## 321. *Conformationally Fixed Olefins. Part III.*[1] *The Stereochemistry of the Reaction of t-Butyl Perbenzoate with 1-Methylene-4-t-butylcyclohexane.*

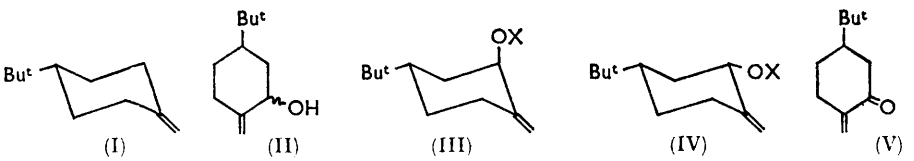
By B. Cross and G. H. Whitham.

The main product from the reaction of 1-methylene-4-t-butylcyclohexane (I) with t-butyl perbenzoate in the presence of cuprous chloride is the benzoate of 2-methylene-*trans*-5-t-butylcyclohexanol (III; X = H). The corresponding *cis*-alcohol (IV; X = H) is obtained by reduction of 2-hydroxymethylene-5-t-butylcyclohexanone (VI) with lithium aluminium hydride. Evidence on which the configurational assignments are made is presented and the stereochemical course of the reaction of t-butyl perbenzoate is discussed.



The reaction of an olefin, possessing an allylic hydrogen, with t-butyl perbenzoate in benzene in the presence of catalytic quantities of cuprous salts usually results in the introduction of an allylic benzoyloxy-group:[2] C:C·CH ⟶ C:C·C(OBz). Allylically rearranged products are not obtained in this reaction and a modified free-radical mechanism has been proposed.[3] So far no studies on the sterochemistry of the reaction have been reported and we have, therefore, investigated this using 1-methylene-4-t-butylcyclohexane[4] (I) as substrate. This compound, which should exist in the chair form shown,[4] is free from strong steric influences at $C_{(2)}$ so that the mode of allylic substitution should be dictated largely by stereoelectronic effects.

The crude product from the reaction of t-butyl perbenzoate with the hydrocarbon (I), which consisted of a mixture of biphenyl, unchanged hydrocarbon, and benzoates, was hydrolysed and chromatographed. The main product, obtained in 26% yield, had $\nu_{max.}$ 3580 (OH) and 3060, 1650, and 904 cm.$^{-1}$ (C=$CH_2$) and the conclusion that it was one of the epimeric 2-methylene-5-t-butylcyclohexanols (II) was borne out by reactions described below. A small amount of another alcohol possessing methylenic infrared absorption was also formed; this could not be obtained free from the major product but was shown to be




(I) (II) (III) (IV) (V)

the epimer of the latter by infrared comparison with a pure sample obtained later in another way. Other hydroxylic materials were also formed but were not investigated after infrared spectra had shown the absence of the exocyclic methylene group.

We made the tentative assignment, on the basis of their order of elution on chromatography,[5] that the major allylic alcohol, eluted first, was the axial isomer (III; X = H), the minor component being the equatorial epimer (IV; X = H). The possibility that epimerisation might have occurred under the alkaline conditions of hydrolysis was excluded by an alternative procedure in which lithium aluminium hydride was used.

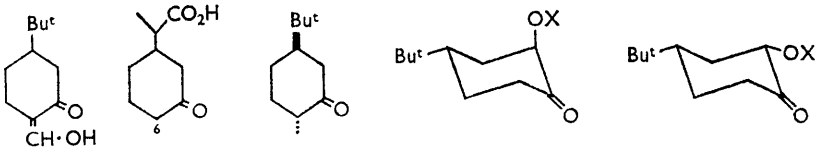
To confirm the assignments (which for convenience of discussion will be assumed to be correct), an alternative route to the minor isomer was required. Attempts to epimerise the alcohol (III; X = H) by potassium t-butoxide in t-butyl alcohol and benzophenone[6]

[1] Part II, Cross and Whitham, *J.*, 1960, 3895.
[2] Kharasch and Sosnovsky, *J. Amer. Chem. Soc.*, 1958, **80**, 756; Kharasch, Sosnovsky, and Yang, *ibid.*, 1959, **81**, 5819.
[3] Denney, Denney, and Feig, *Tetrahedron Letters*, 1959, **15**, 19.
[4] Cross and Whitham, *J.*, 1960, 3892.
[5] Barton, *J.*, 1953, 1027.
[6] Doering and Aschner, *J. Amer. Chem. Soc.*, 1949, **71**, 839.

or aluminium isopropoxide in propan-2-ol and acetone [7] resulted only in the recovery of unchanged material, and attempts to oxidise it to the methylene ketone (V) gave intractable mixtures owing to the ready dimerisation of α-methylenecyclohexanones.[8]

Dreiding and Hartman [9] have shown that 2-methylenecyclohexanol is obtained, along with 1-hydroxymethylcyclohexene and 2-hydroxymethylcyclohexanol, by reduction of 2-hydroxymethylenecyclohexanone with lithium aluminium hydride. It is likely that the 2-methylenecyclohexanol is derived by reduction of 2-methylenecylohexanone formed *in situ*. Thus a new approach to the equatorial allylic alcohol (IV; X = H) would involve reduction of 2-hydroxymethylene-5-t-butylcyclohexanone (VI) by lithium aluminium hydride, which should proceed by way of the unsaturated ketone (V).

Condensation of 3-t-butylcyclohexanone [10] with ethyl formate gave the hydroxymethylene-ketone (VI). That formylation would be expected to occur as shown, and not at $C_{(2)}$, owing to the steric effect of the t-butyl group, is indicated by the analogous case [11] of the ketone (VII) where condensation occurs at $C_{(6)}$. Reduction of the hydroxymethylene-ketone (VI) with an excess of lithium aluminium hydride gave the required allylic alcohol (IV; X = H) in 33% yield. It was chromatographically homogeneous and its infrared spectrum, though different from that of the major allylic alcohol (III; X = H) obtained in the t-butyl perbenzoate reaction, was identical with that of the minor isomer. This confirmed the identity of the latter.




(VI) (VII) (VIII) (IX) (X)

It was next necessary to prove, first, that the two allylic alcohols obtained above were indeed the epimeric 2-methylene-5-t-butylcyclohexanols and, secondly, that the configurations are as tentatively assigned. Their skeletal identity was proved by their rearrangement, when heated with palladium–carbon in methanol, to the same methyl ketone (VIII). Additional confirmation that the two alcohols have the same skeleton and substantiation of the assigned configurations came from the products of ozonolysis of their 3,5-dinitrobenzoates: ozonolysis, by the procedure of Conia and Leriverend,[12] of the 3,5-dinitrobenzoate of the minor alcohol gave a crystalline ketone 3,5-dinitrobenzoate; that of the main alcohol gave a gum which had a different infrared spectrum (in particular, the gum had only one band in the carbonyl region at 1743 cm.$^{-1}$ whereas the crystalline isomer had two bands, at 1751 and 1739 cm.$^{-1}$). Treatment of the gum with 0·1N-perchloric acid in acetone gave the crystalline isomer. These results are best accommodated by an acid-catalysed epimerisation of the axial ester (IX) to the more stable equatorial 3,5-dinitrobenzoate (X).

Additional confirmation of the configurational assignments and conversely, taken in conjuction with the above chemical evidence, that the allylic alcohols (III and IV; X = H) exist predominantly in the chair form in carbon tetrachloride solution is given by their nuclear magnetic resonance spectra. For the alcohol (IV; X = H) the absorption due to the tertiary proton >CH·OH was a broad band at −122·7 cycles/sec. whereas for the alcohol (III; X = H) it was sharper and centred at −133·8 cycles/sec. Examples [13]

[7] Eliel and Ro, *J. Amer. Chem. Soc.*, 1957, **79**, 5992.
[8] Mannich, *Ber.*, 1945, **74**, 554.
[9] Dreiding and Hartman, *J. Amer. Chem. Soc.*, 1956, **78**, 1216.
[10] Whitmore and Pedlow, *J. Amer. Chem. Soc.*, 1941, **63**, 759.
[11] Abe, Harukawa, Ishikawa, Miki, Sumi, and Tuga, *J. Amer. Chem. Soc.*, 1953, **75**, 2567.
[12] Conia and Leriverend, *Compt. rend.*, 1960, **250**, 1078.
[13] Lemieux, Kullnig, Bernstein, and Schneider, *J. Amer. Chem. Soc.*, 1957, **79**, 1005; 1958, **80**, 6098; Smith, Marx, Garbarini, Foell, Origoni, and Goodman, *ibid.*, 1960, **82**, 4619.

show that equatorial protons absorb at lower fields than axial protons (average difference *ca.* 0·3 p.p.m.[14]) and that absorption bands due to axial protons are broader, owing to more pronounced axial–axial coupling patterns. Supplementary evidence is given by the nuclear magnetic resonance spectra of the acetates (III and IV; X = Ac).

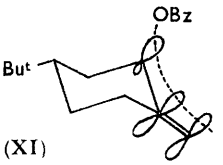
*Infrared Spectra.*—The strong absorption bands in the 900 cm.$^{-1}$ region associated with the compounds containing an exocyclic methylene group are tabulated. A small but distinct shift to higher frequencies is observed for compounds with α-oxygenated substituents. Thus an equatorial α-substituent causes a shift of 4—9 cm.$^{-1}$ and an axial α-substituent a somewhat larger shift of 15—20 cm.$^{-1}$. The markedly reduced ε values noted for some α-substituted methylenic compounds, where free rotation about the =C–CX– bond can occur,[15] were not observed with these more rigid systems.

*Infrared absorption bands in the* 900 *cm.*$^{-1}$ *region.*

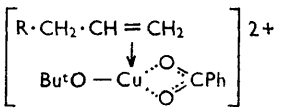
| | X = H | | | X = CO·$C_6H_3(NO_2)_2$ | | X = Ac | |
|---|---|---|---|---|---|---|---|
| Compound ..... | I | IV | III | IV | III | IV | III |
| Band (cm.$^{-1}$) ..... | 890 | 894 | 905 | 899 | 910 | 894 | 909 |

*Discussion.*—The major allylic substitution product from the reaction of t-butyl perbenzoate with 1-methylene-4-t-butylcyclohexane is therefore the benzoate (III; X = Bz) with an axial benzoyloxy-group. The epimeric benzoate is only formed to a minor extent.

A free-radical mechanism could explain this result. Thus abstraction, by a t-butoxy-radical, of an axial rather than an equatorial α-hydrogen atom should be facilitated by the favourable overlap of the π-orbitals of the double bond with the developing *p*-orbital containing the odd electron. Conversely, on combination of the allylic radical so formed with a benzoyloxy-radical, a stereoelectronic preference for axial insertion would be expected (cf. XI). This situation would thus be the free-radical counterpart of the ionic bromination of cyclohexanones which, under suitable conditions, gives the axial α-bromo-cyclohexanone.[16]




(XI)




(XII)

If, on the other hand, an intermediate complex of the type proposed by Denney, Denney, and Feig [3] (cf. XII) is involved in the t-butyl perbenzoate reaction, then the stereochemical outcome may be determined by the preferred direction of co-ordination of the olefin with the copper complex. In the case of the methylene hydrocarbon (I) co-ordination of the copper complex from the side *trans* to the t-butyl group would direct attack on to the axial hydrogen atom at $C_{(2)}$ [or $C_{(6)}$]. That attack in this sense by a bulky metal complex might be expected is indicated by the reaction of the methylene hydrocarbon (I) with osmium tetroxide, which gives solely the product resulting from attack *trans* to the t-butyl group.[17] A clear decision awaits sharper delineation of the mechanism of the t-butyl perbenzoate reaction. For the present it seems that the presence of small amounts of the equatorial allylic substitution product favours the second alternative. On this basis it could result from co-ordination to a small extent from the less favoured side.

[14] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1959, p. 116.
[15] Barton, de Mayo, and Shafiq, *J.*, 1958, 3314.
[16] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.
[17] Cross and Whitham, unpublished results.

## Experimental

For general remarks see Part I.[4]

*2-Methylene*-trans-5-*t-butylcyclohexanol* (III; X = H).—(*a*) To 1-methylene-4-t-butylcyclohexane (5·2 g.) in dry benzene (600 c.c.) were added cuprous chloride (0·15 g.) and t-butyl perbenzoate (15·4 g.), and the mixture was heated under reflux during 8 hr. [In preliminary experiments the decomposition of t-butyl perbenzoate in benzene at the above concentration in the presence of cuprous chloride was followed by the disappearance of the 1755 cm.$^{-1}$ infrared band (per-ester). After 8 hr. all the per-ester had decomposed, the products being biphenyl, benzoic acid, and t-butyl alcohol.] The mixture was filtered and washed with water. Removal of benzene gave a syrup which was hydrolysed with 20% methanolic potassium hydroxide at 20° under nitrogen during 48 hr. The neutral fraction was obtained as an oil which was chromatographed on alumina. Elution with light petroleum gave biphenyl (1·41 g.), m. p. 69—70°. Further elution with light petroleum–ether (1 : 1) and (1 : 9) gave an oil (1·67 g.) which was rechromatographed. Elution with light petroleum–ether (8 : 2) and (7 : 3) gave the *trans-alcohol* (1·45 g., 26%), b. p. 116—118°/12 mm., $n_D^{20}$ 1·4805, m. p. *ca.* 25° (Found: C, 78·5; H, 11·5. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%), $\lambda_{max.}$ 3580, 1086, 1041, 1018, 983 (OH), 3060, 1650, 905 (C=$CH_2$), 1369 cm.$^{-1}$ (Bu$^t$). Continued elution with light petroleum–ether (6 : 4) gave an oil (0·25 g.). The infrared spectrum of the latter exhibited, in addition to bands due to the *trans*-alcohol, bands at 1089, 1075, 1055, and 894 cm.$^{-1}$ shown later to be characteristic of the *cis*-alcohol (IV; X = H).

Further elution of the original column with ether gave hydroxy-compounds showing no exocyclic methylene absorption in the infrared spectrum.

(*b*) Crude product from the reaction of t-butyl perbenzoate (0·9 g.) with 1-methylene-4-t-butylcyclohexane (0·34 g.) was dissolved in dry ether (10 c.c.), lithium aluminium hydride was added, and the mixture was heated under reflux during 1 hr. Decomposition with water was followed by treatment with aqueous sodium potassium tartrate. Isolation with ether gave an oil which was chromatographed on alumina. Elution with light petroleum gave material (0·16 g.) which was not further investigated; further elution with light petroleum–ether (97 : 3) and (9 : 1) gave an oil (63 mg.) shown by its infrared spectrum to be identical with the *trans*-alcohol obtained as under (*a*).

*2-Methylene*-trans-5-*t-butylcyclohexyl* 3,5-*Dinitrobenzoate*.—3,5-Dinitrobenzoyl chloride (3·03 g.) in dry benzene (60 c.c.) was added at 0° to the *trans*-alcohol (III; X = H) (1·14 g.) in dry benzene (20 c.c.) containing dry pyridine (0·94 g.) and left at 8° during 12 hr. Pyridine hydrochloride was filtered off and the benzene layer was washed with aqueous sodium carbonate and water. Evaporation of the dried solution followed by chromatography of the residue in benzene on alumina gave the 3,5-*dinitrobenzoate* (300 mg.), m. p. 78—80° (from ethanol) raised to 84—85° after two further recrystallisations (Found: C, 59·55; H, 5·8. $C_{18}H_{22}N_2O_8$ requires C, 59·65; H, 6·1%).

*2-Methylene*-cis-5-*t-butylcyclohexanol* (IV; X = H).—3-t-Butylcyclohexanone [10] (15·6 g.) was added to a suspension of dry sodium methoxide (from sodium, 4 g.) in dry benzene (150 c.c.) under nitrogen. Ethyl formate (16 g.) was added and the mixture was shaken and set aside at 20° for 12 hr. Iced water was added and the aqueous layer was collected. The benzene layer was washed with cold aqueous sodium hydroxide (5 × 50 c.c.), and all the aqueous layers were combined, washed once with ether, and acidified with dilute hydrochloric acid. After addition of salt, isolation with ether gave the 2-hydroxymethylene-5-t-butylcyclohexanone (11·5 g.), b. p. 94—98°/1 mm.

The hydroxymethylene-ketone (11·5 g.) in ether was added to a stirred suspension of lithium aluminium hydride (4 g.) in dry ether (200 c.c.), and the mixture was heated under reflux for 1 hr. After addition of water and sodium potassium tartrate the product was iolated with ether. Distillation gave an oil (5·5 g.), the infrared spectrum of which had a band at 1685 cm.$^{-1}$ (αβ-unsaturated ketone), presumably due to the presence of some ketone (V). The oil was accordingly resubmitted to the reduction sequence with lithium aluminium hydride (1 g.). Isolation as before followed by chromatography on alumina gave the *alcohol* (3·7 g., 33%), b. p. 74°/0·4 mm., $n_D^{19}$ 1·4855, m. p. *ca.* 20° (Found: C, 78·0; H, 11·85%). $\nu_{max.}$ 3560, 1087, 1073, 1054 (OH), 3060, 1650, 894 (C=$CH_2$), and 1367 cm.$^{-1}$ (Bu$^t$). The 3,5-*dinitrobenzoate*, formed as above in 44% yield, was obtained as needles, m. p. 153·5—154°, from light petroleum (b. p. 80—100°)

(Found: C, 59·65; H, 6·45%). The *acetate* had b. p. 65—66°/0·2 mm., $n_D^{21}$ 1·4659 (Found: C, 74·3; H, 10·65. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%).

2-*Methyl-5-t-butylcyclohexanone* (VIII).—(*a*) Palladium–carbon (10 mg.) was added to 2-methylene-*cis*-5-t-butylcyclohexanol (120 mg.) in methanol (8 c.c.), and the mixture was heated under reflux during 2 hr. After filtration, evaporation of the filtrate gave an oil which was chromatographed on alumina (activity I). Elution with light petroleum–ether (98 : 2) and (95 : 5) gave the ketone (60 mg.) as an oil, $\nu_{max.}$ (in $CCl_4$) 1723 cm.$^{-1}$ (C=O). The 2,4-*dinitrophenylhydrazone* formed orange prisms (from ethanol), m. p. 169—170° (Found: C, 58·8; H, 7·0; N, 16·0. $C_{17}H_{24}N_4O_4$ requires C, 58·6; H, 6·95; N, 16·1%).

(*b*) 2-Methylene-*trans*-5-t-butylcyclohexanol (100 mg.) was similarly treated with palladium–carbon to give the methyl ketone (25 mg.). Its infrared spectrum was rich in detail and was identical with that of the ketone obtained as under (*a*). The 2,4-dinitrophenylhydrazone had m. p. undepressed on admixture with that prepared above.

*Ozonolysis of 2-Methylene-5-t-butylcyclohexyl 3,5-Dinitrobenzoates.*—Ozonised oxygen was bubbled through a solution of the *cis*-derivative (94 mg.) in methylene dichloride (2 c.c.) containing pyridine (28 mg.) at −75°. After 10 min. reaction was shown to have ceased by the liberation of iodine from acidic potassium iodide solution by the exit gases. The solution was warmed to 25°, washed with water, saturated aqueous cadmium chloride, and dried. Evaporation followed by crystallisation from methanol gave the 2-(3,5-*dinitrobenzoyloxy*)-cis-4-*t-butylcyclohexanone* (64 mg.) as needles, m. p. 165—166° (Found: C, 56·05; H, 5·7; N, 7·5. $C_{17}H_{20}N_2O_7$ requires C, 56·05; H, 5·55; N, 7·7%).

The *trans*-derivative (150 mg.), ozonised in the same way, gave a gum (120 mg.). A portion (50 mg.) was heated in a 0·1N-solution of perchloric acid in aqueous acetone for 40 min. Addition of water followed by isolation with ether gave material (35 mg.) which crystallised on trituration with methanol and after two recrystallisations from methanol had m. p. 163—165° undepressed on admixture with a sample from the previous preparation. The infrared spectra were identical.

*Nuclear Magnetic Resonance.*—Spectra were measured on a Mullard instrument at 32 mcycles/sec. in carbon tetrachloride with tetramethylsilane as internal reference. Peak positions are in cycles/sec. from tetramethylsilane = 0.

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