the addition of *p*-anisonitrile (6.65 g., 0.05 mole), instead of *p*-toluonitrile. The **α-phenyl-4-methoxybenzoin ketimine hydrochloride** (10 g.), precipitated in the indicated work-up, was recrystallized from ethanol–ether–chloroform and melted at 205–210° dec.

Anal. Calcd. for $C_{21}H_{20}ClNO_2$: C, 71.28; H, 5.70; Cl, 10.02; N, 3.96. Found: C, 70.75; H, 5.81; Cl, 9.51; N, 3.62.

To 5.0 g. of the precipitated hydrochloride was added 50 ml. of 18% hydrochloric acid and the resulting solution was refluxed for 6 hr. Upon cooling the aqueous acid was decanted from a crystalline mass which had formed. This solid was ground in a mortar and pestle, washed with water, and dried. The yield was 4.1 g. of product, m.p. 58–63°, which could not be crystallized from a variety of solvents, although the oil which separated from mixed solvents containing water would always eventually crystallize upon standing. Elemental analysis indicated that the material obtained this way is a hydrate of **α-phenyl-4-methoxybenzoin**.

Anal. Calcd. for $C_{21}H_{18}O_3 \cdot H_2O$: C, 74.98; H, 5.99. Found: C, 74.02; H, 5.99.

Preparation of the known **α-phenylbenzoin** and its ketimine were accomplished in an exactly analogous manner from benzophenone and benzonitrile. Attempts to prepare **α-anisyl-4-methoxybenzoin** in an analogous manner from *p*-methoxybenzophenone and anisonitrile were not successful.

Reductions with Metal Hydrides. XVIII. Reductions of Ketones with Lithium Aluminum Hydride–Aluminum Chloride and Hydride Transfer from the Resulting Alcohol Complexes[1]

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This paper is concerned with two types of reduction: (1) application of the previously described "mixed hydride" (probably $HAlCl_2$) reduction under conditions of kinetic and thermodynamic control to camphor and norcamphor (bicyclo[2.2.1]heptan-2-one), and (2) reductions with alkoxyaluminum dichlorides, $RR'CHOAlCl_2$, by hydride transfer. (1) In the mixed hydride reduction, under kinetic control, norcamphor gives 95–96% of the less stable *endo*-norborneol (rest *exo*) and camphor gives 66–71% of the less stable isoborneol (rest 10–11% borneol and 2–8% camphene), hydride approaching from the less hindered side in both cases. Equilibration of norborneols with excess ketone leads to 89–90% of the more stable *exo* isomer (rest *endo*), but fails in the case of isoborneol where dehydration to camphene occurs instead. An improved method of mixed hydride equilibration is described. (2) The alkoxyaluminum dichlorides formed from ketone (or alcohol) and mixed hydride in turn function as reducing agents. In $RR'CHOAlCl_2$ reduction, an I-strain series is observed in that the isobornyloxy derivative is a better reducing agent than cyclopentyloxy which, in turn, is better than cyclohexyloxyaluminum dichloride. Conversely, 4-*t*-butylcyclohexanone was reduced more readily than cyclopentanone or norcamphor; camphor was least readily reduced by alkoxyaluminum dichlorides. Isobornyloxyaluminum dichloride is a fairly stereoselective reducing agent in that it produces largely axial alcohols in the reduction of cyclohexanones. The reaction is synthetically useful for the stereoselective reduction of higher ketones, such as 3-cholestanone (whose reduction products can be readily freed of residual isoborneol).

Reductions and Equilibrations with Mixed Hydride.—In a previous publication[1] we have described the reduction of various cyclohexanones with lithium aluminum hydride–aluminum chloride ("mixed hydride", probably[2b,c] effectively $AlHCl_2$). Under conditions of kinetic control, mixtures are produced which are ordinarily richer in the less stable (axial) alcohol than those obtained with $LiAlH_4$ alone. Under conditions of thermodynamic control, *i.e.*, in the presence of a small excess of ketone (which provokes a reversible hydride transfer), the more stable (equatorial) alcohol results almost to the exclusion of its epimer.

We have now applied the reaction to camphor and norcamphor. Our results and those of the earlier work[2a] are summarized in Table I which, for the sake of comparison, also contains results of reduction with lithium aluminum hydride alone and of equilibration with aluminum alkoxide (Meerwein–Ponndorf–Oppenauer), the latter at slightly higher temperatures.

TABLE I

Ketone reduced	Stable alcohol	% equatorial or stable alcohol in product obtained by			
			$LiAlH_4$–$AlCl_3$		
		$LiAlH_4$	Kinetic	Thermo-dynamic	M–P–O[a]
4-*t*-Butylcyclohexanone	*trans*	89[b]	80[b]	99.5[b]	79[c]
4-Methylcyclohexanone	*trans*	81[c]	77[b]	92[b]	70[c]
4-Phenylcyclohexanone	*trans*	91[b]	86[b]	99[b]	79[b]
3-Cholestanone	β	91[d]	83[d]	100[d]	84[e]
3,3,5-Trimethylcyclohexanone	*cis*	45[f]	15[f]	100[f]	94[g]
Norcamphor	*exo*	9[h,i]	4[j]	89[j]	80[h]
Camphor	Borneol (*endo*)	10[k]	27[j]	l	71[h]

[a] Meerwein–Ponndorf–Oppenauer equilibration with aluminum isopropoxide–isopropyl alcohol–acetone. [b] Reference 2a. [c] E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957). [d] Reference 3. [e] H. R. Nace and G. L. O'Connor, *J. Am. Chem. Soc.*, **73**, 5824 (1951). [f] Reference 4. [g] E. L. Eliel and H. Haubenstock, *J. Org. Chem.*, **26**, 3504 (1961). [h] C. F. Wilcox, M. Sexton, and M. F. Wilcox, *ibid.*, **28**, 1079 (1963). [i] R. Howe, E. C. Friedrich, and S. Winstein, *J. Am. Chem. Soc.*, **87**, 379 (1965). [j] This work. [k] D. S. Noyce and D. B. Denney, *J. Am. Chem. Soc.*, **72**, 5743 (1950). [l] Equilibration does not occur; isoborneol is destroyed and forms camphene.

The reduction of norcamphor proceeds normally. As in the instances earlier described[2a,3,4] mixed hydride gives less of the stable (*exo*) isomer under conditions of kinetic control than does $LiAlH_4$ (Chart I). Apparently steric hindrance to approach from the *endo* side (to give *exo* alcohol) is more severe for mixed hydride than for $LiAlH_4$. Equilibration of the nor-

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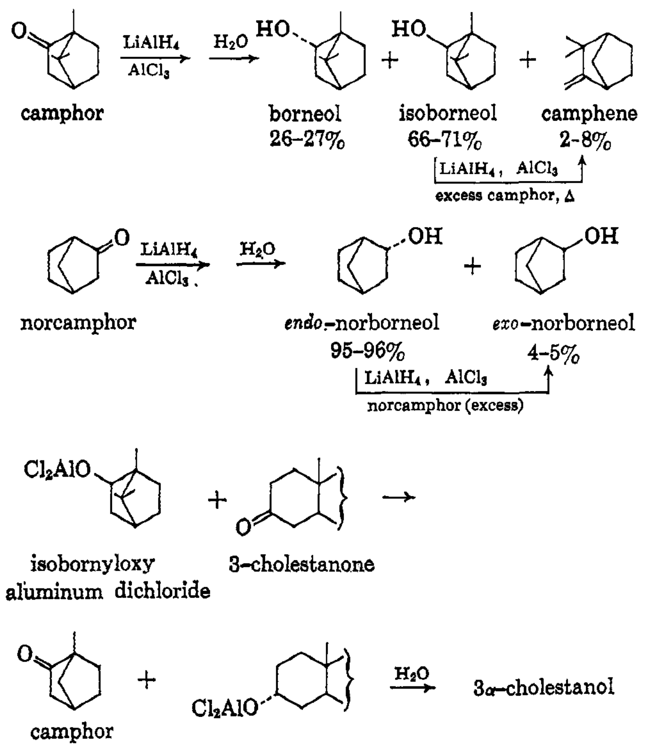
(1) Paper XVII: E. L. Eliel and J. Roy, *J. Org. Chem.*, **30**, 3092 (1965).

(2) (a) E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960); (b) E. L. Eliel, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **22**, 129 (1961); (c) see also E. L. Eliel and T. J. Brett, *J. Org. Chem.*, **28**, 1923 (1963).

(3) J.-C. Richer and E. L. Eliel, *ibid.*, **26**, 972 (1961).

(4) E. L. Eliel and H. Haubenstock, *ibid.*, **26**, 3504 (1961).

CHART I



borneol complexes gives the stable (*exo*) isomer in higher proportion than the Meerwein–Ponndorf–Oppenauer equilibration, also in accordance with earlier observations in other systems.[2a,3,4] The reduction of camphor, however, is atypical. In this case mixed hydride gives *more* of the stable *endo* isomer (borneol) than $LiAlH_4$ alone.[5] This has been previously ascribed[2b] to a nonclassical carbonium ion derived from the ketone which blocks approach from the *endo* side. Unfortunately, however, no definite evidence for such an ion has come forth and it remains in the realm of speculation. Equilibration of the mixed hydride complex derived from isoborneol failed[6]; in the presence of a small amount of either camphor or acetone (or even *t*-butyl alcohol), the isoborneol complex was quickly destroyed by conversion to camphene and only the borneol complex remained. Large amounts of camphor seemed to stabilize the isoborneol complex but did not promote its conversion to borneol. The experiments described below suggest that hydride transfer from an isobornyloxy complex to camphor does not take place at a reasonable rate and therefore equilibration cannot occur.

In the course of this phase of the investigation we have been able to effect an improvement in the equilibration method which is described in the experimental part as applied to the synthesis of *trans*-4-*t*-butylcyclohexanol.[2a] The preparation of this compound by mixed hydride equilibration requires an excess of ketone (4-*t*-butylcyclohexanone). Since, however, a *large* excess of ketone is not desired (because it interferes with the purification of the *trans* alcohol), careful control of the amount of ketone and hydride was necessary which, in turn, required the use of standardized hydride solutions. We have now found that a liberal excess of hydride (not necessarily standardized) may be used; the excess hydride is then destroyed by means of an excess of *t*-butyl alcohol (which does not interfere in the equilibration) and equilibration is finally effected by adding a *small* amount of 4-*t*-butylcyclohexanone.

Reduction with Mixed Hydride Complexes.—The equilibration of epimeric alcohols through complexes with "mixed hydride" involves, in its essential step, a hydride transfer (eq. 1). An analogous hydride transfer, but involving a ketone different from that corresponding to the alcohol, would lead to an equilibrium of the type shown in eq. 2. Equilibria of this kind, but involving the free alcohols, have been previously investigated.[7] It was hoped that in the present approach equilibrium would be reached rapidly (as it was in the epimerizations described in eq. 1) and that, perhaps, the position of equilibrium would be influenced in a significant way by use of the $ROAlCl_2$ complex instead of the free alcohol, ROH.

$$RR'CHOAlCl_2 + RR'CO \rightleftharpoons RR'CO + epi\text{-}RR'CHOAlCl_2 \quad (1)$$

$$R_1R_2CHOAlCl_2 + R_3R_4CO \rightleftharpoons R_1R_2CO + R_3R_4CHOAlCl_2 \quad (2)$$

In this event, it turned out that the equilibrium described in eq. 2 could, in general, not be reached because of the marked tendency of some of the ketones involved, especially acetone and cyclopentanone, to enter into condensation reactions.[8] The experiments reported in the sequel are therefore of a semiquantitative rather than a quantitative nature; they do, nevertheless, give a rough indication of the position of the equilibria involved in eq. 2. Obviously, if $R_1R_2CHOAlCl_2$ is a good reducing agent and R_3R_4CO is a good oxidizing agent, the reaction described by eq. 2 will generally proceed well from left to right but not from right to left. Contrariwise, if the reaction (2) proceeds well from right to left but not from left to right, it can be taken as an indication that $R_3R_4CHOAlCl_2$ is a good reducing agent and R_1R_2CO a good oxidizing agent.

A number of combinations were investigated with the results shown in Table II. The results indicate that cyclohexanones are more readily reduced than cyclopentanone (entries 1 *vs.* 2, 15 *vs.* 14) which is similar in reactivity to norcamphor (entries 2 *vs.* 3, 6 *vs.* 7, 14 *vs.* 16; also 10 *vs.* 11); camphor is hardly reduced at all. (This, along with the tendency of isoborneol to be converted to camphene under the conditions of the reaction, explains why isoborneol cannot be equilibrated to borneol by means of camphor; the reduction of the camphor is simply too slow.) In a mixture of cyclopentanone and 4-*t*-butylcyclohexanone (see Experimental Section), the latter is reduced preferentially, as might have been predicted. Table II

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(5) In camphor, unlike in norcamphor, the *exo* side is less accessible and the corresponding *exo* alcohol less stable because of the overhanging *gem*-dimethyl group: *cf.* E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 304.

(6) Indications to the contrary in ref. 2b were found to be in error.

(7) H. Adkins, R. M. Elofson, A. G. Rossow, and C. C. Robinson, *J. Am. Chem. Soc.*, **71**, 3622 (1949); see also B. J. Yager and C. K. Hancock, *J. Org. Chem.*, **30**, 1174 (1965).

(8) This finding suggests that epimerizations of the type expressed in eq. 1 may also fail when the ketone moiety involved is readily condensed, *e.g.*, in the case of substituted cyclopentanols or diastereoisomeric acyclic carbinols. We have, however, achieved equilibration in at least one case of the latter type, *viz.*, 3-phenyl-2-butanol: B. P. Thill, Ph.D. Dissertation, University of Notre Dame, 1963.

TABLE II

REDUCTION OF KETONES BY HYDRIDE TRANSFER FROM ALKOXYALUMINUM DICHLORIDES

Alcohol	Entry no.	Ketone	Time, hr.	Mole ratio, alcohol–ketone	% reduction or oxidation[a]
Isopropyl alcohol	1	4-*t*-Butylcyclohexanone	2	2:1	92 (R)
	2	Cyclopentanone	2	2:1	44 (R)
	3	Norcamphor	0.5	4:3	22 (R)
	4	Camphor	2	2:1	2 (R)[b]
4-*t*-Butylcyclohexanol	5	Acetone	2	1:2	5–22 (O)
Cyclohexanol	6	Cyclopentanone	0.25	1:1	~5 (R)[c]
	7	Norcamphor	0.5	4:3	8 (R)
	8	Camphor	3	3:1	<1 (R, O)
Cyclopentanol	9	Acetone	2	1:2	~3 (O)[d]
	10	Cyclohexanone	2	2:1	>95 (R)
	11	Norcamphor	0.5	4:3	21 (R)
	12	Camphor	3	3:1	~0 (R)[e]
Isoborneol	13	Acetone	0.5	1:2	~100 (O)[f]
	14	Cyclopentanone	0.25	1:2	Incomplete (O)[g]
			0.25	1:3	Complete (O)[h]
	15	Cyclohexanone	0.25	1:2	~100 (O)[i]
	16	Norcamphor	0.5	4:3	~100 (R)

[a] (R) means that extent of reduction was measured [alcohol/(alcohol + ketone) in reduction product]. (O) means that extent of oxidation was measured [ketone/(ketone + alcohol) in oxidation product]. [b] Also 4% camphene was formed; this may indicate additional reduction to isoborneol followed by dehydration. [c] Also higher boiling condensation products. Gas chromatography (internal standard) indicated 55% cyclopentanol plus cyclopentanone recovered. [d] Also higher boiling condensation products; cyclopentanol plus cyclopentanone recovery 70%. [e] 3–4% camphene formed. [f] 3–12% camphene formed. [g] 53–60% camphene. [h] 15–20% camphene. [i] Almost no camphene.

also shows that isobornyloxyaluminum dichloride[9] is a good reducing agent, cyclohexyloxyaluminum dichloride is poor, and cyclopentyloxyaluminum dichloride and isopropoxyaluminum dichloride are intermediate and similar to each other in reducing power. The results thus generally follow an I-strain[10] series: the cyclohexanone to cyclohexanol reduction is easier than cyclopentanone to cyclopentanol or norcamphor to norborneol. (A precise comparison of norcamphor with cyclopentanone was not possible because of the much greater tendency of cyclopentanone to undergo condensation reactions in competition with reduction.) The camphor to borneol–isoborneol reduction is even less facile, presumably owing to the steric effect of either the adjacent 1-methyl substituent or the overhanging *gem*-dimethyl groups. The observed similarity of acetone and cyclopentanone has its parallel in other systems.[10b]

The proportions of the epimeric alcohols obtained from 4-*t*-butylcyclohexanone and norcamphor[11] in the reduction with various alkoxyaluminum dichlorides are of interest. 4-*t*-Butylcyclohexanone gives 93% *trans* (stable) alcohol when reduced with the 2-propanol derivative. In view of the bulkiness of the reducing agent, it is unlikely that the *trans* product results from kinetically-controlled reduction; rather it appears that equilibration has occurred during the reduction, but not the same extent as in the treatment of the 4-*t*-butylcyclohexyloxyaluminum dichloride with 4-*t*-butylcyclohexanone described earlier in which over 99% *trans* isomer is formed in 2 hr.[2a] Presumably the presence of a reducing agent other than 4-*t*-butylcyclohexanol retards the equilibration process by slowing reoxidation of any *cis* alcohol formed initially. Similar observations were made with norcamphor which yields 76% *endo*-norborneol (unstable isomer) with isopropoxyaluminum dichloride, 83% *endo* isomer with cyclohexyloxyaluminum dichloride, and 91% *endo* isomer with cyclopentyloxyaluminum dichloride. This compares with 95–96% *endo* isomer in kinetically controlled reduction with mixed hydride and 10–11% *endo* isomer in thermodynamically controlled equilibration with mixed hydride–norcamphor. Here, clearly, the product of alkoxyaluminum dichloride reduction is far from equilibrated.

Since camphor is not readily reduced by alkoxyaluminum dichlorides, it cannot oxidize these derivatives readily and therefore would not be expected to promote appreciable equilibration. In accordance with this expectation, reduction of 4-*t*-butylcyclohexanone with isobornyloxyaluminum dichloride gave very largely the less stable *cis*-4-*t*-butylcyclohexanol (80–92%) and reduction of norcamphor with the same reagent gave nearly exclusively the less stable isomer, *endo*-norborneol (over 97%). These reductions are of interest because, in general, it is not easy to obtain the less stable alcohol by reduction of the corresponding ketones. A number of other reductions were therefore carried out with the results shown in Table III. In all cases the less stable alcohol was the principal reduction product. Clearly, isobornyloxyaluminum chloride, besides avoiding equilibration, is a reagent which, because of its size, is subject to marked "steric approach control."[12]

There are two other methods (other than catalytic hydrogenation, which rarely gives over 80% of the unstable isomer[13]) known to produce the less stable epimeric alcohol in high purity by reduction of a ketone: reduction with isopropyl alcohol–chloroiridic acid–

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[9] The assumption will be made in the sequel that the reducing agents are alkoxyaluminum dichlorides: *cf.* ref. 2c.

[10] As proposed by H. C. Brown; for summaries see (a) ref. 5, pp. 265–269; (b) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Division, John Wiley and Sons, Inc., New York, N. Y., 1965, pp. 195, 196.

[11] In the small amount of reduction of camphor with isopropoxyaluminum dichloride the only alcohol formed is borneol. However, this observation may not be significant, since camphene is also formed and isoborneol may be transformed to camphene under the reaction conditions.

[12] As suggested by W. G. Dauben: *cf.* ref. 5, pp. 245, 304; ref. 10b, p. 115 ff; and J.-C. Richer, *J. Org. Chem.*, **30**, 324 (1965).

[13] *Cf.* E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957).

TABLE III

COMPOSITION OF MIXTURES OF EPIMERIC ALCOHOLS OBTAINED IN REDUCTION OF KETONES WITH ISOBORNYLOXYALUMINUM DICHLORIDE

Ketone	Product, % of epimeric mixture
4-*t*-Butylcyclohexanone	*cis*, 80–92
3-Cholestanone	α, 86–89
Norcamphor	*endo*, 97
2-Methylcyclohexanone	*cis*, 97–98
3-Methylcyclohexanone	*trans*, 91–92
4-Methylcyclohexanone	*cis*, 89–90
2-*t*-Butylcyclohexanone	*cis*, 90
3,3,5-Trimethylcyclohexanone	*trans*, 98

trimethyl phosphite complex[14] and reduction with diisopinocamphenylborane.[15] In comparing the present method with the two previously reported, one must take into account that the camphor and, especially, isoborneol found along with the reaction products in the present work are highly volatile and therefore difficult to separate from relatively low-boiling products, such as methylcyclohexanols or 4-*t*-butylcyclohexanols. For relatively nonvolatile materials, such as 3α-cholestanol, on the other hand, the present method is very convenient, since the by-products are readily sublimed away; other polycyclic ketones should be reducible to axial alcohols in similar fashion.

D. N. is presently engaged in investigating optically active isobornyloxyaluminum chloride as a reagent in asymmetric synthesis. Preliminary experiments with acetophenone indicate that phenylmethylcarbinol is obtained in about 25% optical purity.

A few control experiments were carried out to compare isobornyloxyaluminum dichloride with isobornyloxymagnesium bromide[16] and aluminum isobornyloxide. The results reported in the Experimental Section indicate that neither complex is as good a reducing agent as isobornyloxyaluminum dichloride and neither provides a feasible route to the preparation of the less stable epimeric alcohols.

Experimental Section

***trans*-4-*t*-Butylcyclohexanol.**—Anhydrous aluminum chloride (67 g., 0.5 mole) was placed in a 2-l. three-necked flask equipped with a stirrer, reflux condenser protected with a drying tube, and pressure-equalized addition funnel. The flask was cooled in ice–water and 500 ml. of cold anhydrous ether was added with stirring. When all the aluminum chloride was dissolved, a slurry of 5.5 g. (0.13 mole) of lithium aluminum hydride in 140 ml. of ether was added, the ice bath was removed, and stirring was continued for 0.5 hr. 4-*t*-Butylcyclohexanone (77.5 g., 0.5 mole) in 500 ml. of anhydrous ether was then added at such a rate as to maintain gentle reflux; after the addition was complete, the mixture was gently boiled for 2 hr. *t*-Butyl alcohol (10 ml.) was then added to destroy any excess hydride and refluxing was continued for 0.5 hr., following which 3 g. of 4-*t*-butylcyclohexanone in 20 ml. of ether was added and refluxing was continued for another 4 hr. The reaction mixture was cooled and treated with 100 ml. of water followed by 250 ml. of 10% aqueous sulfuric acid. Separation of the ether layer followed by washing with water, drying over sodium sulfate, and concentration gave a product (85 g.) containing, besides traces of residual solvent, 96% *trans* alcohol, 0.8% *cis* alcohol, and 3.2% ketone (by gas chromatography on Carbowax). Recrystallization from petroleum ether (b.p. 60–70°) gave nearly pure *trans* alcohol, m.p. 75–78° (lit.[2a] 82.5–83°), weight 61 g. (78%). (Additional material may be recovered from the mother liquor.)

The same decomposition procedure using *t*-butyl alcohol could be used to improve the previously described[2a] thermodynamically controlled reduction using acetone or the equilibration[2a] of commercial 4-*t*-butylcyclohexanol (70% *trans* isomer). In each case, the product contained over 98% *trans* alcohol.

Reduction of Camphor. A. With Excess Hydride.—To a cooled "mixed hydride" solution prepared from 10 g. (0.075 mole) of aluminum chloride, 20 ml. of 1 *M* lithium aluminum hydride (0.020 mole), and 80 ml. of ether was added a solution of 10 g. (0.066 mole) of camphor in 50 ml. of ether over a period of 0.5 hr. The solution was stirred at room temperature for 1 hr. and a 25-ml. aliquot was then removed and worked up in the usual way. The residue, after removal of solvent, contained 71% isoborneol, 26% borneol, and 3% camphene (gas chromatographic analysis on Carbowax 20M or diglycerol). The bulk of the reaction mixture was boiled for 1 hr. and worked up to give 8.5 g. of residue which contained 70% isoborneol, 26% borneol, and 4% camphene. In other experiments, the isoborneol content of the product ranged from 66 to 71%, borneol content from 26 to 27%, and camphene content from 3 to 7%.

B. With a Small Excess of Camphor.—Camphor (5.5 g., 0.036 mole) in 40 ml. of ether was reduced with "mixed hydride" prepared from 5 g. (0.038 mole) of aluminum chloride in 40 ml. of ether and 10 ml. (0.01 mole) of 1 *M* ethereal lithium aluminum hydride solution in the cold. The mixture was stirred for 0.25 hr. while it was allowed to warm to room temperature, and an aliquot (10 ml.) was then removed, decomposed, and analyzed. Reflux was started and further aliquots were removed after 1, 2, and 3 hr. The analyses, shown in Table IV (top), indicated rapid destruction of isoborneol under these conditions.

TABLE IV

ANALYSIS OF SAMPLES REMOVED IN REDUCTION OF EXCESS CAMPHOR WITH MIXED HYDRIDE

Time, hr.	Camphene, %	Camphor, %	Isoborneol, %	Borneol, %
		Small Excess of Camphor		
Initial	2.8	6.3	64.0	26.9
1	12.8	5.9	54.9	26.3
2	65.2	6.7	0	27.1
3.5	66.3	5.8	0	27.9
		Large Excess of Camphor		
Initial	1.2	50.9	33.1	14.9
1	3.0	50.7	31.3	15.0
2	4.5	50.3	29.4	15.8
3.5	13.7	49.8	21.2	15.2
4[a]	17.7	49.7	18.0	14.6

[a] *t*-Butyl alcohol added after 3.5 hr.

C. With a Large Excess of Camphor.—The above experiment was repeated except that the amount of camphor was doubled (11.0 g., 0.072 mole). In this case, the destruction of the isoborneol was much slower (Table IV, bottom).

Reduction of Norcamphor. A. In the Presence of Excess "Mixed Hydride."—A solution of 8.8 g. (0.08 mole) of norcamphor in 50 ml. of ether was reduced as described above by "mixed hydride" prepared from 12.5 g. (0.0935 mole) of aluminum chloride, 100 ml. of ether, and 25 ml. (0.025 mole) of 1 *M* ethereal lithium aluminum hydride. The mixture was stirred at room temperature for 1.5 hr. and then an aliquot (50 ml.) was worked up in the usual way. Analysis required a 30-ft. Carbowax 20M column with the following temperature programming: 0.5 hr. at 150°, 0.5 hr. at 175°, then temperature raised to 200°. It indicated 95–96% *endo*-norborneol and 4–5% *exo*-norborneol. The mixture was crystallized from *n*-hexane to give white plates of *endo*-norborneol, m.p. 153–153.5° (lit.[17] m.p. 152–153°).

B. With Excess Norcamphor.—To the remainder of the above reaction mixture was added 3.5 ml. of *t*-butyl alcohol followed by 2 g. of norcamphor. The mixture was refluxed overnight and then worked up. The product (8.0 g.) was a viscous liquid whose analysis indicated it to contain *exo*-norborneol and *endo*-norborneol in a 89–90 to 10–11 ratio, along with approximately 35% norcamphor.

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[14] Y. M. Y. Haddad, H. B. Henbest, J. Husbands, and T. R. B. Mitchell, *Proc. Chem. Soc.*, 361 (1964).

[15] H. C. Brown and D. B. Bigley, *J. Am. Chem. Soc.*, **83**, 3166 (1961).

[16] G. Vavon and A. Antonini, *Compt. rend.*, **232**, 1120 (1951); A. Streitwieser and J. R. Wolfe, *J. Am. Chem. Soc.*, **79**, 903 (1957).

[17] H. Toivonen, *Ann. Acad. Sci. Fennicae*, [A II] **72**, 1 (1956).

C. Equilibration of *exo*-Norborneol.—Four grams of commercially available *exo*-norborneol (Aldrich Chemical Co.), m.p. 130°, was converted to the $ROAlCl_2$ complex as described elsewhere.[2a] A few drops of *t*-butyl alcohol were added, followed by 1 g. of norcamphor. The mixture was refluxed for 16 hr., worked up in the usual way, and analyzed as described above. The viscous residue (5 g.) contained about 20% norcamphor; the ratio of *exo*- to *endo*-norborneol was 92:8.

Reduction of 4-*t*-Butylcyclohexanone with Isopropoxyaluminum Dichloride.—This reduction is described as typical of those summarized in Table II. To a stirred solution of 12 g. (0.09 mole) of aluminum chloride in 80 ml. of ether was added 20 ml. of 1.1 *M* ethereal lithium aluminum hydride (0.022 mole) in the fashion described earlier. This was followed by 6 g. (0.1 mole) of 2-propanol in 15 ml. of ether. After 0.5 hr., 7.0 g. (0.045 mole) of 4-*t*-butylcyclohexanone was added in 15 ml. of ether. The solution was refluxed and aliquots were removed, worked up in the usual way, and analyzed at intervals. After 1, 2, and 22 hr., the composition was 4-*t*-butylcyclohexanone, 4.6, 3.5, and 1.9%; *cis*-4-*t*-butylcyclohexanol, 3.0, 4.2, and 3.1%; and *trans*-4-*t*-butylcyclohexanol, 92.4, 92.3, and 95.0%.

Similar reduction of camphor and analysis after 1, 2, and 22 hr. gave camphor, 100, 94.8, and 91.3%; borneol, 0, 1.6, and 1.1%; camphene, 0, 3.6, and 7.6%; and isoborneol, none at any time.

Cyclopentanone after 2 hr. gave a product containing cyclopentanone and cyclopentanol in a 56:44 ratio. Analysis using an internal gas chromatographic standard revealed that the total of the two compounds accounted for only 55% of the material. Higher boiling materials, presumably condensation products of cyclopentanone, were also observed.

Reductions with Cyclohexyl- and Cyclopentyloxyaluminum Dichlorides.—A mixture of 7.7 g. (0.05 mole) of *cis*- and *trans*-4-*t*-butylcyclohexanol (30:70) was converted to the $ROAlCl_2$ complex in similar fashion as described above. After destruction of any excess hydride with *t*-butyl alcohol, 5.8 g. (0.1 mole) of acetone was added. After 2 hr. of reflux, only 4–5% of the material was oxidized to 4-*t*-butylcyclohexanone, the remainder still being alcohol. Apparently the *cis* alcohol was oxidized preferentially, since it now constituted only about 15% of the alcohol fraction. Some higher boiling impurities were observed; undoubtedly some 4-*t*-butylcyclohexanone was lost by condensation. Addition of more acetone increased the 4-*t*-butylcyclohexanone–4-*t*-butylcyclohexanol ratio to about 20:80.

Oxidation of cyclopentyloxyaluminum dichloride [from 5 g. (0.0375 mole) of aluminum chloride in 40 ml. of ether, 10 ml. (0.01 mole) of 1 *M* $LiAlH_4$ solution, and 3.5 g. (0.04 mole) of cyclopentanol in 10 ml. of ether] with acetone (4.7 g., 0.08 mole) was similarly unsuccessful. Work-up after 2 hr. of reflux, followed by gas chromatographic analysis using cyclohexanol as an internal standard, indicated 70% recovery of cyclopentanol (68%) and cyclopentanone (2%), the remainder having been converted to higher boiling material.

Cyclopentanone was also ineffective in oxidizing the $ROAlCl_2$ complex of an equivalent amount of cyclohexanol; after 15 min. at reflux the cyclopentanol–cyclopentanone ratio in the product was 1:20 and the cyclohexanol-cyclohexanone ratio was 40:1.

In contrast, cyclohexanone was quite effective in oxidizing the complex of cyclopentanol, the ratio of cyclohexanol–cyclohexanone being *ca.* 20:1 after 2 hr. with a 100% excess of cyclopentanol and about 1:1 with a stoichiometric amount of cyclopentanol.

Both the cyclopentanol and cyclohexanol complexes failed to reduce camphor, no borneol or isoborneol and only a trace of camphene being formed, as evidenced by gas chromatography.

Reduction of a Cyclopentanone–4-*t*-Butylcyclohexanone Mixture with Isopropoxyaluminum Dichloride.—The alcohol derivative was prepared from 6.0 g. (0.1 mole) of isopropyl alcohol as described above and there was added to it a mixture of 4.2 g. (0.05 mole) of cyclopentanone and 7.7 g. (0.05 mole) of 4-*t*-butylcyclohexanone. After 1.5 hr. of reflux the mixture was decomposed and worked up in the usual way. Gas chromatographic analysis of the product indicated a 4-*t*-butylcyclohexanol–4-*t*-butylcyclohexanone ratio of 24:1 (composition of alcohol: 96% *trans* and 4% *cis*), whereas the cyclopentanol-cyclopentanone ratio was only 1:5.5.

Reductions with Isobornyloxyaluminum Dichloride.—To 12.5 g. (0.0935 mole) of aluminum chloride in 100 ml. of dry ether was added 25 ml. of 1 *M* ethereal lithium aluminum hydride (0.025 mole) as described earlier, followed by a solution of 15.4 g. (0.1 mole) of isoborneol in 60 ml. of ether. The solution was stirred with cooling throughout. After the isoborneol addition was complete (0.5 hr.), 2–3 ml. of *t*-butyl alcohol in a little ether was added until hydrogen evolution ceased[18]; then the desired ketone (0.2 mole) was added dropwise with srtiring. After 0.25–0.5 hr. the reaction mixture was worked up. Acetone effected quantitative oxidation to camphor containing but a little camphene (3–12%). Cyclohexanone also effected complete oxidation to camphor. Cyclopentanone, in contrast, gave much camphene (53–60%) and left some unreacted isoborneol (3–11%). To effect complete consumption of isoborneol required 0.3 mole of cyclopentanone; after 0.25 hr. at reflux nearly all the isoborneol was used up and only 15–20% of the product was camphene, the remainder being camphor.

4-*t*-Butylcyclohexanone.—To the isobornyloxyaluminum dichloride reagent prepared as described immediately above and treated with *t*-butyl alcohol as there described was added 10 g. (0.066 mole) of 4-*t*-butylcyclohexanone in 30 ml. of ether dropwise with stirring. The addition required 0.25 hr. during which time the reaction mixture was allowed to warm to room temperature. An aliquot worked up following an additional 20-min. stirring contained *cis*-4-*t*-butylcyclohexanol and its *trans* isomer in a 90:10 ratio, in addition to camphor, camphene, and isoborneol. To the bulk of the reaction mixture was added several milliliters of *t*-butyl alcohol and the solution was boiled for 2 hr. and worked up.[19] The product contained *cis*- and *trans*-4-*t*-butylcyclohexanol in an 80:20 ratio. In other experiments the ratio ranged from 85:15 to 92:8. In all cases the product was contaminated with camphor, isoborneol, and camphene.

The material from several runs (80 g. of crude material) containing camphene, camphor, and about 20% isoborneol and having a *cis–trans* ratio of 84:16 was dissolved in 100 ml. of dry benzene and treated with 60 g. of zinc chloride at reflux for 5 hr. The solution was cooled and extracted with water, the water extract being cleared with ether. The combined ether–benzene layer was washed with water, dried over potassium carbonate, and concentrated. Isoborneol was still present (7.5%) but could be largely removed, along with camphene and camphor, by chromatography on alumina. The column was first eluted with benzene; subsequent elution with ether gave largely 4-*t*-butylcyclohexanol (*cis–trans* ratio 80:20) along with traces of isoborneol and another impurity. *cis*-4-*t*-Butylcyclohexanol may be isolated from this mixture through the *p*-nitrobenzoate, as described elsewhere.[13]

Other ketones were similarly reduced with isobornyloxyaluminum dichloride and the products were analyzed gas chromatographically with the results shown in Table III.

3-Cholestanone.—The preparation of isobornyloxyaluminum dichloride described above was scaled down to 5 g. (0.0375 mole) of aluminum chloride, 10 ml. of 1 *M* ethereal lithium aluminum hydride (0.01 mole), 6.2 g. (0.04 mole) of isoborneol, and 65 ml. of ether. 3-Cholestanone (3 g., 0.008 mole) in 40 ml. of ether was added dropwise over 0.25 hr. Stirring was continued for 0.25 hr. at room temperature and 1 hr. at reflux. The solution was cooled and decomposed with 25 ml. of 10% sulfuric acid. Extraction of the aqueous layer with ether, drying over potassium carbonate, and concentration gave the crude product which was freed of camphene, isoborneol, and camphor by steam distillation or heating at 200–220° (0.1 mm.). The residual white solid (2.9 g.), m.p. 173–183°, was treated in three different ways.

Crystallization from ethanol produced pure 3α-cholestanol, m.p. 185–186° (lit.[20] m.p. 186–187°), in about 70% yield.

Chromatography of the crude material on alumina indicated it to contain *ca.* 86% of 3α-cholestanol with 14% of the 3β isomer.

Treatment of the crude material with acetic anhydride–pyridine (3 hr., steam bath) converted it to the acetate, m.p.

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(18) Prolonged contact of the reagent with *t*-butyl alcohol should be avoided, as it converts isobornyloxyaluminum dichloride to camphene. When 1 g. of *t*-butyl alcohol was added to the reagent prepared from 5.0 g. of isoborneol and the mixture was refluxed and sampled periodically, the camphene-isoborneol ratio in the solution was 2.6:97.4 initially, 57.1:42.9 after 15 min., and 100:0 after 30 min. Addition of excess isoborneol or borneol to the complex promoted similar conversion to camphene.

(19) It had been hoped (see footnote 18) that *t*-butyl alcohol would lead to the destruction of the isoborneol by conversion to easily removed camphene. However, this dehydration is evidently much retarded when camphor is in excess (*cf.* the similar results in Table IV).

(20) C. W. Shoppee, *J. Chem. Soc.*, 1138 (1946).

80–92°, in 99% yield. The optical rotation was $[\alpha]^{32}\text{D}$ +28.1° corresponding to 89% 3α- and 11% 3β-cholestanyl acetate.[3] In a second run, a value of $[\alpha]^{30}\text{D}$ + 26.4° corresponded to 80% of the 3α isomer.

Reduction of Norcamphor with Alkoxyaluminum Dichlorides.—In a typical experiment, isopropoxyaluminum dichloride was prepared as described earlier from 5 g. (0.0375 mole) of aluminum chloride in 40 ml. of ether, 10 ml. of 1 *M* ethereal $LiAlH_4$ (0.01 mole), and 2.4 g. (0.04 mole) of isopropyl alcohol in 10 ml. of ether. The chilled solution was brought to room temperature and, after hydrogen evolution ceased, 3.3 g. (0.03 mole) of norcamphor in 20 ml. of ether was added with stirring (10 min.) and the solution was refluxed for 0.5 hr. It was then cooled and worked up in the usual way and the residue was analyzed for residual norcamphor, *exo*-norborneol, and *endo*-norborneol as described earlier. The results of this experiment and similar ones employing cyclopentanol and cyclohexanol instead of isopropyl alcohol are entered in Table II. The *exo–endo* ratio of the alcohols was 23.8:76.2 with isopropyl alcohol, 8.8:91.2 with cyclopentanol, and 16.8:83.2 with cyclohexanol.

When isobornyloxyaluminum dichloride was used as reducing agent, analytical difficulties arose because of overlap of the *exo*-norborneol and camphor peaks in the gas chromatogram. Fortunately, there was no residual norcamphor in this case (*cf.* Table II), so the product was treated with an excess of lithium aluminum hydride which reduced the camphor to borneol and isoborneol, whereupon gas chromatographic analysis could be effected as described before, indicating 96.5% *endo* and 3.5% *exo* isomer.

Miscellaneous Reductions. 4-*t*-Butylcyclohexanone and Isobornyloxymagnesium Bromide.—To the Grignard reagent prepared from 11 g. (0.1 mole) of ethyl bromide and 2.4 g. (0.1 g.-atom) of magnesium in 80 ml. of dry ether was slowly added a solution of 15.4 g. (0.1 mole) of isoborneol in 50 ml. of dry ether with cooling and stirring until gas evolution ceased. The apparatus was then set for downward distillation, 180 ml. of dry benzene was added, and the solvent was distilled through a Vigreux column until the overhead temperature reached 70°. To the homogeneous solution was then added 5.1 g. (0.033 mole) of 4-*t*-butylcyclohexanone in 10 ml. of benzene. The solution was stirred for 3 hr. at room temperature and then decomposed with water and dilute acid. The benzene layer was separated, washed with water, dried, and concentrated. The gas chromatogram of the product indicated very little camphor (less than 5% of the original isoborneol), large amounts of unchanged 4-*t*-butylcyclohexanone and isoborneol, and only traces of 4-*t*-butylcyclohexanol, indicating that little reduction had occurred.

When the reaction was repeated with 2 hr. of reflux, some reduction occurred. The extent of oxidation to camphor now was about 20% and the extent of reduction to 4-*t*-butylcyclohexanol about 22%. The alcohol portion was largely *trans* isomer (81%) with but 19% *cis*.

4-*t*-Butylcyclohexanone and Aluminum Isobornyl Oxide.—Redistilled aluminum tri-*t*-butoxide (14 g., 0.17 mole) was dissolved in 100 ml. of dry toluene and heated to reflux. Part of the toluene (20 ml.) was allowed to distil to entrain any free *t*-butyl alcohol that might have been present. Isoborneol (5.1 g., 0.033 mole) was then added and the solution was refluxed for 4 hr. The apparatus was then set for downward distillation and two portions of 25 ml. of solvent were removed. The first portion was found, by gas chromatography using isopropyl alcohol as an internal standard, to contain 2.52 g. (0.034 mole) of *t*-butyl alcohol, whereas the second portion was free of *t*-butyl alcohol. Thus, the theoretical amount of *t*-butyl alcohol was evolved, though it is not clear whether the alkoxide formed was of the type $ROAl(O\text{-}t\text{-}Bu)_2$ or a mixture of $(RO)_3Al$ and $Al(O\text{-}t\text{-}Bu)_3$ and possibly even $(RO)_2Al(O\text{-}t\text{-}Bu)$ where R = isobornyl. To the remaining solution was added 2.5 g. (0.0165 mole) of 4-*t*-butylcyclohexanone in 30 ml. of toluene and the mixture was stirred at room temperature for 1 hr. An aliquot of the reaction mixture (10 ml.) was worked up and analyzed at this stage but only about 10% camphor was formed; the proportion of *cis*- and *trans*-4-*t*-butylcyclohexanol in the small amount of reduced product formed was 70:30. The solution was then boiled for 0.5 hr. This virtually completed the reduction but, apparently, also produced considerable equilibration, since now the ratio of *cis*- to *trans*-4-*t*-butylcyclohexanol was 1:2.

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Synthesis of 1-Olefins and α-Substituted Allylic Compounds by Free-Radical Addition of Acetylene[1]

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α-Substituted allyl alcohols, amines, esters, and ketones were produced when the appropriate substrate was added to acetylene in a free-radical reaction initiated by di-*t*-butyl peroxide. 1-Olefins were produced when isoparaffins or cycloparaffins underwent reaction. Products were identified from physical properties, including infrared and n.m.r. spectra. The reaction was carried out in a high-pressure 1-l. autoclave at 140°. Acetylene partial pressure was maintained at 100 to 200 p.s.i. during reaction. Isoparaffins, cycloparaffins, and compounds containing a functional group underwent reaction. At the conditions employed, acetylene addition took place at the secondary hydrogen of cycloparaffins, at tertiary hydrogen, or at hydrogens adjacent to an activating group. The yield of monoadduct based on di-*t*-butyl peroxide increased as the amount of peroxide used was decreased.

Free-radical additions to acetylene which produce new carbon–heteroatom bonds are well known. The literature on these reactions has been reviewed by Stacey, *et al.*[2] However, the addition of radicals to acetylene to form carbon–carbon bonds has not been studied extensively. Bartok and Lucchesi[3] reported 3-methyl-1-butene as a product of the radiation-initiated addition of propane to acetylene. Schluback, *et al.*,[4] prepared 2,5-hexanedione by the addition of acetylaldehyde to acetylene initiated by benzoyl peroxide. The competitive addition of methyl radicals to acetylene and ethylene was studied by Gazith and Szwarc[5] who found that the addition of methyl radicals to acetylene has a slightly higher activation energy than the addition to ethylene, and that the rate of addition is about 30 times

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(2) F. W. Stacey and J. F. Harris, Jr., *Org. Reactions*, **13**, 150 (1963).

(3) W. Bartok and P. J. Lucchesi, *J. Am. Chem. Soc.*, **81**, 5918 (1959).

(4) H. R. Schluback, V. Franzen, and E. Dahl, *Ann.*, **587**, 124 (1959).

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