A Study of the Geometry of a 1-Substituted Cyclohexyl Free Radical

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Cyclic alcohols of known configuration and conformation with bulky groups in either the 3-position, the 4-position, or in both positions have been added to an olefin by a free-radical reaction involving the 1-hydrogen of the alcohol. In every case, it was found that both the *cis* and *trans* configurations formed the same intermediate free radical and thus gave the same ratio of products. The products were formed by an approximate 66:34 ratio of equatorial to axial attack of olefin on a planar, intermediate free radical except in the coprostanols in which the ratio was reversed. It was found that a complete product separation and analysis could be done by thin layer chromatography.

The *chemical* evidence for establishing the geometry of an intermediate free radical has been derived chiefly from three types of reactions. First, an optically active substrate was caused to produce potentially asymmetric free radicals which upon dimerization or reaction with another radical could result in optically active products. An example is the free-radical chlorination of optically active amyl chloride which gave inactive dichloride as the product of interest.[2]

The second type of reaction is an addition of radical fragments to an olefin which could produce a potentially asymmetric intermediate radical. The addition product would be formed by stereospecific *trans* addition providing the intermediate free radical exists in a pyramidal configuration. This is typified by the addition of thiolacetic acid to both *cis*- and *trans*-2-chloro-2-butene which gave the same mixture of thiolesters from both olefins (90% *threo* and 10% *erythro*).[3]

The third type of reaction is a free-radical addition of a potentially asymmetric radical to an olefin. The addition product, as in former cases, would be active or inactive depending upon whether the free radical were pyramidal or planar. This type of reaction is exemplified by the addition of optically active 2-butanol to 1-octene where the product could be optically active, but was found to be inactive.[4] If the addition occurred rapidly in a solvent cage, it is possible that the product would be optically active.

$$\underset{\text{active}}{CH_3CH_2C^*HOHCH_3} \xrightarrow[(R\cdot)]{CH_2{=}CH{-}C_6H_{13}} CH_3CH_2CHOH(CH_3)CH_2CH_2C_6H_{13}$$

inactive

In the present study, a fourth type of reaction was investigated to obtain further evidence for the structure of a free radical. This reaction required neither an optically active starting material nor an olefin of known configuration; moreover, the geometry of the intermediate radical need not be deduced from the optical activity of the products. Instead, a cyclohexyl derivative of known conformation and configuration was used to produce a radical which originally existed in a known conformation. The cyclohexyl derivatives utilized were the 3- and 4-*t*-butylcyclohexyl and steroidal alcohols, since both the configuration and the conformation of their substituents are easily determined. This is because the *t*-butyl group is always equatorial, and both equatorial and axial hydroxyl groups have sufficiently characteristic infrared spectra.[5] Since hydrogen atom abstraction has been shown to occur on the carbon atom bearing the hydroxyl group,[6] the original conformation of the intermediate free radical is known from the conformation of the hydroxyl group.

Therefore, the products from the free-radical addition of the cyclohexyl alcohols to an olefin can be used to decide the geometry of the intermediate radical. For, in the event that the radical were pyramidal, the conformation of the hydroxyl group would be either axial or equatorial. If the radical were planar, then the hydroxyl group should be neither axial nor equatorial. Lastly, the intermediate free radical may preferentially exist in one of the two possible conformations; this preference also can be established from the products.

Results

Evidence to establish the geometry of an intermediate free radical was obtained from the free-radical addition reactions of secondary cyclohexyl alcohols to olefins. Three systems were investigated, the free-radical reaction of 1-octene with 3-*t*-butylcyclohexanol, 4-*t*-butylcyclohexanol, and steroidal alcohols, *viz.*, the 3-cholestanols and the 3-coprostanols. Both conformational isomers of the above alcohols were available and studied. The tertiary alcohols resulting from the addition reactions were isolated in yields expected for these starting materials (*ca.* 30%).[6] In all the reactions, both of the possible isomeric tertiary alcohols were obtained, and their per cents were determined. Table I contains the results from the study of the 3- and 4-*t*-butylcyclohexanols, and Table II contains the results from the study of the steroids.

The authentic tertiary alcohols were prepared from the Grignard addition of octylmagnesium bromide to the appropriate ketones. The assignment of the configuration of the authentic tertiary alcohols was made on the basis of a difference in the infrared absorption spectra of the isomeric alcohols, particularly in the absorption of the hydroxyl group.[5] The product ratios of the isomeric tertiary alcohols were determined and are given in Table III.

(1) (a) IBM Research Laboratory, San Jose 14, Calif. (b) From the Ph.D. thesis of R. J. Albers, June, 1963; previous communication, *J. Org. Chem.*, **27**, 4708 (1962).

(2) M. S. Kharasch, H. C. Brown, and T. H. Chao, *J. Am. Chem. Soc.*, **62**, 3455 (1940); see also, P. S. Skell, D. L. Tuleen, and P. O. Readio, *ibid.*, **85**, 2850 (1963).

(3) F. G. Bordwell and N. P. Neureiter, *ibid.*, **82**, 5354 (1960).

(4) R. J. Gritter, Ph.D. dissertation, University of Chicago, Chicago, Ill., 1955.

(5) A. R. H. Cole, P. R. Jeffries, and G. T. Mueller, *J. Chem. Soc.*, 1212 (1959).

(6) W. H. Urry, F. W. Stacey, E. S. Huyser, and O. O. Juveland, *J. Am. Chem. Soc.*, **76**, 450 (1954).

TABLE I

REACTIONS OF 3- AND 4-*t*-BUTYLCYCLOHEXANOLS

Alcohol (no.), mmole	1-Octene, mmole	*t*-Butyl peroxide, mmole	Time (hr.), temp. (°C.)	Product (mg.), conversion (%)	Axial hydroxyl product, %
cis-3 (I) 0.790	0.080	0.016	1.0, 150	1.0, 5	68
cis-3 (II) 0.640	0.064	0.054	16.0, 135	4.6, 27	60
cis-3 (III) 0.640	0.064	0.054	1.0, 150	6.6, 39	65
cis-3 (IV) 0.640	0.064	0.054	48, *a*	5.0, 29	64
cis-3 (V) 1.750	0.175	0.059	48, *a*	4.4, 9	62
trans-3 (I) 0.640	0.064	0.054	1.0, 150	2.7, 16	67
trans-3 (II) 1.870	0.187	0.065	48, *a*	5.0, 10	64
trans-3 (III) 0.640	0.064	0.054	48, *a*	7.1, 41	68
trans-4 (I) 0.690	0.069	0.028	2,0 135	5.8, 31	61
trans-4 (II) 0.640	0.064	0.054	1.0, 150	8.6, 50	58
trans-4 (III) 0.650	0.064	0.054	48, *a*	3.4, 20	61
trans-4 (IV) 0.640	0.064	0.054	48, *a*	1.3, 8	59
trans-4 (V) 1.600	0.160	0.067	48, *a*	2.5, 6	57
cis-4 (I) 0.640	0.064	0.054	1.0, 150	6.5, 39	60
cis-4 (II) 0.640	0.064	0.054	16, 135	7.3, 43	57
cis-4 (III) 0.640	0.064	0.054	1.0, 150	5.7, 33	59
cis-4 (IV) 0.650	0.065	0.027	48, *a*	3.5, 20	59
cis-4 (V) 0.650	0.065	0.054	48, *a*	5.9, 34	64
cis-4 (VI) 0.650	0.064	0.054	48, *a*	3.4, 20	63

[a] Ultraviolet.

In most reactions, the products were separated and identified by thin layer chromatography. Authentic compounds and products were shown to have identical retentions (R_f) and to give the same positive color tests on thin layer chromatoplates. The isolations of the products were, in many cases, done by thin layer chromatography. For this end, a new technique was developed for detecting products on a thin layer plate without partial destruction of the compound.[7] Relative amounts of products were established by measuring areas and correlating these with standards. The accuracy of this method is within 5%.

Discussion

This study has contributed evidence for the postulate that an intermediate free radical is planar. In all the systems studied, both of the possible 1-octene addition products were formed, and the *cis* products (like **2**) predominated. In addition, both isomeric secondary alcohols gave the same mixture of isomeric products, both at room temperature and at 150°. These

(7) R. J. Gritter and R. J. Albers, *J. Chromatog.*, **9**, 392 (1962).

TABLE II

REACTIONS OF STEROIDS

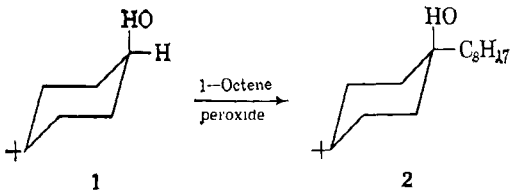
Steroid (mmole)	1-Octene, mmole	*t*-Butyl peroxide, mmole	Time (hr.), temp. (°C.)	Product (mg.), conversion (%)	3-Hydroxy isomer (%)
β-Cholestanol (1.280)	0.051	0.270	16, 135	2.7, 10	α (63)
β-Cholestanol (1.280)	0.102	0.195	16, 135	7.0, 14	α (65)
α-Cholestanol (1.280)	0.102	0.195	16, 135	22.1, 43	α (57)
Epicoprostanol (1.280)	0.102	0.195	16, 135	11.1, 22	α (56)
Epicoprostanol (1.280)	0.102	0.195	16, 135	12.0, 24	β (62)
Epicoprostanol (0.256)	0.020	0.054	1.0, 150	3.2, 32	β (64)
Coprostanol (0.256)	0.020	0.054	1.0, 150	3.7, 37	β (64)

TABLE III

GRIGNARD REACTION OF KETONES WITH OCTYLMAGNESIUM BROMIDE

Ketone	Isomer (%)	Isomer (%)
3-*t*-Butylcyclohexanone	*trans* (68)	*cis* (32)
4-*t*-Butylcyclohexanone	*cis* (63)	*trans* (37)
3-Cholestanone	α (65)	β (35)
3-Coprostanone	β (65)	α (35)

experimental facts are adequately explained by the formation of a planar cyclohexyl radical, which agrees with the e.s.r. evidence of Fessenden.[8]



1 2

Nonetheless, the preponderance of axial hydroxyl product (in the coprostanols, the β isomer is the axial hydroxyl) may suggest that the intermediate free radical preferentially exists in the equatorial conformation. To test this hypothesis a study of the Grignard addition reaction was made.

The compositions of the products from the addition of octylmagnesium bromide to the corresponding ketones show that an attachment on the *planar* carbonyl carbon produces substantially the same isomeric products in the same ratio as from the free-radical addition reactions. The results are compared in Table IV. Emphatically, one can conclude that the geometry of the intermediate free radical is the same as the geometry of the carbonyl carbon, namely, planar. Thus, the preponderance of axial hydroxyl product from both reactions arises from the steric restriction to axial attack by the olefin or octylmagnesium bromide. This is readily seen on examination of Dreiding models.

In no case did the per cent difference between the products from the Grignard and the radical addition reactions exceed 3%. Moreover, the per cent of equatorial product from the Grignard reaction was always

(8) R. W. Fessenden, *Quart. Rep. Mellon Inst.*, April–June, 1961, mentioned by M. C. R. Symons, *Nature*, **198**, 1196 (1963).

TABLE IV

COMPARISON OF GRIGNARD AND FREE-RADICAL REACTIONS[a]

Reaction	3-*cis*	3-*trans*	4-*trans*	4-*cis*	Epicoprostanol	Coprostanol	β-Cholestanol	α-Cholestanol
Free radical, heat	65	67	60	59	36	36	64	57
Free radical, ultraviolet	64	66	60	62				
Grignard	68	68	63	63	35	35	65	65

[a] % Axial hydroxyl product, average values.

greater. One cannot conclude from this small but definite difference that the free radical has a conformational preference, because this can be explained easily by the difference of the reactions.

The conclusion from this work can be compared to the work of Eliel and Acharya[9] who studied the Hunsdiecker reaction with *cis*- and *trans*-4-*t*-butylcyclohexanecarboxylic acid. The 4-*t*-butylcyclohexyl radical from both the *cis* and *trans* acid gave the same mixture of products; in this mixture the *trans* bromide predominated. The equilibrated per cent of *trans* bromide was determined to be 77[10] while the free-radical reaction gave 65%. However, Greene and coworkers[11] have reported in a recent communication that, although the 4-*t*-butylcyclohexyl radical produced from both the *cis* and *trans* isomers of dimethyl(4-*t*-butylcyclohexyl)carbinyl hypochlorite gives the same mixture of products, the *cis* product predominated (66%). Hart and Lau[12] found that the decomposition of the diacyl peroxides of the *cis*- and *trans*-4-*t*-butylcyclohexanecarboxylic acids in 1,1,2,2-tetrabromoethane gave as minor products the *cis*- and *trans*-4-*t*-butylcyclohexyl bromides in nearly the same ratio from either starting material. Although the *trans* product was predominant, it was formed in significantly lower amount than the equilibrium value. It is evident that further work is necessary to clarify the varied results mentioned above, for the systems seem to react in different ways.

Experimental

Preparation of *cis*- and *trans*-3-*t*-Butylcyclohexanol.—3-*t*-Butylcyclohexanone was prepared by the 1,4-addition of *t*-butylmagnesium chloride to 2-cyclohexenone according to the procedure of Whitmore and Pedlow,[13] modified in the following manner: the ketone was isolated as its sodium bisulfite addition product which on decomposition by base gave 3-*t*-butylcyclohexanone (62.5 g. of 2-cyclohexanone gave 35.0 g. of product, 35 yield).

A portion (0.074 mole, 11.5 g.) of the ketone dissolved in 200 ml. of absolute alcohol was reduced quantitatively with hydrogen using 5.0 g. of W-5 Raney nickel as catalyst. The isomeric 3-*t*-butylcyclohexanols (1.5 g.) were chromatographed over 150 g. of acidic, activity grade II alumina, using 10% benzene in pentane as developer. Pure *trans*-3-*t*-butylcyclohexanol (m.p. 63–64°; acid phthalate m.p. 154–155°, lit.[14] m.p. 154.5–155.5°) was eluted first, then the *cis* isomer (acid phthalate m.p. 136–137, lit.[14] m.p. 136–137).

Preparation of *cis*- and *trans*-4-*t*-Butylcyclohexanol.—Into a solution of 0.123 mole of sodium dichromate (78.0 g.), 50 ml. of water, 90 ml. of concentrated sulfuric acid, and 300 ml. of water at ice bath temperature was added dropwise during a period of 0.5 hr. a solution of 0.127 mole of 4-*t*-butylcyclohexanol (20.0 g.) in 100 ml. of benzene. The reaction mixture was stirred until no alcohol could be detected by thin layer chromatography. The benzene layer was separated and washed with 20 ml. of a 5% bicarbonate solution and two portions of a saturated salt solution. The benzene layer was flash evaporated, and the resulting ketone was crystallized from pentane; 12.6 g. (76% yield) of pure ketone and 4.2 g. of crude ketone, recovered from the mother liquors, were obtained (m.p. 49–50° lit.[14] m.p. 49–50°). The mixture of isomeric alcohols was prepared by the quantitative reduction of 4-*t*-butylcyclohexanone (0.013 mole, 2.0 g.) in 50 ml. of acetic acid with hydrogen using platinum oxide as catalyst. The reaction mixture was diluted with 100 ml. of water, neutralized with sodium carbonate, and extracted with pentane. The alcohols were chromatographed over 200 g. of acidic, activity grade II alumina; a pentane–15% benzene solution was used as developer. The *cis* alcohol was eluted first, then the *trans* (*cis* m.p. 74.5–75.5°, lit.[14] m.p. 72–75°; *trans* m.p. 79–80°, lit.[14] m.p. 81–82°).

Preparation of β-Cholestanol.—β-Cholestanol was prepared from the reduction of cholesterol in 56% yield according to the procedure of Bruce[15] (m.p. 141–142°, lit.[15] m.p. 141–142°).

Preparation of α-Cholestanol.—Cholestanone was prepared from the bichromate oxidation of β-cholestanol in 65% yield according to procedure of Bruce[16] (m.p. 128–130°, lit.[16] m.p. 129–130°). Cholestanone (0.013 mole, 5.00 g.) was dissolved in 100 ml. of acetic acid and reduced quantitatively using 0.1 g. of platinum oxide as catalyst. The catalyst was removed by filtration, and the solvent was flash distilled. The product was hydrolyzed by a 5% solution of sodium hydroxide in 95% alcohol at reflux temperature. On cooling, the product containing a mixture of α- and β-cholestanol crystallized. The dried product was chromatographed over 150 g. of acidic, activity grade II alumina. The first fraction contained 4.1 g. of α-cholestanol (m.p. 179–180°, lit.[17] m.p. 180–181°). The second fraction contained 0.1 g. of β-cholestanol.

Preparation of Epicoprostanol.—Cholestenone was prepared in 81% yield by the Oppenauer oxidation of cholesterol according to the procedure of Oppenauer[18] (m.p. 79–80, lit.[18] m.p. 79–80). Epicoprostanol was made from the quantitative reduction of cholestenone according to a modified procedure of Ruzicka.[17] The products obtained as shown by thin layer chromatography were α- and β-cholestanol and epicoprostanol. The mixture was chromatographed over 100 g. of acidic, activity grade III alumina using pentane–15% benzene as developer. The second eluent was epicoprostanol (0.7 g., 70% yield; m.p. 112–113°, lit.[17] m.p. 110–111°).

Preparation of Coprostanol.—Coprostanone was prepared from the reduction of cholestenone according to the procedure described by Ruzicka[17] (m.p. 57–58°, lit.[17] m.p. 61–62°). Coprostanol was prepared from the reduction of coprostanone in glacial acetic acid according to the procedure of Ruzicka[17] (m.p. 95–100°, lit.[17] m.p. 101–102°). Although thin layer chromatography indicated only one product, the melting point indicated the product to be impure. Repeated recrystallization failed to give a better melting point.

Preparation of *cis*- and *trans*-1-Octyl-3-*t*-butylcyclohexanol.—Into a Morton flask, equipped with condenser and drying tube, dropping funnel, and stirring bar, was placed 0.052 g.-atom of magnesium (1.27 g.). Enough anhydrous ether was added to cover the magnesium, and 0.053 mole (9.0 ml.) of 1-bromooctane,

(9) E. L. Eliel and R. V. Acharya, *J. Org. Chem.*, **24**, 151 (1959).
(10) P. Klaeboe, J. L. Lothe, and K. Lunde, *Acta Chem. Scand.*, **10**, 1465 (1956).
(11) F. D. Greene, C. C. Chu, and J. Walia, *J. Am. Chem. Soc.*, **84**, 2463 (1962).
(12) H. Hart and H. H. Lau, *ibid.*, **81**, 4897 (1959).
(13) F. C. Whitmore and G. W. Pedlow, *ibid.*, **63**, 758 (1941).
(14) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).
(15) W. F. Bruce and J. O. Ralls, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 139.
(16) W. F. Bruce, *ibid.*, p. 191.
(17) L. Ruzicka and J. Meyer, *Helv. Chim. Acta*, **17**, 1407 (1934).
(18) R. V. Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

dissolved in 50 ml. of anhydrous ether, was added during a period of 2 hr. The reaction mixture was allowed to stir for 1 hr. after which 0.013 mole (2.00 g.) of 3-*t*-butylcyclohexanone (see above), dissolved in 75 ml. of anhydrous ether, was added during a period of 0.5 hr. and allowed to stir another 4.0 hr. The Grignard adduct was cooled to ice-bath temperature and decomposed by 55.0 ml. of 10% sulfuric acid. The ether layer was separated and washed twice with 25 ml. of 5% sodium bicarbonate and twice with 25 ml. of water. Flash evaporation of the solvent left 3.2 g. of a mixture of four products: *cis*- and *trans*-1-octyl-3-*t*-butylcyclohexanol (3.0 g., 85% yield) and *cis*- and *trans*-3-butylcyclohexanol (0.2 g., 10% yield). The ratio of the tertiary alcohols was 68:32 *cis* to *trans*. A portion of the reaction mixture (0.100 g.) was spotted on a 20 × 20 cm. thin layer chromatoplate, developed by benzene, and separated into its components, affording pure *cis*- and *trans*-1-octyl-3-*t*-butylcyclohexanol. The conformation of the products was established by infrared analysis on the basis that the axial hydroxyl absorbs at 2.9 μ and the equatorial hydroxyl at 3.0 μ.[5]

Anal. Calcd. for $C_{18}H_{36}O$: C, 80.52; H, 13.52. Found: C, 79.46; H, 12.94.

Preparation of *cis*- and *trans*-1-Octyl-4-*t*-butylcyclohexanol.—Authentic *cis*- and *trans*-1-octyl-4-butylcyclohexanol was prepared from the reaction of octylmagnesium bromide with 4-*t*-butylcyclohexanone using the same method which was used for the synthesis of the *cis*- and *trans*-1-octyl-3-*t*-butylcyclohexanol. The mixture of isomeric tertiary alcohols was obtained in 73% yield. Determination of conformation was made on the same basis as that used for the 1-octyl-3-*t*-butylcyclohexanols. The ratio of *trans* to *cis* was 63:37 (*trans* m.p. 81.5–82.0°, *cis* m.p. 61.1–62.5°).

Anal. Calcd. for $C_{18}H_{36}O$: C, 80.52; H, 13.52. Found: C, 80.70; H, 13.49.

Preparation of α- and β-3-Octylcholestan-3-ol.—Into a Morton flask, equipped with condenser and drying tube, dropping funnel, and stirring bar, was placed 0.054 g.-atom of magnesium (1.32 g.) and 10 ml. of anhydrous ether. To this was added during a period of 1.0 hr., 0.052 mole of 1-bromooctane (9.1 ml.) dissolved in 75 ml. of anhydrous ether. The solution was stirred 1.0 hr. and, subsequently, 0.018 mole of cholestanone (6.98 g.) in 50 ml. of anhydrous ether was added. The reaction mixture was refluxed overnight, after which the addition product was decomposed with 56 ml. of 5% sulfuric acid. The ether layer was separated and washed three times with 25 ml. of water. Thin layer chromatography showed four products: two tertiary alcohols, α- and β-3-octylcholstan-3-ol in a ratio of 65:35, and α- and β-cholestanol.

Anal. Calcd. for $C_{35}H_{64}O$: C, 83.92; H, 12.88. Found: C, 83.71; H, 12.76.

Preparation of α- and β-Octylcoprostan-3-ol.—The 3-octylcoprostan-3-ols were prepared from the reaction of octylmagnesium bromide with coprostanone under the same conditions that were used to prepare the 3-octylcholestan-3-ols. Thin layer chromatography showed that three products had formed, *viz.*, α- and β-3-octylcoprostan-3-ol and epicoprostanol. The ratio of β to α was determined to be 65:35.

Anal. Calcd. for $C_{35}H_{64}O$: C, 83.92; H, 12.88. Found: C, 84.06; H, 12.97.

Free-Radical Reactions of 3- and 4-*t*-Butylcyclohexanols.—The experimental procedures for the free-radical reactions of *cis*- and *trans*-3- and 4-*t*-butylcyclohexanols were essentially the same in all cases; Table I should be referred to for particular differences. Two representative reactions are given below.

***cis*-4-*t*-Butylcyclohexanol.**—Into a 5-mm. glass tube was placed 0.64 mmole of *cis*-4-*t*-butylcyclohexanol (100.0 mg.), 0.064 mmole of 1-octene (10.0 μl.), and 0.054 mmole of *t*-butyl peroxide (10.0 μl.). The tube was deaerated, sealed, and placed in a 150° constant temperature bath for 1.0 hr. The contents were placed on a 20 × 20 cm. thin layer chromatoplate and developed in benzene–25% chloroform solution. Two products were isolated, *cis*- and *trans*-1-octyl-4-*t*-butylcyclohexanol (6.5 mg., 39% yield based on 1-octene). A small portion of the mixture of the products was spotted on another chromatoplate to determine the ratio of the products from their areas (see below). The ratio of *cis* to *trans* was found to be 60:40.

***cis*-3-*t*-Butylcyclohexanol.**—A 5-mm. quartz tube was charged with 0.064 mmole of *cis*-3-*t*-butylcyclohexanol (0.100 g.), 0.064 mmole of 1-octene (10.0 μl.), and 0.054 mmole of *t*-butyl peroxide (10.0 μl.). The tube was deaerated, sealed, and irradiated for 48 hr. by a Hanovia ultraviolet light source (the half-life of the peroxide under these conditions was calculated to be 24 hr.). The products were separated from the starting material by thin layer chromatography as above. The isolated 1-octyl-3-*t*-butylcyclohexanols amounted to 5.0 mg. (29% yield based on 1-octene), and the ratio of *trans* to *cis* tertiary alcohols calculated from their areas was 64:36.

Free-Radical Reaction of Steroidal Alcohols. Coprostanol (Representative Run).—Into a 5-mm. glass tube were placed 0.256 mmole of coprostanol (0.100 g.), 0.020 mmole of 1-octene (3.0 μl.), and 0.054 mmole of *t*-butyl peroxide (10.0 μl.). The tube was deaerated, sealed, and heated at 150° for 1.0 hr. in a constant temperature oil bath. The contents were spotted on a 20 × 20 cm. chromatoplate and developed by a benzene–25% chloroform solution. The products obtained were coprostanone (2.5 mg.) and β- and α-3-octylcoprostan-3-ol (3.7 mg., 39% yield). The mixture of products was spotted on a chromatoplate, developed in the solvent system used above, and, from the areas, the ratio of tertiary alcohols was determined to be 64:36 β to α.

Thin Layer Chromatography Technique.[7]—Products were both identified and isolated by thin layer chromatography. Up to 100 mg. of compound was spotted on a 20 × 20 cm. thin layer plate and developed with an appropriate solvent. The zones of silica gel which contained the products were made visible by spraying with water until saturation occurred. The zones were marked and, after the plate was dried, were removed mechanically. The products were then eluted from the silica gel by reagent grade ether.

The procedure followed to identify products by thin layer chromatography was to compare R_f values of authentic compounds and unknowns when spotted on the same starting point and develop by three different solvents to determine whether a resolution could be obtained. If the R_f values of authentic were the same and if no separation could be obtained, the identification was positive.

Thin layer chromatography also has been shown to be a useful tool for quantitative determinations. In this work it was used for determining the relative amounts of isomeric tertiary alcohols, products from both Grignard and free-radical addition reactions. The mixture of alcohols together with a standard mixture was applied to a chromatoplate, developed by a suitable solvent, and made visible by concentrated sulfuric acid or aluminum chloride in chloroform. The areas were measured directly or by tracing on paper and were corrected by means of the standard mixture which allowed for slight variations from plate to plate. The standard deviation of this method of analysis is within ±2.5%.

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