

The Chemistry of Organoborates. Part II.¹ High Yield Syntheses of Trialkylmethanols by the Cyanoborate Process²

By Andrew Pelter* Michael G. Hutchings, Keith Rowe, and Keith Smith, Departments of Chemistry, University College of Swansea, Singleton Park, Swansea SA2 8PP, and University of Manchester, Manchester M13 9PL

Treatment of trialkylcyanoborates with an excess of trifluoroacetic anhydride induces three migrations from boron to carbon and conditions are defined for the migration of alkyl groups of differing bulk. Oxidative work-up of the reactions gives trialkylmethanols in good yield.

A CHEMICAL target of great synthetic significance is the replacement of the boron atom of an organoborane by a carbon atom bearing a functional group (*i.e.* $\geq\text{B} \rightarrow \geq\text{C-X}$). In this way all the unique properties associated with hydroboration³ and other organoborane-forming reactions⁴ are transferred in a predictable fashion to a stable carbon framework and provide valuable synthetic possibilities for organic chemistry. So far this objective has been attained in two ways. The first utilises carbon monoxide as the one-carbon unit and requires vigorous conditions⁵ whilst the second uses the anion derived from dichloromethyl methyl ether and the reaction medium is thus strongly basic.⁶ We now report that the cyanoborate process represents an alternative, high yield reaction sequence

needing neither special apparatus nor strong base. Oxidative work-up yields trialkylmethanols (*i.e.* $\geq\text{B} \rightarrow \geq\text{C-OH}$).

RESULTS AND DISCUSSION

(a) *Tri-n-alkylcyanoborates*.—In Part I¹ we observed that in solvents other than bis-(2-methoxyethyl) ether (diglyme) the reaction of even 1 equiv. of trifluoroacetic anhydride (TFAA) with a tri-*n*-alkylcyanoborate resulted, after oxidation, in a mixture of trialkylmethanol and dialkyl ketone. That the third migration from boron to carbon should occur so readily suggested that further studies might define conditions in which the product of a triple migration would predominate.

We first attempted to induce the third migration by

⁵ (a) H. C. Brown, *Accounts Chem. Res.*, 1969, **2**, 65; (b) H. C. Brown and M. W. Rathke, *J. Amer. Chem. Soc.*, 1967, **89**, 2737; (c) E. Negishi and H. C. Brown, *Synthesis*, 1972, 197.

⁶ (a) H. C. Brown and B. A. Carlson, *J. Org. Chem.*, 1973, **38**, 2422; (b) H. C. Brown, J. J. Katz, and B. A. Carlson, *ibid.*, p. 3968.

¹ Part I, A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe, preceding paper.

² A. Pelter, M. G. Hutchings, and K. Smith, *Chem. Comm.*, 1971, 1048.

³ H. C. Brown, 'Hydroboration,' Benjamin, New York, 1962.

⁴ K. Smith, Ph.D. Thesis, Manchester University, 1971.

heating the intermediate (1) after removal of solvents and any excess of TFAA. However, this procedure was unsuccessful. More fruitful was the use of an excess of TFAA as shown in Table 1. For the ensuing

gave isolated yields of 85% tri-n-butyl-, 86% tri-n-hexyl-, and 81% tri-n-octyl-methanol.

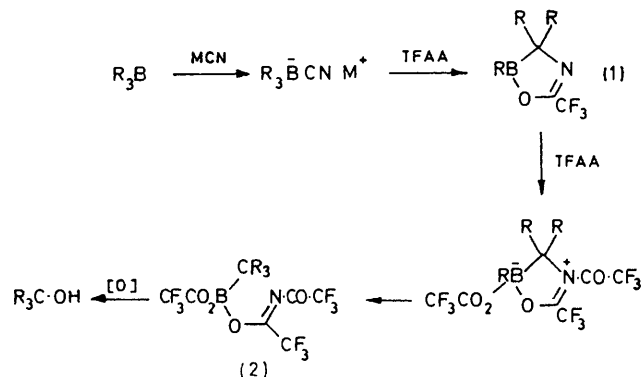
(b) *Cyanoborates containing Secondary Alkyl Groups.*—The mild conditions used for tri-n-alkylcyanoborates

TABLE 1^a
Investigation of the preparation of tri-n-alkylmethanols

Alkyl group	Solvent	Volume (ml)	TFAA (equiv.)	Time (h)	Temp. (°C)	Products	
						Ketone (%)	Trialkyl-methanol (%)
n-Hexyl	THF	30	1.1	1	-40 → R.T. ^c	31	36
	THF	25	2.0	1	0 → R.T.	27	78
	THF	25	3.0	1	0 → R.T.	2	98
	DG ^b	25	1.04	2	0 → R.T.	94	5
	DG	20	1.2	1	-63 → R.T.	80	17
	DG	25	2.0	1	0 → R.T.	10	86
	Et ₂ O	30	1.1	1	-78 → R.T.	20	46
	Et ₂ O	30	2.0	1	0 → R.T.	8	90
n-Butyl	Et ₂ O	10	3.0	1.5	0 → R.T.	1	96
n-Butyl	Et ₂ O	15	3.0	2	0 → R.T.	7	89
n-Octyl	Et ₂ O	15	3.0	1.5	0 → R.T.	15	85
n-Hexyl	CH ₂ Cl ₂	25	1.1	1	0 → R.T.	26	39
	Hexane	20	1.1	1	0 → R.T.	13	49
	Hexane	20	2.0	1	0 → R.T.	27	79
	Hexane	25	3.0	1	0 → R.T.	29	75

^a In this and all other Tables detailing exploratory experiments the reactions were carried out on a 10 mmolar scale and the products estimated by quantitative g.l.c. Preparative reactions are indicated by an asterisk and then the yield given is of isolated product. ^b DG = diglyme. ^c R.T. = room temperature.

reaction we propose the sequence shown in Scheme 1, the stages prior to the intermediate (1) having been firmly established in the preceding paper.



SCHEME 1

Several points emerge from Table 1. In particular, for good yields in mild conditions, an excess of TFAA is an absolute requirement regardless of solvent. We recommend that as a standard procedure 3 mol. equiv. of TFAA to one of the tri-n-alkylcyanoborate should be used. In the presence of such an excess, use of any of the solvents tried resulted in an efficient reaction. The rate was slightly enhanced in diglyme as compared with tetrahydrofuran (THF) but for convenience the latter solvent may well be preferred.

The practical procedure is notable for its simplicity and mildness. It consists of adding 3 equiv. of TFAA to the tri-n-alkylcyanoborate in THF at 0° and stirring the reaction mixture at room temperature over 3 h. Oxidation then yields the trialkylmethanol, isolated by dry column chromatography. Preparative reactions

were unsuccessful in the case of cyanoborates containing secondary alkyl groups. Indeed in diethyl ether, light petroleum, or dichloromethane, or in the presence of nitromethane or dimethyl sulphoxide⁷ no product of a triple migration could be formed at all. A systematic study (Table 2) indicated that the most convenient solvent for this reaction was diglyme.

TABLE 2^a
Production of tricyclopentylmethanol from cyanotri-cyclopentylborate^b

Solvent	Volume (ml)	Time (h)	Temp. (°C)	Products	
				Ketone (%)	Tricyclo-pentyl-methanol (%)
No solvent	0	1	0 → R.T. ^c	93	7
Et ₂ O	10	1	0 → R.T.	95	Trace
Et ₂ O	15	2	0 → 35	95	Trace
Et ₂ O	15	3	0 → R.T.	98	Trace
CH ₂ Cl ₂	25	1	0 → R.T.	98	0
Hexane	20	1	0 → R.T.	99	0
Hexane	20	3	0 → R.T.	97	0
Hexane	20	1.5	0 → 40	97	Trace
THF	20	1	0 → R.T.	45	56
THF	20	3	0 → R.T.	38	65
DG ^d	20	3	0 → R.T.	21	79
DG	20	6	0 → R.T.	9	91

^a See first footnote to Table 1. ^b 3 mol. equiv. TFAA were used in each experiment. ^c R.T. = room temperature. ^d DG = diglyme.

For preparative purposes the reaction was warmed at 40° for 6 h, and in this way isolated yields of 86% tricyclopentyl- and 80% tricyclohexyl-methanol were obtained.

In order to determine whether the third migration

⁷ M. G. Hutchings, Ph.D. Thesis, Manchester University, 1972.

involved free radicals, both radical initiators and inhibitors were tested in the reaction of cyanotricyclopentylborate with an excess of TFAA. No gross or systematic effects were noted and therefore the third migration is not radical in character.

Cyanodicyclohexyl-*n*-octylborate was studied (Table 3). In this case a slight modification of the diglyme procedure using 6 equiv. of TFAA was satisfactory and a 92% yield of dicyclohexyl-*n*-octylmethanol could be obtained. Nonetheless, comparison of the THF results

TABLE 3^a
Reactions of cyanodicyclohexyl-*n*-octylborate

Solvent for double migration	Solvent for third migration	TFAA (equiv.)	Temp. (°C)	Time (h)	Products		
					Ketone (%)	Trialkyl-methanol (%)	Olefin (%)
DG ^b	DG	6	20	6	27	69	4
DG	DG	13	20	6	15	80	5
DG	DG	6	40	6	3	94	4
DG	DG	6	40	8	1	92*	4
THF	THF	6	20	6	49	45	6
THF	THF	6	40	6	18	75	7
THF	THF	6	40	10	6	89	7
THF	THF	6	60	6	6	87	7
THF	THF-Pyridine (9:1)	6	20	6	19	72	11
THF	THF-Pyridine (6:4)	6	20	6	17	64	20
DG	DG-Pyridine (6:4)	6	20	6	17	62	21
THF	THF-Pyridine (3:7)	6	20	6	14	69	17
THF	Pyridine	6	20	6	12	74	16
THF	Pyridine	6	60	6	Trace	82	16
THF	Pyridine	6	60	3	8	78	15
THF	Pyridine	0	82	16	10	80	10
Pyridine	Pyridine	6	20	4	ca. 8	ca. 4	Trace
Pyridine	Pyridine	6	20	20	8	4	Trace

^a See first footnote to Table 1. ^b DG = diglyme.

TABLE 4^a
Reactions of cyanotris-(2-*exo*-norbornyl)- and cyanotris-(*trans*-2-methylcyclopentyl)-borate

Alkyl group	Solvent for double migration	Solvent for third migration	Time (h)	Products		
				Ketone (%)	Trialkyl-methanol (%)	Olefin (%) from double migration
2- <i>exo</i> -Norbornyl	DG ^b	DG	8	32	53	17
	DG	DG	18	23	58	19
	DG	DG-Pyridine (9:1)	18	7	73	21
	DG	DG-Pyridine (9:1)	24	Trace	79*	18
	DG	DG	8	57	43	4
<i>trans</i> -2-Methylcyclopentyl	DG	DG	18	2	88	3
	DG	DG-Pyridine (9:1)	8	3	87	4
	DG	DG-Pyridine (9:1)	10	Trace	85*	ca. 4

^a See first footnote to Table 1. ^b DG = diglyme.

In certain cases the reaction was still rather slow, but addition of a basic solvent (pyridine or dimethylformamide) to the reaction mixture overcame this problem. The amount of basic solvent added is important since it sometimes promotes the production of an olefin derived from two B-C migrations [*e.g.* (3) and (4)].



with and without added pyridine clearly shows the increase in rate associated with the presence of pyridine. However, the presence of too much pyridine lowered the yield of trialkylmethanol with concomitant increase in the yield of olefin. For poorly migrating secondary groups the use of 10% (v/v) of pyridine is justified.

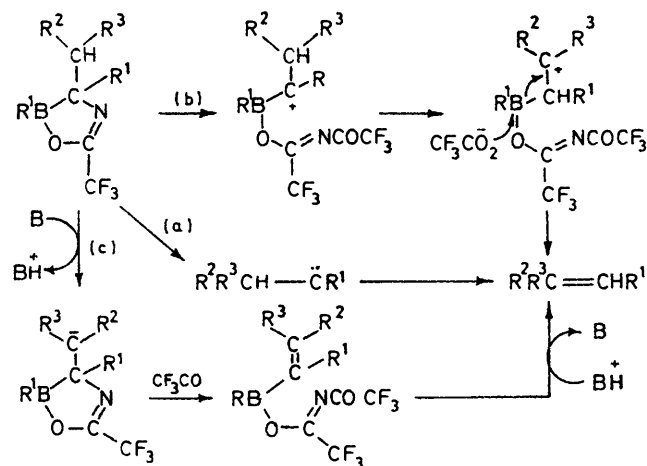
The results with cyanotris-(*trans*-2-methylcyclopentyl)-borate and cyanotris-(2-*exo*-norbornyl)borate are in Table 4. For these compounds 6 equiv. of TFAA and a reaction temperature of 40° were used. The presence of 10% pyridine allows the isolation of 85% tris-(*trans*-2-methylcyclopentyl)methanol with little by-product. The norbornyl case, in which the olefinic product is formed very readily, and indeed in some experiments⁷ on using an excess of basic solvent becomes the major product, provides a more critical test. Even in this case, however, an isolated yield of 79% tris-(2-*exo*-norbornyl)methanol was readily achieved in 10%

pyridine in diglyme without any enhancement in olefin formation.

It should be noted that in most cases the simple diglyme procedure is satisfactory and the need to use 10% pyridine for the third migration arises only occasionally for the migration of *s*-alkyl groups.

A further alternative for obtaining the trialkylmethanol without substantial quantities of olefinic by-product consists of heating the intermediates from a double migration with acetic anhydride. Oxidation then gives the trialkylmethanol. Heating the intermediate (1) for an extended period with pyridine alone can also cause a third migration (Table 3).

The origin of the olefinic by-product is of interest and if it could be produced in good yield the reaction would be of synthetic value. By sampling we have shown that the olefin is present before oxidative work-up and three mechanisms (Scheme 2) can be envisaged.



Mechanism (a) proceeds through a carbene intermediate that rearranges to the olefin, (b) involves the rearrangement of an incipient carbonium ion α to a trivalent boron atom, followed by elimination of boron, whilst (c) involves proton abstraction by a base and hydrolysis of an alkenylborane by the conjugate acid of the base. At present, we have not chosen among these alternatives. A very similar reaction has been noted⁸ in the reaction of the anion of dichloromethyl methyl ether with borinic acid esters and this has been developed into a synthetic procedure,⁹ whose mechanism is also unclear.

(c) *Trialkylcyanoborates containing a Tertiary Alkyl Group*.—In view of the increased ease of the third migration of secondary alkyl groups in the presence of a basic solvent, we decided to use the optimal solvent mixture to test whether or not it were possible to cause a tertiary alkyl group to migrate^{6b} in the cyanoborate process. In practice this proved not too difficult and di-*n*-octylthexylmethanol (thexyl = 1,1,2-trimethyl-

propyl) was obtained from the corresponding cyanoborate in an isolated yield of 70% by the use of 6 equiv. of TFAA at 40° for 10 h. Similarly 64% di-*n*-hexylthexylmethanol was produced.

Conclusions.—By the use of an excess of TFAA it is possible to induce all three alkyl groups of a trialkylcyanoborate to migrate from boron to carbon. The third migration of a primary group proceeds in ether solvents at low temperatures whilst for secondary groups diglyme is the best solvent and warming to 40° may be required. In difficult cases the use of 10% pyridine in diglyme as solvent is effective and this mixture may be used for the migration of tertiary groups. The method is thus a mild and versatile procedure for the replacement of boron in a trialkylborane by a hydroxy-carbon group.

EXPERIMENTAL

The apparatus and reagents used were as already described¹ and reaction products were separated by dry column chromatography on silica gel pre-treated with diethylamine and reactivated at 100° for 3 h.

All trialkylmethanols gave the expected i.r. and mass spectra, and, where possible, were compared with authentic samples. Physical constants were taken on distilled or recrystallised samples.

Procedure (a).—*Preparation of tri-*n*-hexylmethanol*. Potassium cyanotri-*n*-hexylborate (10 mmol) in THF (10 ml) was prepared from cyclohexene (3.75 ml, 30 mmol), diborane (10 mmol of BH_3), and KCN (0.684 g, 10.5 mmol), as previously described.¹ Trifluoroacetic anhydride (TFAA) (4.1 ml, 30 mmol) was added at 0° and the mixture was kept at room temperature for 3 h before the excess of TFAA was removed at the pump.

Oxidation and extraction were carried out as for the preparation of ketones.¹ The crude product was transferred with the aid of a little pentane to a dry neutralised silica gel column, which was eluted first with pentane (50 ml) and then with dichloromethane (2×150 ml). The latter fractions gave tri-*n*-hexylmethanol (2.38 g, 86%), b.p. 110–112° at 0.1 mmHg (lit.,¹⁰ 121–123° at 0.2 mmHg); n_D^{23} 1.4446; ν_{max} (film) 3400 cm^{-1} [Found: m/e , 199.2062. Calc. for $\text{C}_{13}\text{H}_{27}\text{O}$ ($M^+ - \text{C}_6\text{H}_{13}$): m/e , 199.2062].

*Tri-*n*-butylmethanol*. The procedure as before from but-1-ene (1.68 g) gave tri-*n*-butylmethanol (1.69 g, 84.5%); n_D^{23} 1.4438 (lit.,¹¹ n_D^{20} 1.4445); ν_{max} (film) 3400 cm^{-1} [Found: m/e , 143.1437. Calc. for $\text{C}_9\text{H}_{19}\text{O}$ ($M^+ - \text{C}_4\text{H}_9$): m/e , 143.1436].

*Tri-*n*-octylmethanol*. This was prepared as above from oct-1-ene (4.65 ml); yield 2.97 g (81.5%); n_D^{23} 1.4562 (lit.,^{5b} n_D^{20} 1.4565); ν_{max} (film) 3400 cm^{-1} [Found: m/e , 255.2689. Calc. for $\text{C}_{17}\text{H}_{35}\text{O}$ ($M^+ - \text{C}_8\text{H}_{17}$): m/e , 255.2688].

Procedure (b).—*Tricyclohexylmethanol*. Potassium cyanotri-cyclohexylborate (10 mmol) in diglyme (10 ml) was prepared from cyclohexene (3.04 ml, 30 mmol), diborane (10 mmol of BH_3), and KCN (0.684 g, 10.5 mmol) as previously described.¹ TFAA (8.2 ml, 60 mmol) was added at 0° and the flask was then warmed to 40° for 6 h. Excess of TFAA was removed at the pump and the mixture was oxidised and extracted in the normal way. Chromatography as above gave tricyclohexylmethanol (2.39 g, 86%),

¹⁰ M. E. D. Hillman, *J. Amer. Chem. Soc.*, 1962, **84**, 4715.

¹¹ J. M. Church, F. G. Whitmore, and R. V. McGrew, *J. Amer. Chem. Soc.*, 1934, **56**, 180.

⁸ B. A. Carlson and H. C. Brown, *J. Amer. Chem. Soc.*, 1973, **95**, 6876.

⁹ H. C. Brown, personal communication.

pure by g.l.c. Recrystallisation from pentane gave a sample (2.21 g, 79%), m.p. 93–94° (lit.,^{5b} 94.5–95°; lit.,¹² 92–93°); ν_{\max} (mull) 3620 cm^{-1} [Found: C, 82.0; H, 12.2%; m/e , 195.1747. Calc. for $\text{C}_{16}\text{H}_{34}\text{O}$: C, 82.0; H, 12.3%. Calc. for $\text{C}_{13}\text{H}_{23}\text{O}$ ($M^+ - \text{C}_6\text{H}_{11}$): m/e , 195.1749].

Tricyclopentylmethanol. Procedure (b) using cyclopentene (2.64 ml) gave the methanol (2.03 g, 86%); n_D^{23} 1.5125 (lit.,^{5b} n_D^{20} 1.5128); ν_{\max} (film) 3500 cm^{-1} ; b.p. 105° at 0.1 mmHg (lit.,^{5b} 152–153° at 2 mmHg) [Found: C, 81.5; H, 12.0%; m/e , 167.1436. Calc. for $\text{C}_{18}\text{H}_{28}\text{O}$: C, 81.4; H, 11.9%. Calc. for $\text{C}_{11}\text{H}_{19}\text{O}$ ($M^+ - \text{C}_5\text{H}_9$): m/e , 167.1436].

Procedure (c).—*Dicyclohexyl-n-octylmethanol*. Potassium cyanodicyclohexyl-n-octylborate (10 mmol) was prepared in diglyme (9 ml) in the usual way¹ from KCN (0.684 g, 10.5 mmol) and dicyclohexyl-n-octylborane (10 mmol) [prepared from cyclohexene (2.02 ml, 20 mmol), diborane (10 mmol of BH_3), and oct-1-ene (1.56 ml, 10 mmol)³]. TFAA (1.5 ml, 11 mmol) was added at 0° and the mixture allowed to warm to 25° over 30 min after which more TFAA (6.95 ml, 50 mmol) was added, followed by pyridine (1 ml). The flask was warmed to 40° for 10 h and the excess of TFAA removed at the pump. Oxidation was carried out as usual with 5*N*-NaOH (5 ml) and 50% H_2O_2 (5 ml). The normal work-up gave dicyclohexyl-n-octylmethanol (2.84 g, 92%), m.p. 31–32°; ν_{\max} (film) 3470 cm^{-1} (Found: C, 81.9; H, 13.1. Calc. for $\text{C}_{21}\text{H}_{40}\text{O}$: C, 81.8; H, 13.0%; m/e , 290.2973 [Calc. for $\text{C}_{21}\text{H}_{38}$ ($M^+ - \text{H}_2\text{O}$): m/e , 290.2973], 225.2218 [Calc. for $\text{C}_{15}\text{H}_{26}\text{O}$ ($M^+ - \text{C}_6\text{H}_{11}$): m/e , 225.2218], and 195.1749 [Calc. for $\text{C}_{13}\text{H}_{23}\text{O}$ ($M^+ - \text{C}_8\text{H}_{17}$): m/e , 195.1749].

Tris-(trans-2-methylcyclopentyl)methanol. Procedure (c) was used, starting with 1-methylcyclopentene (3.23 ml, 30 mmol); yield 2.38 g (85.5%); n_D^{23} 1.4910; ν_{\max} (film) 3610 cm^{-1} (Found: C, 81.8; H, 12.1. Calc. for $\text{C}_{19}\text{H}_{34}\text{O}$: C, 82.0; H, 12.2%; m/e , 260.2504 [Calc. for $\text{C}_{19}\text{H}_{32}$ ($M^+ - \text{H}_2\text{O}$): m/e , 260.2504]; and 195.1749 [Calc. for $\text{C}_{13}\text{H}_{23}\text{O}$ ($M^+ - \text{C}_6\text{H}_{11}$): m/e , 195.1749].

Tris-(exo-2-norbornyl)methanol. Prepared by procedure (c) from norbornene (2.82 g, 30 mmol) this yielded 2.49 g (79%); m.p. 137° (lit.,^{5b} 137–137.5°), ν_{\max} (film) 3600 and 3500 cm^{-1} [Found: C, 83.9; H, 10.9%; m/e , 219.1755. Calc. for $\text{C}_{22}\text{H}_{34}\text{O}$: C, 84.1; H, 10.8%. Calc. for $\text{C}_{15}\text{H}_{23}\text{O}$ ($M^+ - \text{norbornyl}$): m/e , 219.1749].

Di-n-hexylthexylmethanol. Potassium cyanodi-n-hexylthexylborate (10 mmol) was prepared in diglyme (9 ml) as previously described.¹ TFAA (1.5 ml, 11 mmol) was added at 0° and the mixture allowed to warm to 25° over 30 min. TFAA (6.95 ml, 50 mmol) followed by pyridine (1 ml) were then added and the mixture was held at 40° for 18 h. Excess of TFAA was pumped off and the normal oxidation and work-up yielded *di-n-hexylthexylmethanol* (1.82 g, 64%) in the dichloromethane (4 × 100 ml) eluate; n_D^{25} 1.4538, ν_{\max} (film) 3500 and 3600 cm^{-1} [Found: C, 80.5; H, 14.2%; m/e , 266.2973. $\text{C}_{19}\text{H}_{40}\text{O}$ requires C, 80.3; H, 14.1%. $\text{C}_{19}\text{H}_{38}$ ($M^+ - \text{H}_2\text{O}$) requires m/e , 266.2973].

Di-n-octylthexylmethanol. This was prepared as above from hexene (2,3-dimethylbut-2-ene) (1.18 ml, 10 mmol) and oct-1-ene (3.08 ml, 20 mmol), yield 2.38 g (70%); n_D^{25} 1.4560; ν_{\max} (film) 3500 and 3600 cm^{-1} [Found: C, 81.2; H, 14.3%; m/e , 322.3599. $\text{C}_{23}\text{H}_{48}\text{O}$ requires C, 81.2; H, 14.1%. $\text{C}_{23}\text{H}_{46}$ ($M^+ - \text{H}_2\text{O}$) requires m/e , 322.3599].

Olefinic Products (3) and (4) from Two Migrations.—The olefins were isolated as the minor products from experiments designed to yield the two alcohols, dicyclohexyl-n-octyl- and tris-(2-*exo*-norbornyl)-methanol. The olefins were present in the pentane eluate from chromatography of the crude, neutral extracts. The yield of any one experiment is detailed in Tables 3 and 4. (*Norbornan-2-ylidene*)-(2-*exo*-norbornyl)methane (4) had b.p. 175° at 765 mmHg; $n_D^{21.5}$ 1.5089 (Found: C, 89.1; H, 10.9%; M^+ , 202.1721. $\text{C}_{15}\text{H}_{22}$ requires C, 89.1; H, 10.9%; M , 202.1721). G.l.c. examination showed that the compound exists as a pair of isomers, peak ratio 5:1, running at 7.3 and 6 min on a 4% PEGA column programmed from 50 to 190° at 12° min^{-1} . A similar observation has been made previously.⁹

Nonylidene-cyclohexane (3) had b.p. 209° at 760 mmHg; $n_D^{21.5}$ 1.4599 (Found: C, 84.5; H, 13.4%; M^+ , 208.2191. $\text{C}_{15}\text{H}_{28}$ requires C, 86.5; H, 13.5%; M , 208.2191).

M. G. H. and K. R. thank the S.R.C. for maintenance grants.

[4/1231 Received, 24th June, 1974]

¹² P. Bartlett and A. Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 141.