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A DEFINITIVE INVESTIGATION OF THE REACTION OF CYCLOPENTADIENE WITH *cis*-3,4-DICHLOROCYCLOBUTENE: A LITERATURE CORRECTION

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Abstract: Structural assignments are made to the three adducts derived from the title reaction. ^{1}*H-n.m.r.,* ^{13}*C-n.m.r. and euroshift data are used to support the new structures.*

In order to better understand the factors contributing to the specificities in cycloaddition reactions, it is essential to know the correct structures of the reaction products. A case in point is the reaction of cyclopentadiene with *cis*-3,4-dichlorocyclobutene which was reported to form a single product, assigned the *endo,syn*-stereochemistry. The high stereospecificity of this reaction was a point of interest, since it represented a case where attack appeared to occur onto the sterically more encumbered side of the dienophile. However, the original structural assignment is now shown to be incorrect which invalidates any previous conclusions, including those seeking to invoke a role for the chlorine atoms.[1]

The reaction of *cis*-3,4-dichlorocyclobutene (1) with cyclopentadiene (2) was first reported by Nenitzescu and his co-workers to yield a single product in high yield.[2] The supporting evidence offered for the *endo,syn*-stereochemical assignment seemed well founded, and it is to their credit that, despite marked advances in isolation techniques and structural evaluations, their assignment has remained essentially unchallenged for the last decade. In that time numerous examples of *cis*-3,4-dichlorocyclobutene acting as a dienophile or a dipolarophile have appeared in the literature, but no stereochemical assignments have been made to many of the products.[3]

Our own interest in the cycloaddition reactions of cyclobutenes in general, and *cis*-3,4-dichlorocyclobutene in particular, has led us to investigate their reaction with a variety of cyclic dienes. As the results of our investigations became available it was apparent that the

Nenitzescu result was in conflict with the general observation that [π^4s + π^2s] cycloaddition occurred preferentially from the side opposite to that of the substituents on the cyclobutene ring.[4] Although *syn*-addition to *cis*-3,4-dichlorocyclobutene is known to occur in 1,3-dipolarphilic reactions it is not normally observed in the sterically more sensitive [π^4s + π^2s] cycloadditions.[5] In order to evaluate the stereochemistry of the adduct from the reaction between cyclopentadiene and *cis*-3,4-dichlorocyclobutene the reaction has been reinvestigated and indeed new stereochemical assignments have been necessary. We now report evidence which shows that the reaction yields primarily the *endo,anti*-isomer (3), with minor amounts of the *exo,syn*-isomer (4) and even smaller amounts of the *endo,syn*-isomer (5) (Scheme 1).

Reaction of cyclopentadiene and *cis*-3,4-dichlorocyclobutene was carried out initially at 40° (4 hr) and subsequently at 150° (2 hr). Distillation, followed by preparative VPC (15% carbowax 20 M on chromosorb W. 10' x ¼", 182°) yielded one major (isomer A) and two minor adducts (isomer B and isomer C) in an overall yield of 85% (ratio A:B:C = 31:4:1). The major product, which corresponds in physical properties to the Nenitzescu result was subjected to hydrogenation (10% Pd/C, ether) to yield the dihydro product (12). Significantly the H3,4-protons of the hydrogenated product now resonate at δ 4.8 (see insert fig. 1), which is close to that observed in isomers B and C. We attribute the high field shift of the H3,4-protons in isomer A to the anisotropy of the stereochemically adjacent $\Delta^{7,8}$ double bond, which is removed upon hydrogenation. This suggests that isomer A has the *endo,anti*-structure (3). Additional support for this *endo,anti*-stereochemical assignment was obtained by an L.I.S. study on the *endo*-alcohol (11) derived from isomer A by hydroboration, oxidation to the ketone and reduction with sodium borohydride (Scheme 2). The shift data are summarised in figure 2 and clearly show that protons H3,4 must be geometrically proximate to the coordinating hydroxyl group, as required in the *endo,anti*-isomer (3).

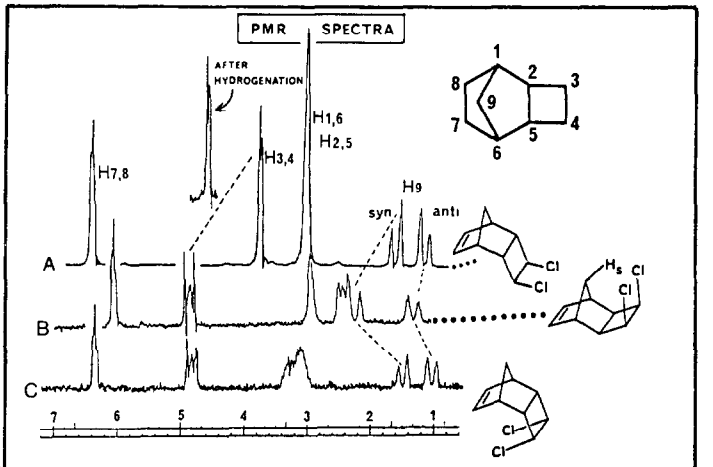


FIG. 1. 60 MHz pmr spectra of isomers A, B & C

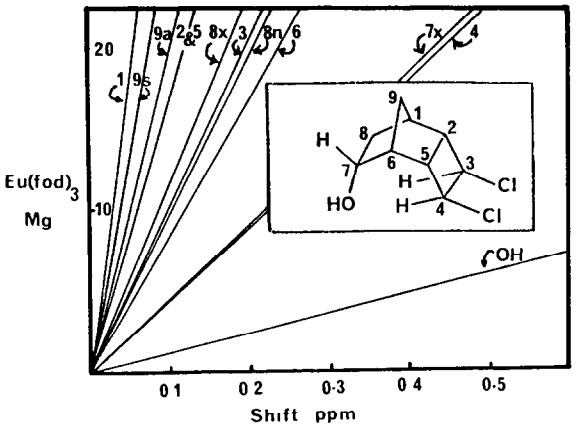


FIG. 2. L.I.S. study of *endo*-alcohol (11)

The reaction of isomers A, B, C, with potassium t-butoxide was most revealing since they all yield dehydrochlorinated products, which now shows that this reaction has NO diagnostic value for stereochemical assignments of the type employed by Nenitzescu.

However it did serve to interrelate these adducts since isomers A and C gave the same *endo*-fused product (7)(fig. 3), while isomer B yielded the *exo*-fused product (8)(fig. 4). Further stereochemical assignments were made

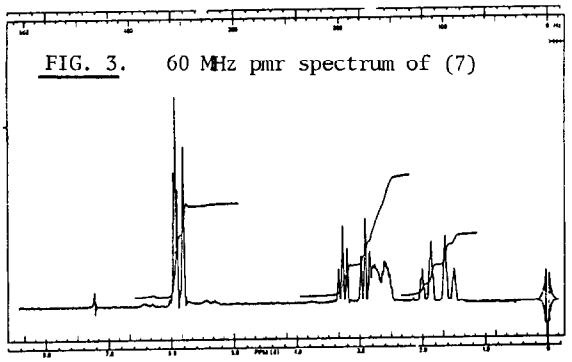


FIG. 3. 60 MHz pmr spectrum of (7)

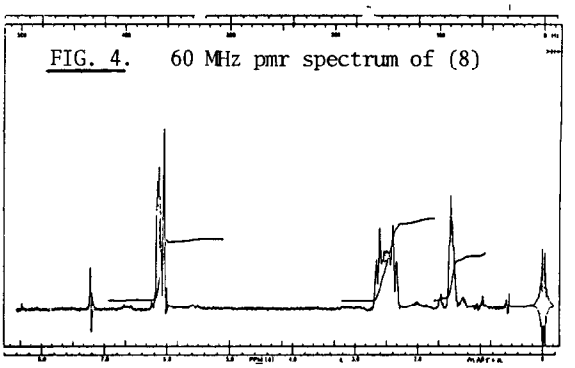
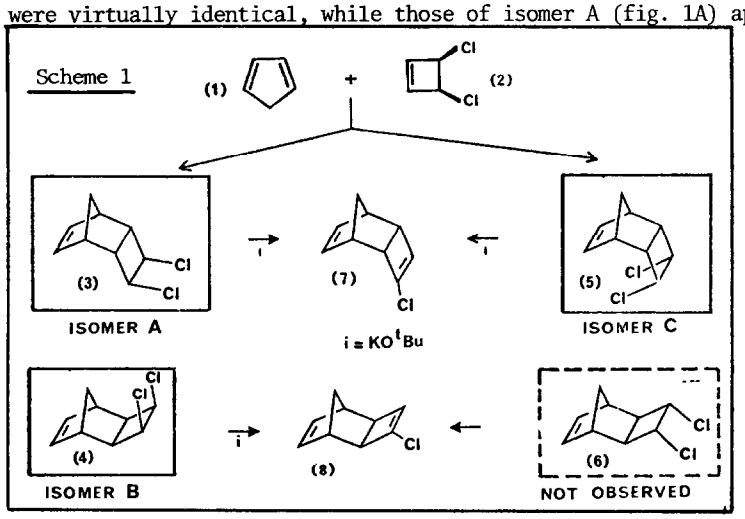
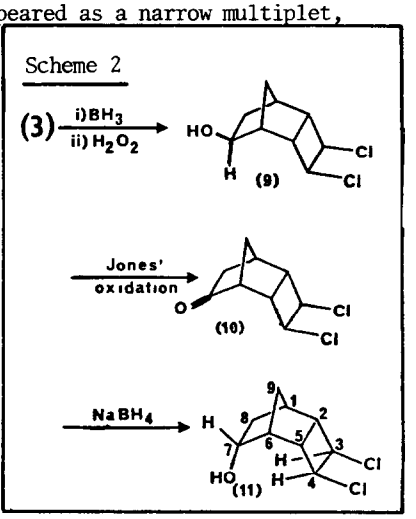


FIG. 4. 60 MHz pmr spectrum of (8)

on the basis of proton couplings about the cyclobutane ring. Clearly isomers B (fig. 1B) and C (fig. 1C) were related, since the coupling patterns for the downfield methine protons H3,4 were virtually identical, while those of isomer A (fig. 1A) appeared as a narrow multiplet,





typical of other *anti*-fused systems of this type (c.f. ref. 3, 4). A comparison of the chemical shifts of the *syn*-H9-bridge protons in these isomers lends additional support for these assignments. Isomer B, in which the *syn*-H9 proton is shifted downfield by about 0.75 ppm from the corresponding proton in either isomer A or isomer C is so shifted due to steric compression.[6] Correspondingly the upfield shift of the bridging C9-carbon in the ^{13}C-nmr of isomer C (see table 1), is quite distinctive, and is possibly due to a through space inductive effect,[7] which could only operate in this isomer.

We can assign, therefore, the *endo,anti*-stereochemistry to isomer A, the *exo,syn*-stereochemistry to isomer B and the *endo,syn*-chemistry to isomer C.

Table 1

^{13}C-nmr spectra of adducts (3), (4) and (5)

	VINYL	BRIDGEHEAD	CYCLOBUTYL	CH-Cl	METHYLENE
	C7,8	C1,6	C2,5	C3,4	C9
(3)	136.2	44.8	50.6	55.9	53.1
(4)	137.0	44.2	43.1	54.9	44.1 *
(5)	135.7	48.0	46.6	57.6	51.8

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