azacubane system. This method also provides for the facile syntheses of fused azetidines that are of considerable current interest.[8]

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References and Notes:

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6. General procedure for the Diels-Alder reactions of **1**: To a solution of **1** (1 mmol) in toluene in an Ace screw cap pressure tube was added the diene (1.1 mmol) and the resulting solution was heated in an oil bath maintained at 110 °C for 2 hours. The reaction mixture was allowed to cool and then concentrated under reduced pressure to give a residue that was purified by column chromatography on silica gel eluting with ethyl acetate/hexane (4:2).
7. Spectral data for **3**: m.p: 136-138 °C; IR (KBr): 2985(m), 1607(m), 1523 (vs), 1342 (vs), 1168 (vs), 1009(m), 853 (s) Cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (d, J = 9.3 Hz, 1H), 1.68 (d, J = 9.3 Hz, 1H), 2.62-2.75 (m, 1H), 2.87-2.95 (m, 1H), 3.12-3.25 (m, 2H), 3.63(t, J = 8.4 Hz, 1H), 4.52 (dd, J = 8.1, 4.5 Hz, 1H), 6.25-6.37 (m, 2H), 7.98 (m, 2H), 8.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.42, 43.06, 46.38, 49.09, 51.29, 68.65, 124.30, 128.30, 133.34, 136.54, 144.40, 156.72.
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