Tetrahedron Letters No. 54, pp.4781-4784, 1969. Pergamon Press. Printed in Great Britain.

REACTION OF AZODICARBOXYLATES WITH 2,4-CYCLOHEXADIENONES;
1,4-CYCLOADDITION AND 'ENE' REACTIONS

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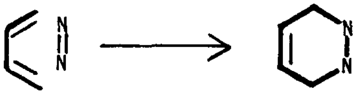
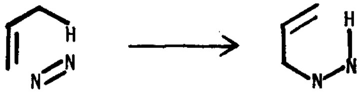
(Received in the USA 9 April 1969: received in the UK for publication 17 October 1969)

Azodicarboxylates generally react with dienes by one of two paths.[2] With less hindered dienes and/or cisoid dienes or azodicarbonyl compounds, 1,4-cycloaddition is most common. Alternatively, the 'ene' or 'addition-abstraction' reaction may be favored, particularly if the Diels-Alder reaction is conformationally or sterically hindered.[3] In this paper we describe the reactions of two closely related 2,4-cyclohexadienones with dimethyl azodicarboxylate. Both ketones are cisoid dienes, but one reacts by 1,4-cycloaddition whereas the other, though less hindered, gives an 'ene' adduct.

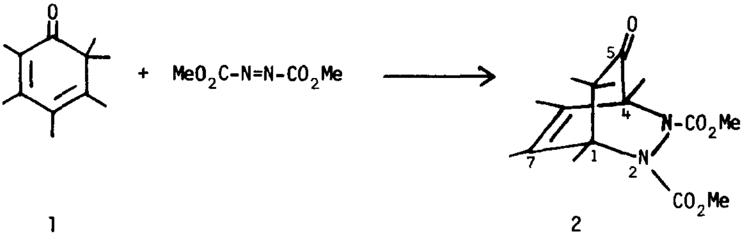


1,4-cycloaddition



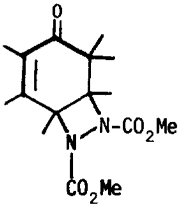
'ene' reaction

When a chloroform solution of hexamethyl-2,4-cyclohexadienone 1[4] and dimethyl azodicarboxylate was allowed to stand at room temperature for 2-3 days, a white crystalline adduct was obtained in 99% yield, mp 161-3° (hexane).[5,6] The nmr spectrum showed no vinyl protons, thus eliminating all possible 'ene' structures. We assign the adduct structure 2 on the following spectroscopic evidence. Strong carbonyl absorptions at 1742 and 1727 cm^{-1} eliminate the 2 + 2 structure 3, which should show a conjugated carbonyl. The ir and nmr spectra do not, however, readily distinguish 2 from the less likely 4. This was accomplished by examining the



1 2

nmr spectrum of adduct prepared from the partially labeled dienone 1'.[7] Unlabeled adduct



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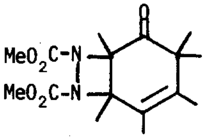

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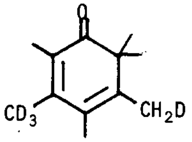
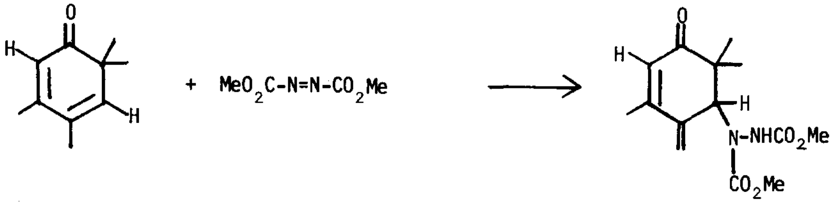


1'

(from 1) had a methyl at τ 8.24 (q, J=1.2 Hz) and three methyls at τ 8.13 (s), 8.10 (s) and 8.07 (q, J=1.2 Hz); the quartets must be the adjacent allylic methyls and the singlets are the bridgehead methyls (in 2 or 4). In the adduct from 1', the quartet at τ 8.24 was absent, whereas that at τ 8.07 had become a singlet; further, the singlet at τ 8.10 was reduced in intensity relative to that at τ 8.13. These results are consistent only with structure 2 for the adduct.[8]

When tetramethyl dienone 5 was similarly treated with dimethyl azodicarboxylate, a white crystalline adduct, mp 154-6° (ether-pentane) was isolated in 70% yield. Structure 6 is assigned on the basis of spectral data.[9] The ir spectrum ($CHCl_3$) showed intense bands at 1757,



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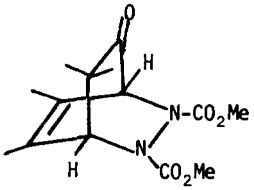
6

1710, 1660 and 1590 cm^{-1} (showing both conjugated and non-conjugated carbonyls), 925 cm^{-1} (terminal methylene) and 3385 cm^{-1} (N-H stretch[10]).

The nmr spectrum ($CDCl_3$) showed only three C-methyls — singlets at τ 8.96 and 8.84, and a doublet at τ 7.96 (J=0.7 Hz). This eliminates the 1,4-cycloaddition structure 7, which has four C-methyls.[11] The uv spectrum (CH_3OH) showed an intense band at 272 nm (ε 13,000) which eliminates the alternative 'ene' structure 8 but is reasonable for 6.[12]



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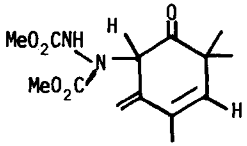

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The difference between the behavior of dienones 1 and 5 toward dimethyl azodicarboxylate depends on a delicate balance between several factors. The absence of methyl groups at the diene termini in 5 should enhance its reactivity toward dienophiles, relative to 1.[14] However, azodicarboxylates are electrophilic dienophiles,[2] and the electron-donating ability of the additional methyls in 1 may counterbalance their steric effect.

Dienone 5 should be much more reactive than 1 in the 'ene' reaction because of less substitution at the vinyl positions.[2] Exclusive attack of nitrogen at C-5 rather than C-2 suggests that nucleophilic attack by nitrogen may lead hydrogen transfer. It should also be noted that the hydrogen which is transferred (from the C-4 methyl) is much less acidic than the hydrogens on the C-3 methyl.

These studies are being extended. The chemistry of the adducts is also being investigated (see following paper).

Acknowledgement. We are indebted to the National Science Foundation and the National Institutes of Health for grants in support of this research.

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1. National Institutes of Health Predoctoral Fellow at Michigan State University, 1967-68.
2. For reviews, see B. T. Gillis in "1,4-Cycloaddition Reactions", ed. by J. Hamer, Academic Press, New York, 1967, pp. 143-177; E. Fahr and H. Lind, Angew. Chem. Internat. Ed., **5**, 372 (1966).
3. For a recent striking example, see E. K. von Gustorf, Tetrahedron Letters, 4693 (1968).
4. H. Hart, P. M. Collins and A. J. Waring, J. Am. Chem. Soc., **88**, 1005 (1966).
5. Anal: Calcd. for $C_{16}H_{24}N_2O_5$: C, 59.25%, H, 7.46%; N, 8.64%.
   Found: C, 59.38%; H, 7.49%; N, 8.69%.

6. In an earlier paper[4] we reported the preparation of the diethyl azodicarboxylate adduct of 1. The assumption of a structure analogous to 2 is now validated.

7. Slight modification of the labeling procedure described in ref. 4 gave a product with complete label at C-3 and partial label at C-5.

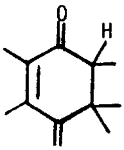
8. The labeling experiment permits a nearly complete assignment of the methyl signals as follows: τ 8.94, 8.92 (C-6), τ 8.24 (C-8), τ 8.07 (C-7), τ 8.13 (C-4), τ 8.10 (C-1), and τ 6.28 (O-methyls).

9. Anal: Calcd. for $C_{14}H_{20}N_2O_5$: C, 56.74%; H, 6.80%; N, 9.45%.
Found: C, 56.72%; H, 6.88%; N, 9.47%.

10. When the solution was concentrated, a broad band appeared at 3275 cm^{-1} (H-bond); this disappeared on dilution.

11. Other peaks in the nmr spectrum of 6, and their tentative assignments are: τ 6.42, 6.29 (O-methyls), τ 4.86 (tertiary C-H), τ 4.42, 4.30 (methylene protons), τ 4.30 (remaining vinyl proton coupled with the methyl at τ 7.96) and τ 3.12 (N-H).

12. The similar dienone i has a λ_{max} 280 nm (ε 13,800).[13]



i

13. H. Hart and D. W. Swatton, *J. Am. Chem. Soc.*, **89**, 1874 (1967).

14. Indeed, 5 is more reactive than 1 toward other dienophiles such as 2-butyne; unpublished results.