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THE PREPARATION OF *CIS*- AND *TRANS*-2-ALKYL-NN-DIMETHYLCYCLOHEXYLAMINES

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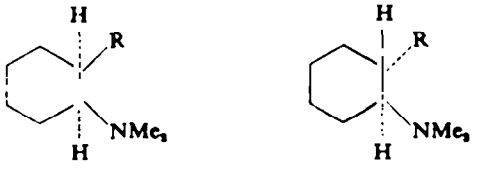
Abstract—Mixtures of *cis*- and *trans*-2-alkyl-NN-dimethylcyclohexylamines have been prepared by standard methods and the majority have been separated into pure isomers by preparative VPC.

STUDIES of the thermal decomposition of quaternary ammonium hydroxides required the synthesis of pure *cis*- and *trans*-2-alkyl-NN-dimethylcyclohexylamines (I and II respectively). Numerous methods[1] are available, but the methods involving reduction, when applied to the preparation of C-alkylcyclohexylamines, are rarely stereospecific. Furthermore, the methods which are claimed to be stereospecific (e.g. the Hofman,



Curtius, Schmidt and Lossen degradations of cyclohexane carboxylic acids or derivatives; the ammonolysis of cyclohexyl *p*-toluenesulphonates; the reaction of cyclohexyl *p*-toluenesulphonates with sodium azide, with subsequent reduction) suffer from the obvious disadvantage that they are useful only if the starting material is itself stereochemically pure.

Our investigations required the pure amines I and II containing a variety of alkyl substituents R. The obvious starting materials were 2-alkylphenols, or 2-alkylcyclohexanols, or 2-alkylcyclohexanones. Many of these compounds are commercially available, an exception being the case of R = isobutyl. However, 2-iso-butylcyclohexanone was prepared without difficulty by an aldol condensation of cyclohexanone and isobutyraldehyde, followed by reduction of the C—C double-bond. Catalytic hydrogenation of 2-alkylcyclohexanone oximes over PtO_2 proceeded slowly and gave moderate yields of 2-alkylcyclohexylamines in which *cis*-isomers formed the major component (Table 1). Reduction of the oximes with sodium in boiling ethanol gave moderate to good yields of the primary amines containing a preponderance of the *trans*-isomers (Table 2). Attempts to separate the mixtures of *cis*- and *trans*-2-alkylcyclohexylamines by analytical VPC, using the columns developed by Feltkamp and Thomas,[2] were not successful. However, under the same conditions, all the

[1] Houben-Weyl, *Methoden Der Organischen Chemie*, Band XI, I, Georg Thieme Verlag, Stuttgart (1957); W. Theilheimer, *Synthetic Methods of Organic Chemistry* Vol. 1–18. S. Karger, Basel (1946–1964); W. Huckel and K-D. Thomas, *Liebigs Ann.* **645**, 177 (1961); A. K. Bose, J. F. Kistner and L. Farber, *J. Org. Chem.* **27**, 2925 (1962); J. L. Pinkus, G. Pinkus and T. Cohen, *Ibid.* **27**, 4356 (1962).

[2] H. Feltkamp and K-D. Thomas, *J. Chromat.* **10**, 9 (1963).

corresponding *cis*- and *trans*-2-alkyl-NN-dimethylcyclohexylamines, obtained by methylating the mixtures of primary amines, were separated satisfactorily on the analytical scale (see Fig. 1). The proportions of *cis*- and *trans*-bases in the mixtures were calculated from the area under the peaks, and are reported in Tables 3, and 4; the corresponding retention times are given in Table 5. In most cases, the separations were successfully extended to a preparative scale (Table 5). In one case, that of 2-methyl-NN-dimethylcyclohexylamine, a preparative separation of *cis*- and *trans*-amines was also achieved by fractional distillation up a spinning band column. The preferred method for synthesising *cis*- rich 2-ethyl-NN-dimethylcyclohexylamine involved catalytic hydrogenation of 2-ethyl-NN-dimethylaniline.

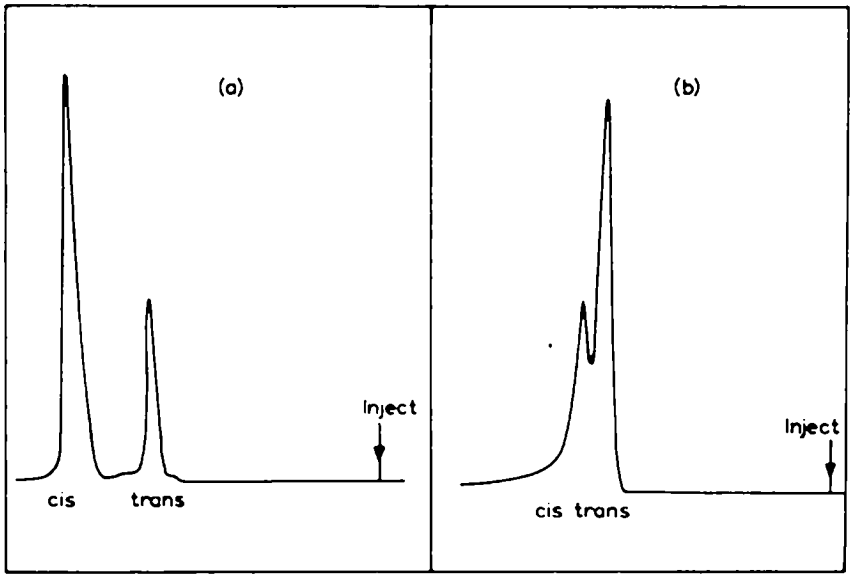


Fig. 1. Separation by analytical VPC of *cis*- and *trans*-2-alkyl-NN-dimethylcyclohexylamine (I and II respectively)
(a) a typical separation (R = iso-butyl)
(b) the most difficult separation (R = t-butyl)

The stereochemistry of both the primary and tertiary amines was established by PMR spectral studies: some of the details of these studies have already been published[3] and the remainder are now reported in Tables 6 and 7.

EXPERIMENTAL

NMR spectra were recorded on a Perkin–Elmer R. 10 spectrometer operating at 60 Mc/s.

Analytical vapour phase chromatography. A Perkin–Elmer 800 Gas Chromatograph was used with N_2 as carrier gas. The 12′ × ¼″ column was packed with Carbowax 20 M (5%) on a support of alkali-treated Chromosorb W. The column temp was varied between 120° and 130°; the injector temp was varied between 250° and 300°. The isomer proportions quoted below were calculated from the curves by the triangulation method, and are estimated to be accurate to ±2%.

Preparative vapour phase chromatography. A Wilkens Autoprep A700 Gas Chromatograph was used, with He as carrier gas. The 25′ × ⅜″ column was packed with Carbowax 20M (25%) on alkali-treated Chromosorb W. The temp of the column was varied between 135° and 145°; the injector temp was varied between 250° and 300°.

[3] H. Booth, N. C. Franklin and G. C. Gidley, *Tetrahedron* **21**, 1077 (1965).

TABLE 1. FORMATION OF cis-2-ALKYLCYCLOHEXYLAMINES FROM 2-ALKYLCYCLOHEXANONE OXIMES

Alkyl	Crude Product Yield	B.p.°/mm	Derivative	Recrystallizing solvent	m.p.°	Analyses Found C;	H;	N	Formula	Required C;	H;	N
Me	59	56–63/11	phthaloyl	sublimed 100°/ 0·1 mm.	122–123	74·0;	6·9;	5·8	$C_{16}H_{17}NO_2$	74·1;	7·0;	5·8
Et	62	70–75/10	phthalamic acid	EtOH—H_2O	155–157	69·6;	7·9;	5·0	$C_{16}H_{21}NO_2$	69·8;	7·7;	5·0
			phthaloyl	EtOH—H_2O	101–103	74·4;	7·6;	5·3	$C_{16}H_{19}NO_2$	74·7;	7·4;	5·5
Pr	30	71–74/12	—	—	—	—	—	9·5	$C_9H_{19}N$[a]	—	—	9·9
			phthaloyl	l. pet. 100–120°	60–61	75·1;	7·4;	5·3	$C_{17}H_{21}NO_2$	75·2;	7·8;	5·2
			picrate	EtOH	178–179	48·6;	5·7;	15·3	$C_{15}H_{22}N_4O_7$	48·6;	6·0;	15·1
iso-Pr	48	61–64/1·7	—	—	—	—	—	—	—	—	—	—
Bu	44	92–99/15	—	—	—	77·3;	13·9;	8·8	$C_{10}H_{21}N$[b]	77·4;	13·6;	9·0
			acetyl	EtOH—H_2O	93–94	73·2;	12·0;		$C_{12}H_{23}NO$	73·0;	11·8	
			picrate	C_6H_6	138–139	49·7;	6·2;	14·8	$C_{16}H_{24}N_4O_7$	50·0;	6·3;	14·6
			picrolonate	C_6H_6—CH_3OH	192–193	56·9;	6·7;	16·9	$C_{20}H_{29}N_5O_5$	57·3;	7·0;	16·7
iso-Bu	57	42–48/0·2	—	—	—	—	—	—	—	—	—	—
sec-Bu	54	47–52/0·35	3,5-dinitrobenzoic acid salt	EtOAc	172–174	—	—	11·3	$C_{17}H_{23}N_3O_6$	—	—	11·4
tert-Bu	47	85–90/13	—	—	—	—	—	—	—	—	—	—
cyclohexyl[c]	61	85–92/1	phthalamic acid	H_2O	112–114	—	—	4·2	$C_{20}H_{27}NO_2$	—	—	4·3
			picrate	EtOH	154–156	52·7;	6·4;	13·5	$C_{18}H_{27}N_4O_7$	52·7;	6·4;	13·7

Notes:

[a] Data for free base, b.p. 81–83°/18 mm, purified through the phthaloyl deriv.

[b] Data for free base, b.p. 93–97°/16 mm, purified through the picrate.

[c] Cf. H. Booth, F. E. King and J. Parrick, *J. Chem. Soc.* 2302 (1958).

TABLE 2. FORMATION OF trans-2-ALKYLCYCLOHEXYLAMINES FROM 2-ALKYLCYCLOHEXANONE OXIMES

Alkyl	Crude Product Yield	B.p.°/mm	Derivative	Recrystallizing solvent	m.p.°	Analyses Found C;	H;	N	Formula	Required C;	H;	N
Me	67	60–64/9	phthaloyl	EtOH	105–106	73·4;	6·9;	5·9	$C_{16}H_{17}NO_3$	74·1;	7·0;	5·8
Et	60	60–64/12	phthaloyl	EtOH	74–75	74·4;	7·7;	5·2	$C_{16}H_{19}NO_3$	74·7;	7·4;	5·5
			picrate	EtOH	199–200[a]	—	—	—	—	—	—	—
Pr	—	69–70/10	3,5-dinitrobenzoic acid salt	H_2O	180–181	54·4;	6·4;	11·6	$C_{16}H_{23}N_3O_6$	54·4;	6·6;	11·9
			phthaloyl	l. pet. 100–120°	88–89	75·1;	7·5;	—	$C_{17}H_{21}NO_3$	75·2;	7·8;	5·2
			picrate	EtOH	166–168[b]	—	—	—	—	—	—	—
iso-Pr	64	80–82/9	phthaloyl	EtOH	88–89	74·7;	7·5;	4·9	$C_{17}H_{21}NO_3$	75·2;	7·8;	5·2
			picrate	EtOH	195–197[c]	—	—	—	—	—	—	—
Bu	74	85–87/9	acetyl	EtOH—H_2O	108–109	73·3;	11·8.	—	$C_{12}H_{23}NO$	73·0;	11·8:	—
			phthaloyl	l. pet. 100–120°	80–81	75·8;	7·5;	5·2	$C_{18}H_{23}NO_3$	75·8;	8·1;	4·9
			picrate	EtOH	141–142[d]	50·1;	6·1;	14·9	$C_{16}H_{24}N_4O_7$	50·0;	6·3;	14·6
			picrolonate	EtOH	191–192	57·1;	7·0;	16·4	$C_{20}H_{29}N_5O_6$	57·3;	7·0;	16·7
sec-Bu	62	44–46/0·25	3,5-dinitrobenzoic acid salt	EtOAc–EtOH	178–179	55·5;	6·8;	11·7	$C_{17}H_{25}N_3O_6$	55·6;	6·9;	11·4
			phthaloyl	EtOH	88–89	—	—	5·0	$C_{18}H_{23}NO_3$	—	—	4·9
tert-Bu	-	e	phthalamic acid[f]	EtOH	196–197	—	—	4·3	$C_{18}H_{25}NO_3$	—	—	4·6
			phthaloyl	EtOH	128–129	75·7;	8·1;	—	$C_{18}H_{23}NO_3$	75·8;	8·1.	—
cyclohexyl	55	84–96/0·75	3,5-dinitrobenzoic acid salt	EtOAc—EtOH	206—208	58·2;	7·3;	10·5	$C_{19}H_{27}N_3O_6$	58·0;	6·9;	10·7
			hydrochloride	—	214–216[g]	—	—	—	—	—	—	—
			phthaloyl	EtOH	112–113	77·1;	8·1;	4·5	$C_{20}H_{25}NO_3$	77·0;	7·9;	4·7
			picrate	EtOH	192–194	52·5;	6·1;	13·3	$C_{18}H_{27}N_4O_7$	52·7;	6·4;	13·7

Notes:

[a] F. E. King, J. A. Barltrop and R. J. Walley, *J. Chem. Soc.* 277 (1945) give m.p. 198–199°.

[b] S. Fujise, *Bull. Inst. Phys. Chem. Res. Tokyo* **8**, 27 (1929) gives m.p. 168–169°.

[c] J. von Braun and O. Bayer, *Ber. Dtsch. Chem. Ges.* **58**, 391 (1925) give m.p. 195° for picrate of hydrogenation of 3-methylindole.

[d] mixed m.p. with *cis*-picrate, 125–135°.

[e] not distilled.

[f] stereochemistry uncertain.

[g] H. Booth, F. E. King and J. Parrick, *J. Chem. Soc.* 2302 (1958) give m.p. 215–216°.

TABLE 3. FORMATION OF cis-2-ALKYL-NN-DIMETHYLCYCLOHEXYLAMINES FROM PRIMARY AMINES

Alkyl	Crude product Yield %	B.p.°/mm	Composition (by VPC) % *cis*	% *trans*	Derivative	Recrystallizing solvent	M.p.°	Analyses Found C; H; N	Formula	Required C; H; N
Me	67	167–176/747	69[a]	31	3,5-dinitrobenzoic acid salt	EtOAc—EtOH	136–138	54·4; 6·5; 11·4	$C_{16}H_{23}N_5O_6$	54·4; 6·6; 11·9
					picrate	EtOH	211–213	48·6; 5·8; 15·1	$C_{16}H_{22}N_4O_7$	48·6; 6·0; 15·1
Et[b]	*c*	60–61/6	80[d]	20	picrate	EtOH	162–163[e]	- - - - —	—	— — —
Pr	*c*	85–90/1	96	4	picrate	EtOH	173–174[f]	— — —	—	— — —
iso-Pr	63	33–36/0·2	91	9	picrate	EtOAc—EtOH	174–175	51·3; 6·7; 13·6	$C_{17}H_{24}N_4O_7$	51·3; 6·6; 13·7
Bu	77	84–86/1·3	74	26	—	—	—	79·1; 13·7; 7·6	$C_{10}H_{23}N$[g]	78·7; 13·7; 7·7
					picrate	EtOH	126–128	52·6; 6·4; 13·3	$C_{16}H_{24}N_4O_7$	52·4; 6·8; 13·6
iso-Bu	*c*	85–90/11	68[h]	27	methiodide	Me_2CO	207–208	48·5; 8·7; 3·9	$C_{10}H_{24}NI$	48·0; 8·6; 4·4
sec-Bu	*c*	50–57/1	70	30	methiodide	Me_2CO	175–176	47·9; 8·6; 4·3	$C_{10}H_{24}NI$	48·0; 8·6; 4·3
tert-Bu	79	68–72/1·1	>95	<5	—	—	—	- - - - - -	—	— — —
cyclohexyl[i]	65	104–106/3	85	15	methiodide	Me_2CO	137–139	— — 3·8	$C_{15}H_{30}NI$	— — 4·0

Notes:

[a] the pure *cis*-base (100% pure by VPC), b.p. 171–172°/741 mm, $n_D^{24.6}$ 1·4571, was obtained from the mixture by distillation up a 2½′ spinning band column.

[b] prepared by hydrogenation of 2-ethyl-NN-dimethylaniline.

[c] not recorded.

[d] the pure *cis*-base (100% pure by VPC), b.p. 64–65°/7 mm, $n_D^{21.6}$ 1·4603, was isolated from the mixture through the picrate.

[e] F. E. King, D. M. Bovey, K. G. Mason and R. L. St. D. Whitehead, *J. Chem. Soc.* 250 (1953) give 159°.

[f] S. Fujise, *Sci. Papers Inst. Phys. Chem. Res., Tokyo* **8**, 185 (1928).

[g] data for free base (100% pure by VPC), separated by preparative VPC.

[h] mixture also contains 5% impurity, probably NN-dimethylcyclohexylamine (VPC).

[i] methylation carried out on the primary amine 'purified' through the picrate.

TABLE 4. FORMATION OF trans-2-ALKYL-NN-DIMETHYLCYCLOHEXYLAMINES FROM PRIMARY AMINES

Alkyl	Crude product Yield %	B.p.°/mm	Composition (VPC) % *cis*	% *trans*	Derivative	Recrystallizing solvent	m.p.°	Analyses Found C; H; N	Formula	Required C; H; N
Me	*a*	165–170/742	10	90[b]	picrate	EtOH	154–155	48·2; 6·2 —	$C_{16}H_{23}N_4O_7$	48·6; 6·0 —
Et	*a*	68–70/12	<10	>90[a]	—	—	—	— — —	—	— — —
Pr	*a*	80–82/9	<10	>90[a]	picrate	EtOH	112–113[d]	— — —	—	— — —
iso-Pr	*a*	60–61/1·5	5	95	picrate	EtOH	162–163	50·9; 6·8 —	$C_{17}H_{26}N_4O_7$	51·3; 6·6 —
Bu	48	94–96/10	<10	>90[a]	picrate	EtOH	118–119	52·1; 6·9 —	$C_{16}H_{24}N_4O_7$	52·4; 6·8 —
sec-Bu	73	*a*	40	60	picrate	EtOAc–C_6H_6	163–164	52·3; 6·8 —	$C_{16}H_{24}N_4O_7$	52·4; 6·8 —
tert-Bu	54	100–102/7	33	67	methiodide	Me_2CO	193–194	— — 4·4	$C_{13}H_{26}NI$	— — 4·3
cyclohexyl	53	90–98/1	10	90[e]	picrate	EtOH	171–172[f]	— — —	—	— — —
					methiodide	Me_2CO	137–140	— — 3·8	$C_{15}H_{30}NI$	— — 4·0

Notes:

[a] not recorded.

[b] the pure *trans*-base (99% by VPC) was obtained from the mixture by distillation up a 2½′ spinning band column.

[c] estimated by NMR.

[d] S. Fujise (see footnote *f*, Table 3) gives 114·5–115·5°.

[e] the pure *trans*-base, b.p. 106°/3 mm., was obtained from the mixture through the picrate.

[f] H. Booth *et al.* (see footnote *g*, Table 2) give 167–168°.

General method of preparation of 2-alkylcyclohexylamines rich in cis-*isomers.* The 2-alkylcyclohexanone oxime (20 g), dissolved in a mixture of glacial AcOH (30 ml) and conc HCl (10 ml), was hydrogenated at room temp and atm press over Adam's PtO_2 (1 g) until absorption of H ceased (5–10 days). The soln was filtered and the filtrate was evaporated under reduced press to a small volume. Unchanged oxime was removed by shaking with ether, and the aqueous phase was then basified and extracted several times with ether. Distillation of the dried (KOH) extracts gave the 2-alkylcyclohexylamine.

General method of preparation of 2-alkylcyclohexylamines rich in trans-*isomers.* The 2-alkylcyclohexanone oxime (25 g) was dissolved in hot dry EtOH (150 ml) and Na (50 g) was added in small pieces during 2½ hr. The mixture was refluxed for 30 min, and then worked up in the usual manner (cf. [4]), a final distillation giving the crude 2-alkylcyclohexylamine.

General method of preparation of phthaloyl derivatives of 2-alkylcyclohexylamines. The cyclohexylamine (1 g) was dissolved, with cooling, in glacial AcOH (5 ml) and treated with powdered phthalic anhydride (1·5 g). The mixture was heated under reflux for 5–6 hr, cooled and poured with stirring

TABLE 5. SEPARATION OF cis- AND trans-2-ALKYL-NN-DIMETHYLCYCLOHEXYLAMINES BY VPC

Alkyl	Retention Times (min)		Purity of base (%) isolated by preparative VPC (Estimated by analytical VPC)	
	cis	*trans*	*cis*	*trans*
Me	5·12	3·72	*a*	*a*
Et	8·08	6·12	*a*	*a*
Pr	7·20	5·52	99·8	*a*
iso-Pr	9·84	8·36	100	99·7
Bu	10·20	7·92	100	*a*
iso-Bu	11·70	7·80	100	—
sec-Bu	6·96	7·64	100	100
tert-Bu	7·72	6·96	*a*	82[b]
cyclohexyl	37·90	29·20	*a*	*a*

Notes:
[a] not separated by preparative VPC.
[b] incomplete separation.

into a sat $NaHCO_3$aq. The insoluble amide was filtered off and crystallized. The related phthalamic acid was sometimes isolated by acidification of the $NaHCO_3$ solution.

N-*Dimethylation* of 2-alkylcyclohexylamines was carried out by the Eschweiler–Clarke method, using formaldehyde and formic acid.

cis-2-*Ethyl*-NN-*dimethylcyclohexylamine.* 2-Ethylaniline (40 g), MeI (114 g), anhyd Na_2CO_3 (85 g) and acetone (230 ml) were heated under reflux during 7 hr. Acetone and excess of MeI were removed by distillation and the residue was extracted with ether. Distillation of the dried (KOH) extracts gave 2-ethyl-NN-dimethylaniline (33·5 g, 68%), b.p. 49–52°/1·2 mm. The tertiary base (10 g) was hydrogenated over W5 Raney Ni in MeOH at 130° and 100 atm. initial press. The mixture was filtered and the filtrate was acidified with 2N HCl and shaken with ether to remove neutral compounds. The aqueous phase was basified and extracted with ether. Evaporation of the dried (KOH) extracts, followed by distillation, gave fraction (a), b.p. 38–40/2 mm (not examined) and fraction (b), crude *cis*-2-ethyl-NN-dimethylcyclohexylamine, b.p. 60–61°/6 mm. (see Table 3).

2-*Isobutylcyclohexanone.* A mixture of cyclohexanone (60 g) and isobutyraldehyde (72 g) was added dropwise, at 0°, to a vigorously stirred mixture of 3% NaOHaq (33 ml) and cyclohexanone (36 g). Next, 3% NaOHaq (67 ml) was added dropwise, with stirring, during 30 min, the temp being maintained at 0°. The mixture was stirred at 0° for a further 5 hr. The organic layer was then

[4] H. Booth and F. E. King, *J. Chem. Soc.* 2688 (1958).

Table 6. Spectral data for N- and 2-substituted cyclohexylamines
(Chemical Shifts in τ values; J in c/s)

Derivative	Solv.	N-Me	α-proton	α-proton ½-band width (c/s)	Misc.
cis-2-Me, NMe_2	1	7·87	*a*	--	Me 9·01[b] (J 7·0)
	2	7·82[b] (J 5·1)	*a*	---	—
		7·85[b] (J 5·1)			
cis-2-Me, NMe_3, MeI	3	6·59	*a*	—	Me 8·78[b] (J 7·0)
cis-2-iso-Pr	1	—	6·95	6	—
cis-2-iso-Pr, NMe_2	1	7·82	*a*	—	—
	2	7·65[b] (J 5·3)	*a*	—	--
trans-2-iso-Pr, NMe_2	1	7·89	*a*	--	—
	2	7·70[b] (J 5·1)	*a*	—	—
		7·85[b] (J 5·1)			
cis-2-iso-Bu	1	—	7·14	7·7	Me 9·13[b] (J 5·2)
cis-2-iso-Bu, NMe_2	1	7·85	*a*	—	--
trans-2-iso-Bu, NMe_2	1	7·83	*a*	--	—
cis-2-sec-Bu	1	—	6·94	6	—
cis-2-sec-Bu, NMe_2	1	7·82	*a*	—	—
	2	7·35[b] (J 5·9)	*a*	—	—
cis-2-sec-Bu, NMe_3, MeI	3	6·50	*a*	---	—
trans-2-sec-Bu	1	—	7·65	~18	—
trans-2-sec-Bu, NMe_2	1	7·86	*a*	---	—
	2	7·68[b] (J 5·5)	*a*	—	—
		7·90[b] (J 5·5)			
cis-2-tert-Bu, NMe_2	1	7·77	7·3	8	Bu^t 8·91
	2	7·57[b] (J 5·5)	*a*	—	—
trans-2-tert-Bu, NMe_2	1	7·90	*a*	—	Bu^t 8·92
	2	7·55[b] (J 5·5)	*a*	---	—
		7·75[b] (J 5·5)			
trans-2-tert-Bu, NMe_3, MeI	3	6·49	*a*	—	Bu^t 8·86
cis-2-cyclohexyl, NMe_3, MeI	3	6·50	*a*	—	—
trans-2-cyclohexyl, NMe_3, MeI	3	6·59	*a*	---	--

Solvents: 1, benzene; 2, benzene and excess of trifluoroacetic acid; 3, chloroform.
Notes:
[a] not seen.
[b] centre of doublet.

Table 7. Spectral data for phthaloyl derivatives of 2-alkylcyclohexylamines

Derivative	Solv.	α-Proton (τ)	Observed splittings (c/s) J_{aa}	J_{ae}
trans-2-iso-Pr	C_6H_6	5·75	11·7	3·8
cis-2-iso-Bu[a]	CCl_4	5·73	12·3	3·8
trans-2-iso-Bu[a]	CCl_4	6·20	11·0	3·9
trans-2-sec-Bu	$CHCl_3$	5·90	11·1	3·4
trans-2-tert-Bu	C_6H_6	5·65	11·1	3·7

[a] present in a mixture of *cis*- and *trans*-imides.

separated, washed with 2N HCl, dried ($MgSO_4$) and heated at 140–145° with anhyd oxalic acid for 2 hr. The organic layer was separated, washed with water, dried ($MgSO_4$) and distilled up a 2½' spinning band column. The fractions collected were examined by PMR, and the fraction b.p. 100–105°/20 mm. was a mixture of isomeric 2-(2'-methylpropenyl)cyclohexanones. This fraction (30 g) was dissolved in EtOH (40 ml) and hydrogenated over 10% Pd–C (1 g) at room temp and atm press (3·9 l. H_2 absorbed; theory 4·4 l.). The mixture was filtered and distilled through the spinning band column. The fraction b.p. 95–98°/15 mm was collected as 2-isobutylcyclohexanone. The derived oxime (93% yield) had b.p. 135–138°/14 mm. The *semicarbazone* formed platelets (EtOH), m.p. 158–159°. (Found: C, 62·9; H, 10·4. $C_{11}H_{21}N_3O$ requires: C, 62·6; H, 10·1%.)

2-s-Butylcyclohexanone oxime. *o*-s-Butylphenol (400 g), dissolved in EtOH (80 ml) was hydrogenated over W5 Raney Ni at 150° and 100 atm initial press. The mixture was filtered, heated to remove EtOH, dissolved in ether and shaken several times with 20% NaOHaq. Distillation of the dried ($MgSO_4$) ethereal soln gave crude 2-s-butylcyclohexanol (380 g, 90%), b.p. 76–80°/2·2 mm, as a mixture of isomers. The foregoing mixture (200 g) was dissolved in glacial AcOH (100 ml) and treated gradually, at 25–30°, with a mixture containing CrO_3 (90 g), water (100 ml) and glacial AcOH (200 ml). The usual method of working-up gave 2-s-butylcyclohexanone (145 g, 70%), b.p. 66–70°/3 mm (lit.[4] 48°/0·7 mm). A mixture of this ketone (145 g), $NaHCO_3$ (130 g), hydroxylamine hydrochloride (108 g) and water (30 ml) was heated at 100° during 5 hr and then treated by ether-extraction. Distillation of the dried ($MgSO_4$) extracts gave 2-s-butylcyclohexanone, b.p. 50–53°/0·9 mm and *2-s-butylcyclohexanone oxime* (92 g, 59%), b.p. 116–118°/4 mm. (Found: C, 71·2; H, 11·0; N, 8·3. $C_{10}H_{19}NO$ requires: C, 71·0; H, 11·3; N, 8·3%.)

2-t-Butylcyclohexanone oxime. *o*-t-butylphenol (200 g), in EtOH (100 ml) was hydrogenated for 5 hr over W5 Raney Ni at 150° and 80 atm initial press. The mixture was filtered, heated to remove EtOH and dissolved in ether. The ether was shaken several times with 30% NaOHaq, dried ($MgSO_4$) and totally distilled. VPC showed that the product was a mixture of *cis*-2-t-butylcyclohexanol (39%), *trans*-2-t-butylcyclohexanol (4%) and 2-t-butylcyclohexanone (57%). Fractional distillation up a 2½' spinning band column gave 2-t-butylcyclohexanone (98 g), b.p. 81–82/14 mm.

The residue of 2-t-butylcyclohexanol (52 g) was oxidized by the method of Schmerling,[4] giving 2-t-butylcyclohexanone (36 g), b.p. 87–89°/19 mm (total recovery of ketone: 134 g). The semicarbazone had m.p. 180–182° (lit.[4] 182–183°).

The ketone (25 g), water (10 ml), hydroxylamine hydrochloride (24 g) and NaOH (13·8 g) were heated at 80° for 12 hr. The usual method of isolation gave *2-t-butylcyclohexanone oxime* (23 g, 84%), m.p. 71–72° from light petroleum, b.p. 40–60°. (Found: C, 71·0; H, 11·2; N, 8·3. $C_{10}H_{19}NO$ requires: C, 71·0; H, 11·5; N, 84%.)

[4] L. J. Dankert and D. A. Permoda, *Chem. Abstr.* **60**, 14405 (1964).
[4] L. Schmerling, *J. Am. Chem. Soc.* **69**, 1121 (1947).