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Structure and Reactivity

I. Deuteration of Substituted Cyclohexenes: Stereoselectivity of Addition and Exchange in the Homoallylic Position

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A series of substituted and deuterium labeled cyclohexenes were deuterated on a Pd/C catalyst, and the products were analyzed by NMR spectroscopy. The compounds were: methyl-2,2,5,5-tetradeuterio-3,4-dimethyl-3-cyclohexenecarboxylate, methyl-2,2,5,5-tetradeuterio-4-*t*-butyl-3-cyclohexenecarboxylate, *cis*- and *trans*-2,5,5-trideuterio-2-alkyl-3-cyclohexenecarboxylic acid methyl ester or nitrile (alkyl being methyl or *t*-butyl). The *cis* isomers underwent exclusive addition on their least hindered side and a stereospecific exchange of the hydrogen located in a *trans* vicinal position with respect to the carboxyl or the cyano groups was noted. This feature was absent for most of the *trans* isomers. The exchange and addition mechanisms are discussed.

INTRODUCTION

The mechanism of alkene hydrogenation on various kinds of catalysts has been widely studied (*1–8*). The results obtained generally fit the Horiuti and Polanyi hypothesis (*9*) of *cis* addition during the first step of the reaction (formation of a carbon–hydrogen bond and a carbon–metal bond). Different secondary exchange processes take place when palladium is used as catalyst, leading mainly to the thermodynamically more stable stereoisomer (*1, 8*).

In previous work we have studied the deuteration of a series of cyclohexenes specifically deuterated in the allylic positions and substituted with a CO_2CH_3 or a CN group in the homoallylic position. The interpretation of the NMR spectra of the products led us to detect the presence of different isotopic modifications (*10–12*). The first results (*10*) showed a partial but stereospecific exchange of a homoallylic hydrogen by a deuterium atom when the addition of deuterium was carried out with 5% palladium on charcoal as catalyst. The stereochemistry of this addition has also been rationalized for some of these derivatives (*12*). In this paper, our purpose is the analysis of the reaction mechanism and the study of the structural parameters which account for these new experimental results.

EXPERIMENTAL METHODS

Materials

The syntheses of the different cyclohexenes were achieved by a Diels-Alder reaction between methyl acrylate (or acrylonitrile), 1,1,4,4-tetradeuterio-2,3-dimethyl-1,3-butadiene, 1,1,4-trideuterio-1,3-pentadiene and 1,1,4-trideuterio-5,5-dimethyl-1,3-hexadiene. The separation of the isomers has been described elsewhere (*10, 13*). In each case, the products obtained after deuteration were isolated by

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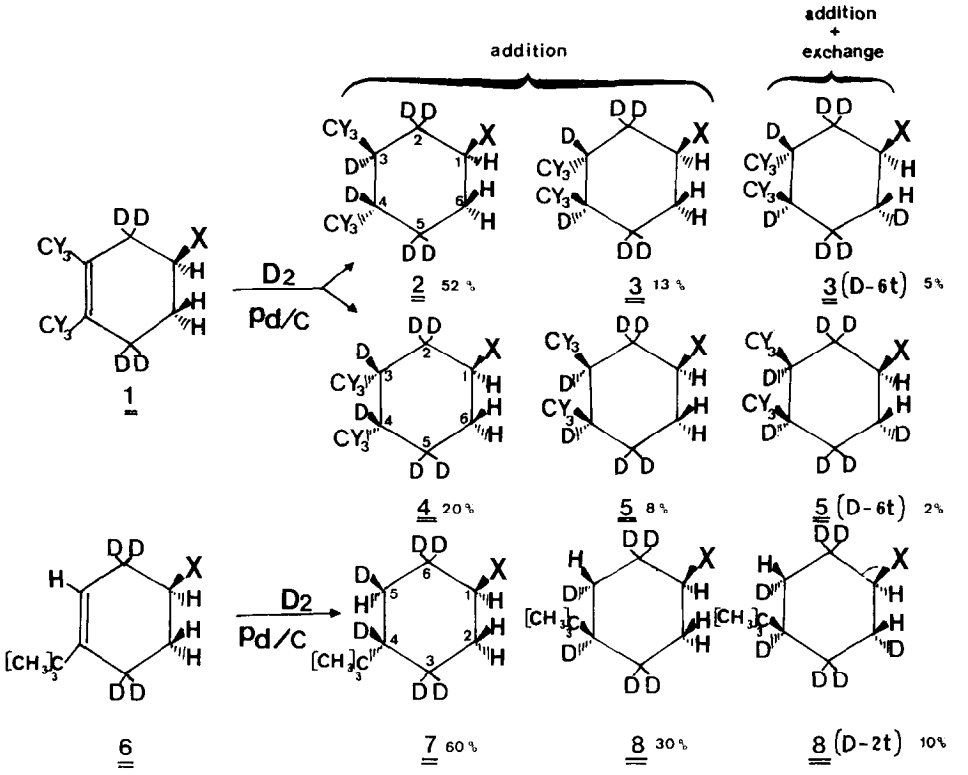

FIG. 1. Deuteration of cyclohexenes substituted on the double bond ($CY_3 = CH_nD_{3-n}$; $X = CO_2CH_3$).

preparative gas chromatography and their purity ($\geq 99\%$) was also checked by NMR. The chromatographic separation of compounds **2**, **3** and **4** + **5** has already been described (*10*), as has also the separation of stereoisomers **7** and **8** (*12*).

Procedures

The addition of deuterium (D_2 from Sté l'Air Liquide) was carried out in anhydrous dioxane at room temperature and atmospheric pressure, with Fluka 5% Pd/C catalyst (10 mg for 100 mg of alkene) previously presaturated with deuterium, according to the method described by Augustine (*14*).

NMR Spectra

The NMR spectra have been described in a previous paper (*12*) and were obtained using a Varian HA 100 spectrometer equipped with a heteronuclear decoupler SD-60 B (NMR Specialities Inc.). The solvent was CS_2 and temperature 303 K.

For compound **8**, the influence of $Eu(fod)_3$–D_{27} (Merck Sharp and Dohme) used as a shift reagent was: *t*-butyl 3.2; H_1 28; H_{2e} 20; H_{2l} 11; H_5 21; the numerals correspond to the slope of the chemical shift as a function of the ratio of the metal to ligand concentrations.

RESULTS

The deuteration of **1** (Fig. 1) gives a mixture of four stereoisomers; 70% of the mixture (*10*) corresponds to compounds **2** and **3** in which methyl substituents are *trans* to one another, and the remaining 30% consists of **4** and **5** with the *cis* orientation of the methyl groups. These ratios can be qualitatively compared with

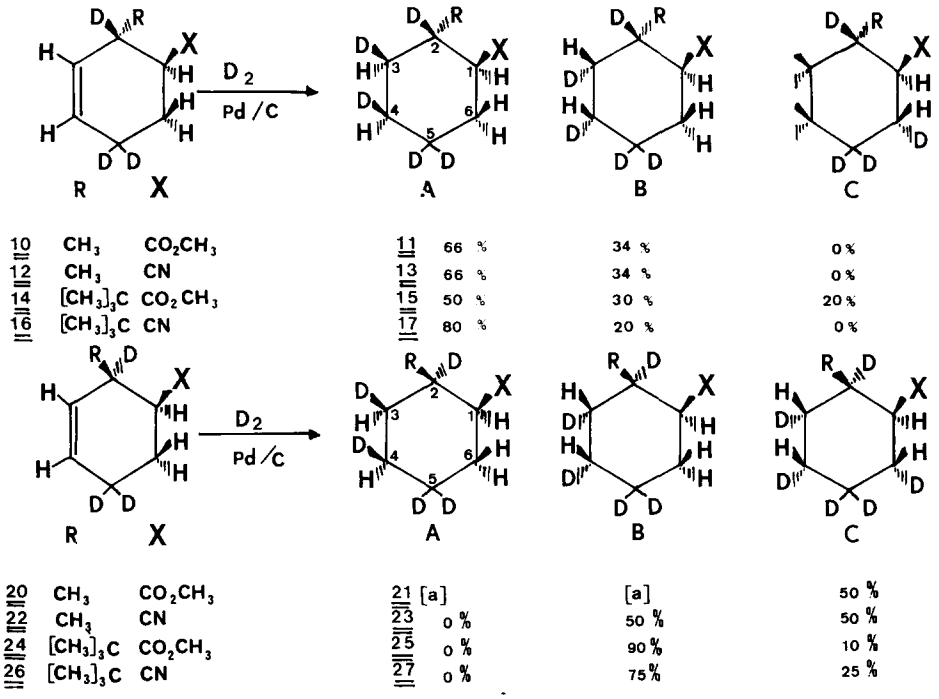

FIG. 2. Deuteration of 3,4-disubstituted cyclohexenes. [a] Percentage can not be determined.

the ones obtained by Sauvage *et al.* (*1*) and Siegel and Smith (*2*) after hydrogenation of 1,2-dimethylcyclohexene (75% of *trans* product) in similar conditions. Another aspect of the reaction is the important exchange of the hydrogens on the methyl groups: their initial deuteration which was 30% in **1** (owing to repeated exchanges of 3,4-dimethylsulfolene with D_2O) rises to 70% in the products (as obtained from the relative integration of the NMR peaks of the methyl and the carbomethoxy groups).

The NMR spectra of stereoisomers **3** and **5** present, for each of the four lines of the protons H_1 and H_{6c}, a supplementary doublet [see spectra of Refs. (*10*, *11*)] which is easily assigned to isotopic modifications **3** (D-6*t*) and **5** (D-6*t*).

The deuteration of **6** occurs with the formation of stereoisomers **7** and **8**. In each case, the *cis* addition of deuterium is confirmed by the appearance of the proton H_5 as a unique peak; the axial position of H_5 in **7** and **8** is implied by its chemical shift (δ = 1.0 ppm),[1] and moreover in **8** by the strong europium-induced shift (see Experimental methods section) which is only consistent with a *syn*-1,3 diaxial position of H_5 and CO_2CH_3. In addition, the NMR spectrum of **8** presents supplementary peaks which are characteristic for **8** (D-2*t*), i.e., a doublet for H_{2c} and a broadening of the transitions for H_1 in good agreement with the existence of a similar doublet.

A stepwise analysis of NMR spectra of *trans* disubstituted cyclohexanes **11**, **13**, **15**, and **17** (*12*) gave evidence for the isotopic modifications A and B (Fig. 2), and is in agreement with a *cis* addition of deuterium to the double bond.[2] The spectrum of **15** is

[1] In *t*-butylcyclohexane, the chemical shifts for protons vicinal to the *t*-butyl group are 1.75 (equatorial) and 0.92 ppm (axial) (15).

[2] The value of the coupling constants between protons H_3 and H_4 (J_{34} = 3.9 Hz) only fits a *cis* arrangement. Long range coupling (*w* path) between diequatorial H_4 and H_{6t} protons of modification A confirms the structure (12).

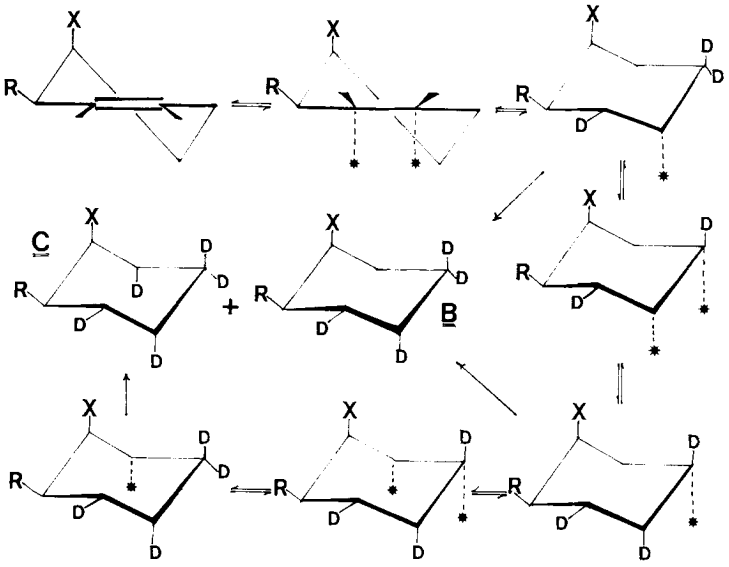

FIG. 3. Classical mechanism for addition and exchange in homoallylic position.

the only one which reveals the presence of the isotopic modification C resulting from a stereospecific exchange (*trans* relative to CO_2CH_3) in the homoallylic position.

For compounds **23**, **25** and **27**, the protons H_3 and H_4 present two isolated NMR signals [after addition of $Eu(fod)_3$ for **25**] whose identification is straightforward (*12*) owing to their chemical shifts, their coupling constants (^3J and ^4J) and for **25**, the effect of the shift reagent. The isotopic modification A is lacking and, consequently, the addition of deuterium to the double bond proceeds exclusively *trans* to the substituents R and X (Fig. 2). For compound **21**, the superposition of different NMR signals occurs, and it is not possible to conclude about the complete lack of **21**-A.

In these last four products, the C type isotopic modifications are present in appreciable amounts, except for **25**-C (Fig. 2).

DISCUSSION

Exchanges in Allylic and Homoallylic Positions

Since the starting molecules are deuterated in the allylic positions, we are not able to appreciate the amounts of exchange in these positions during the deuteration.[3] However, for **1** this kind of exchange leads (Fig. 1) to a mixture of isomers having their methyl groups partially deuterated (up to 60%) in the course of the reaction, and in which the major product is the more thermodynamically stable isomer **2**. This result can be compared to those cited in the literature (*2*, *8*b, *17*); moreover, it shows that the ratio of saturated isomers obtained during the addition of deuterium is not too much modified by a substituent in the homoallylic position.

The addition of hydrogen to compound **20** does not exhibit any allylic exchange of the deuterium in position 2, the H_1 NMR signal of the product being a pure quadruplet without any supplementary peak [cf. spectrum of Ref. (*10*)].

In the course of the deuteration of compounds **6**, **22**, **24**, and **26**, a stereospecific exchange in the homoallylic position is observed. To rationalize this exchange, one

[3] In the course of hydrogenation (Pd/C, CH_3COOD) of *cis*- and *trans*-3,3,6,6-tetradeuterio-4,5-dimethyl-1,2-cyclohexane dicarboxylic acid, Campbell (*16*) pointed out an exchange of 20% of the allylic hydrogens of the ring.

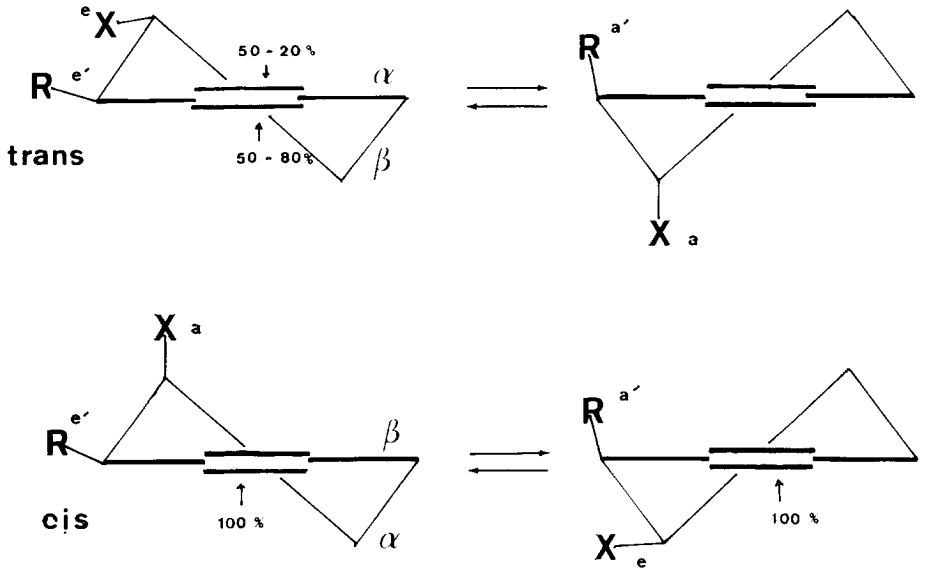

FIGURE 4

can develop several mechanisms. Yet, for all these cyclohexenes, we have proved that *cis* addition to the double bond occurs exclusively and that this process keeps unchanged the stereochemistry of the substituents R and X. For compound **1**, the ratio of **5**(D-6*t*) to **3**(D-6*t*) is exactly that of **4** + **5** to **2** + **3**. All these facts rule out mechanisms proceeding through the deuteration of "desorbed" isomer cyclohexenes or through an exchange on "readsorbed" isomer cyclohexanes.

We must conclude that the exchange of the homoallylic proton occurs before the desorption of the molecule; a sequence of a roll-over mechanism would not lead to stereospecificity (*18*). Figure 3 is in agreement with all the experimental data and shows one of the possible reaction mechanisms.

Factors Governing the Stereoselectivities of Addition and Exchange

For compound **6** and *trans* isomers **10**, **12**, **14**, and **16**, the addition of deuterium takes place on the two sides of the molecule with a marked preference for the β side (*cis* relative to the X group). On the other hand, for *cis* isomers **22**, **24**, and **26**, the addition takes place exclusively on the α side (*trans* relative to X) (Fig. 4).

These stereoselectivities can be interpreted by taking account of:

1. a moderate steric interaction between the surface of the catalyst and the pseudoequatorial (e′) R group in the *trans* isomers; the adsorption of the diaxial conformer must be much more difficult;

2. strong steric repulsions on the β side of *cis* isomers.

The homoallylic exchange never occurs on the carbon bearing the X group, and always proceeds in a *trans* relationship to the vicinal X group. When addition occurs on the β side (deuteration of **1** and **6**), the exchange associated with this addition does not appear: indeed, the isotope modifications **2**(D-6*c*), **4**(D-6*c*), and **7**(D-2*c*) are not formed. On the other hand, there is no exchange for *trans* isomers (Fig. 2) except for the deuteration of **14**. Therefore, the homoallylic exchange occurs quite exclusively for conformers with an axial X group and a pseudoequatorial R group.

This conformational effect may be ascribed to an electronic effect of X on the *anti* C–H bond such as the effect which governs the radical abstraction of a hydrogen *anti* to a C–Br bond (*19*).

CONCLUSION

The use of specifically deuterated cyclohexenes has elucidated the stereochemical course of the deuteration reaction including a stereospecific exchange in the homoallylic position. The phenomenon may be described by steric and electronic effects.

REFERENCES

1. Sauvage, J. F., Baker, R. H., and Hussey, A. S., *J. Amer. Chem. Soc.* **82**, 3874, 6090 (1960).
2. Siegel, S., and Smith, G. V., *J. Amer. Chem. Soc.*, **82**, 6082, 6087 (1960).
3. Shopov, D., and Andreev, A., *Bulg. Acad. Sci., Comm. Dept. Chem.* **2**, 583 (1969).
4. Burwell, R. L., *Accounts Chem. Res.* **2**, 289 (1969).
5. Pecque, M., and Maurel, R., *J. Catal.* **19**, 360 (1970).
6. Hilaire, L., and Gault, F. G., *J. Catal.* **20**, 267 (1971).
7. Smith, G. V., Roth, J. A., Desai, D. S., and Kosco, J. L., *J. Catal.* **30**, 79 (1973).
8. (a) Mitsui, S., Gohke, K., Saito, H., Nanbu, A., Senda, Y., *Tetrahedron* **29**, 1523 (1973); (b) Mitsui, S., Imaizumi, S., Nanbu, A., and Senda, Y., *J. Catal.* **36**, 333 (1975).
9. Horiuti, J., and Polanyi, M., *Trans. Faraday Soc.* **30**, 1164 (1934).
10. Aycard, J. P., Geuss, R., and Bodot, H., *C. R. Acad. Sci.* **275**, 1447 (1972).
11. Aycard, J. P., Geuss, R., Berger, J., and Bodot, H., *Org. Magn. Res.* **5**, 473 (1973).
12. Aycard, J. P., and Bodot, H., *Org. Magn. Res.* **7**, 35 (1975).
13. Aycard, J. P., and Bodot, H., *Org. Magn. Res.* **7**, 226 (1975).
14. Augustine, R. L., "Catalytic Hydrogenation," p. 66. Dekker, New York, 1965.
15. Haddon, V. R., and Jackman, L. M., *Org. Magn. Res.* **5**, 333 (1973).
16. Campbell, J. R., PhD thesis, Queen's University, Kingston, 1969.
17. Hussey, A. S., and Nowack, G. P., *J. Org. Chem.* **34**, 439 (1969).
18. Roth, J. A., Geller, B., and Burwell, R. L., Jr., *J. Res. Inst. Catal. Hokkaido Univ.* **16**, 221 (1968).
19. Simamura, O., *in* "Topics in Stereochemistry," (E. L. Eliel and N. L. Allinger, eds.), Vol. **4**, p. 8. Wiley, New York, 1969.