

[4+2] CYCLOADDITION OF N-ETHOXYCARBONYLAZEPINE AND
5,5-DIMETHOXY-1,2,3,4-TETRACHLOROCYCLOPENTADIENE

John R. Wiseman and Berni P. Chong

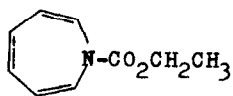
Dept. of Chemistry, Univ. of Michigan, Ann Arbor, Michigan 48104

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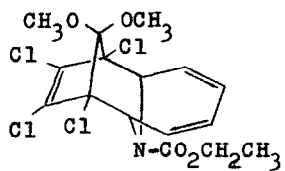
Cycloaddition reactions of azepines have recently generated considerable interest. Three types of cycloaddition reactions involving azepines have been reported: a [4+2] cycloaddition of N-ethoxycarbonylazepine with tetracyanoethylene¹ in which the azepine behaves as a diene, [6+4] dimerizations²⁻⁴ in which the azepines serve as both diene and triene, and a reaction formulated as a [6+2] cycloaddition of N-ethoxycarbonylazepine with nitrosobenzene.⁵ We wish to report the observation of a new type of cycloaddition, a [4+2] reaction in which the 4,5 double bond of N-ethoxycarbonylazepine behaves as a dienophile.⁶

When N-ethoxycarbonylazepine (I) and 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (II) were heated to 100°C for four hours, a colorless, viscous oil III, C₁₆H₁₇NO₄Cl₄⁷, IR (1730 cm⁻¹, str; 1695 cm⁻¹, str; 1605 cm⁻¹, med), was isolated by column chromatography in 30% yield. The simple NMR spectrum, τ 3.16 (2H, d, J=11Hz), τ 5.15 (2H, broad d, J=11Hz), τ 5.82 (2H, q, J=7Hz), τ 6.45 (3H, s), τ 6.52 (3H, s), τ 6.67 (2H, broad s), τ 8.68 (3H, t, J=7Hz), demands a symmetrical structure and is consistent with both IIIa and IIIb. The UV spectrum of III (λ_{max} = 226 m μ , ϵ = 1.2 x 10⁴) is nearly identical to that of VI (λ_{max} = 228 m μ , ϵ = 1.23 x 10⁴)⁸ which contains the same chromophore as IIIb. In contrast, the UV spectrum of VII (λ_{max} = 257 and 267 m μ , ϵ = 7680 and 7870)⁹ which contains a chromophore similar to IIIa is very different from the UV spectrum of III.

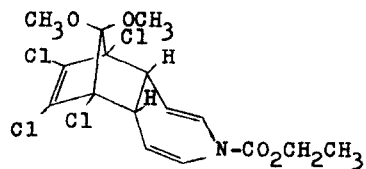
Hydrogenation of III at 50 lbs. pressure for 24 hours with a 5% Pd/C catalyst yielded a crystalline tetrahydro compound IV, C₁₆H₂₁NO₄Cl₄, mp 106.5-108.5°C, IR (1605 cm⁻¹, str), NMR τ 5.93 (4H, q, J=7Hz, superimposed on a multiplet), τ 6.44 (3H, s), τ 6.50 (3H, s), τ 7.21 (4H, multiplet), τ 8.00



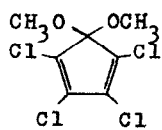
I



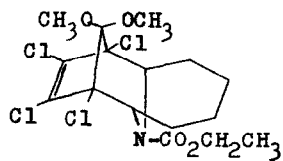
IIIa



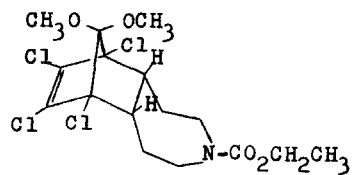
IIIb



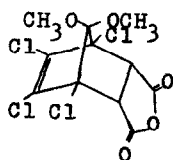
II



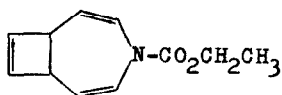
IVa



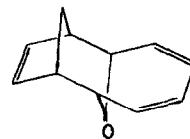
IVb



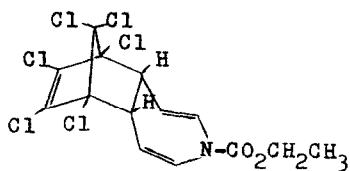
V



VI



VII



VIII

(2H, multiplet), τ 8.78 (5H, t, $J=7\text{Hz}$, superimposed on a multiplet). The NMR spectra of the adduct and the tetrahydroadduct when considered together are not in accord with structures IIIa and IVa. The 2H absorption at τ 6.67 in the NMR spectrum of the adduct III could be logically assigned to the bridgehead protons of IIIa. These protons should appear at higher field in the tetrahydroadduct IV. However, the NMR spectrum of IV shows the lowest field protons at τ 5.93, which would require a downfield shift. Structures IIIb and IVb are consistent with the NMR spectra. The methine protons in IIIb appear at τ 6.67 and are shifted upfield on hydrogenation, appearing at τ 7.21 in the tetrahydroadduct IVb. The fact that the lowest field absorption integrates for only two protons (disregarding $-\text{O}-\text{CH}_2-\text{CH}_3$) is reasonable if the two exo protons α to the nitrogen in IVb are in a different magnetic environment from the two endo protons. This condition is satisfied if the adduct has structure IIIb in the endo configuration.

Confirmation of the spectral assignment was obtained by chemical degradation. The diene II and maleic anhydride were heated at 80°C in benzene overnight and a colorless, crystalline anhydride V, $\text{C}_{11}\text{H}_8\text{O}_5\text{Cl}_4$, mp $96-97^\circ\text{C}$, NMR τ 6.16 (2H, s), τ 6.39 (3H, s), τ 6.45 (3H, s), IR (1880 cm^{-1} , med; 1795 cm^{-1} , str; 1600 cm^{-1} , med), was isolated from the reaction mixture in 93% yield. Oxidative cleavage of the adduct III with permanganate/periodate¹⁰ at room temperature and subsequent sublimation of the product yielded a compound whose NMR and IR spectra were identical to those of V. Thus, the spectral and chemical evidence establish the structure of the adduct as IIIb, formed by a [4+2] cycloaddition in which the central double bond of N-ethoxycarbonylazepine behaves as a dienophile.

N-ethoxycarbonylazepine and hexachlorocyclopentadiene gave a similar adduct VIII, $\text{C}_{14}\text{H}_{11}\text{NO}_2\text{Cl}_6$, mp $103.5-104.0^\circ\text{C}$, in 40% yield. The spectra of the adduct, NMR τ 3.01 (2H, d, $J=11\text{Hz}$), τ 5.07 (2H, broad d, $J=11\text{Hz}$), τ 5.74 (2H, q, $J=7\text{Hz}$), τ 6.43 (2H, broad s), τ 8.68 (3H, t, $J=7\text{Hz}$), IR (1740 cm^{-1} , str; 1695 cm^{-1} , str; 1640 cm^{-1} , str; 1605 cm^{-1} , med), show that it has the same type of structure as the ketal adduct III. In particular, the NMR spectra of III and VIII are

practically superimposable except for the absorption due to the methyl groups of III.

Several attempts to carry out a similar cycloaddition with cyclopentadiene yielded only cyclopentadiene dimer and azepine dimers. Tetracyclone also failed to react.

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References

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