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THE STEREOCHEMISTRY OF THE DIELS-ALDER REACTION OF HETERODIENOPHILES. THE CONFORMATION OF SIX-MEMBERED RINGS. (1,2)

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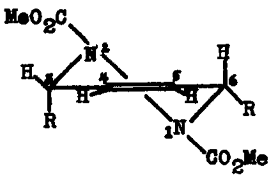
The recent appearance of a communication (3) dealing with results we reported at a meeting early this year (2) prompts us to present additional data we have obtained.

One phenomenon that characterizes many Diels-Alder reactions is its striking stereospecificity. It is probable that the transition states of these reactions retain to a high degree the configurations of the atoms located at the termini of the reacting functional groups. This has been established for the case of carbodienophiles (4) and to a limited extent for the reaction of the heterodienophilic nitroso group (5); however, confirmation of such stereospecificity is lacking for Diels-Alder reactions of azodienophiles (6).

It was anticipated that a suitably substituted Diels-Alder adduct of a dialkyl azodicarboxylate would possess sufficient conformational stability to permit the use of proton magnetic resonance spectroscopy for its structural analysis. Recent reports dealing with derivatives of cyclohexene (7,8) support this expectation. Accordingly, p.m.r.

spectra were determined for adducts (9) of dimethyl azodicarboxylate with *trans, trans*-2,4-hexadiene (1a,$R=CH_3$) and with *trans, trans*-1,4-diphenyl-1,3-butadiene (1b,$R=C_6H_5$).

Two possible configurations exist for these adducts, 1 and 2 in which the substituents at the 3 and 6 positions bear a *cis* and *trans* relationship respectively. If these Diels-Alder reactions are stereospecific and the dienes retain their configurations, the products would be the *cis* isomers, 1. By contrast, *trans* adducts 2, would denote loss of configuration during their formation thereby implying non-stereospecificity of the reactions.



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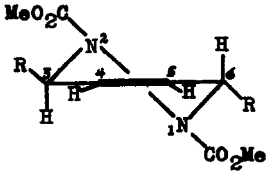


2

a: $R-CH_3$; b: $R=C_6H_5$

Table I summarizes pertinent p.m.r. spectral data for 1a (10), data found for 1b agree with those described recently (3). That the adduct 1a is the *cis* isomer follows from an interpretation of this spectrum.

TABLE I

P.M.R. Spectral Data of Adduct from Dimethyl Azodicarboxylate and *trans*, *trans*-2,4-Hexadiene[a]

H_3[b] 280	$J_{3,4} = 4.0$
H_4[c] 351.1; 347.1; 341.9; 337.9	$J_{4,5} = 9.2$
H_5[d] 329.0; 319.8	$J_{5,6} = 1.4$
H_6[b] 252	$J_{3,5} = 0.7$
	$J_{4,6} = 1.5$

[a] Data are given in c.p.s. downfield from TMS, at 35°.

[b] These bands are broad and show little definition of structure.

[c] Centers of doublets with 1.5 c.p.s. separation.

[d] Centers of quartets with 0.7 c.p.s. separation

(1) There are two methine hydrogen signals: H_3 at 280 c.p.s and H_6 at 252 c.p.s. These diverse chemical shifts are anticipated for la because the axial hydrogen, H_6, is expected to appear upfield from the one that is equatorial H_3 (11). By contrast both methine hydrogen atoms in the *trans* isomer lb are axial and should show the same chemical shifts.

(2) Chemical shifts for the vinyl protons (H_4 and H_5) are different as a consequence of disparate magnetic anisotropic effects of other groups on those two protons. Again, such differences are expected only for the *cis* isomer not for the *trans*. isomer. It is noteworthy that $J_{4,5}$ is 9.2 c.p.s., a value within the normal range for vinyl protons in six-membered rings (12).

(3) As demanded by structure 1a, the coupling constants $J_{3,4}$ and $J_{5,6}$ are not identical: $J_{3,4}$ is 4.0 c.p.s. whereas $J_{5,6}$ is 1.4 c.p.s. This is expected since it is probable that the dihedral angles $\phi_{3,4}$ is 43° whilst $\phi_{5,6}$ is 77° (13).

(4) Two long-range vinyl-allylic proton couplings are evident: $J_{3,5}$ is 0.7 c.p.s. and $J_{4,6}$ is 1.5 c.p.s. Such disparate coupling constants have been reported for systems similar to that in the *cis* configuration 1a and arise from differences in the angular relationship of the coupled protons (14).

Thus, evidence has been obtained to indicate that in the Diels-Alder reaction of dimethyl azodicarboxylate with *trans-trans*-2,4-hexadiene, the diene retains its configuration in forming the adduct. Mechanistically this implies that the Diels-Alder reaction of azodienophiles proceeds *via* a transition state similar to that proposed for carbodienophiles (15)

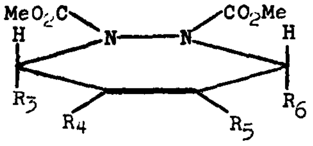
Implicit in the arguments presented above is the conformational stability of the *cis* isomer 1a. Closer examination of this structure reveals that the two O-methyl groups are not equivalent; furthermore the C_3 and C_6 methyl groups are also non-equivalent. The p.m.r. spectrum confirms these non-equivalences (Table II), (10). In view of this, other adducts, 3-10, were examined to ascertain the scope of this phenomenon. At 35° compounds 4 through 10 show equivalent methoxy groups (average chemical shift 224.0 ± 0.5 c.p.s.), while only compound 3 exhibits non-equivalent O-methyl signals.

TABLE II

P.M.R. Spectral Data of Adducts from Dimethyl Azodicarboxylate and Dienophiles[a]

Adduct	O-CH$_3$	Substituent at C$_3$ and C$_6$
1a	222.8; 220.4	93.2; 77.2[b]
1b	229.2; 206.6	447; 428[c]
3	232.5; 196.5	446.5[d]
4	223.5	75.0[e]
5	224.0	---
6	223.0	---
7	224.0	---
8	225.5	---
9	224.0	---
10	223.5	---

[a] Data are given in c.p.s. downfield from TMS, at 35°. [b] Centers of doublets, J = 6.5 c.p.s. [c] The downfield phenyl shows much fine structure while the upfield phenyl is a sharp band with shoulders. [d] Sharp band with shoulders. [e] Center of doublet, J = 6.5 c.p.s.

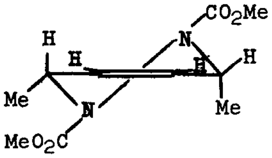


3-10

	R$_3$	R$_4$	R$_5$	R$_6$
3:	C$_6$H$_5$	H	H	H
4:	CH$_3$	H	H	H
5:	H	CH$_3$	H	H
6:	H	CH$_3$	CH$_3$	H
7:	H	H	H	H
8:	H	Cl	H	H
9:	│	H	H	│
	└────────	──── CH$_2$	────	────┘
10:	│	H	H	│
	CH$_2$ ────	────	────	──── CH$_2$

Furthermore. it has been found that at 72 ± 2°, the C_3 and C_6 methyl signals of 1a coalesce and, at 140°, become a sharp doublet centered 84.2 c.p.s. (J = 6.7 c.p.s.); at 82 ± 2° the vinyl protons (H_4 and H_5) coalesce and at 140° give a sharp doublet at 338 c.p.s. (J = 1.3 c.p.s.); at 77 ± 2° coalescence of the H_3 and H_6 methine protons occurs which then separates at 140° into a broad quartet at 267 c.p.s. with J = 6.4 c.p.s.; and finally, the O-methyl signals merge at a lower temperature (55 ± 2°).

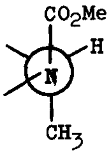
These data are interpreted to mean that at 35° the rate of ring inversion between equivalent conformers 1a and 1a'.



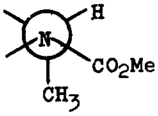
1a'

is slow relative to the rate of the magnetic transitions being analyzed. This assumption is justified since diverse chemical shifts and coupling constants are observed for that adduct. Above 85° average signals are obtained for the ring protons and for the methyl groups because now ring inversion exceeds the frequency of the magnetic transition.

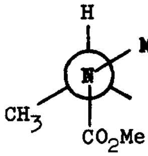
At -5° additional splitting occurs but only at the upfield C-methyl and the upfield methoxy signals. This further splitting is attributed to a reduction of the nitrogen inversion rate so that it becomes slower than the frequency of magnetic transition (16). Because the upfield methyl group (at C_3 in 1a) is fixed in an axial conformation, there will be two non-equivalent conformations for the adjacent methoxy group, 11a and 11b. Hence, when nitrogen inversion slows down, two



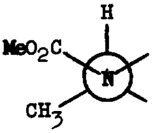
11a



11b



12a



12b

chemical shifts are expected for that methyl group and two for the adjacent methoxy group. By contrast, the downfield equatorial methyl group (at C_6 in 1a) will be in a similar environment regardless of the conformation of its adjacent methoxy group, 12a and 12b.

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