323. *Stereoisomeric Pairs of Cyclic Quaternary Ammonium Salts. Part IV.*[1] *Interconversion of* N-*Benzyl*-N-*Methyl Quaternary Iodides in Hot Chloroform, and General Theoretical Discussion of Reactions Involving a Change Between Co-ordination Numbers* 3 *and* 4 *at a Six-ring Atom*

By James McKenna, Jean M. McKenna, and J. White

There is no evidence that isomerisation follows quaternisation in the reactions described in Part I, so that isomer proportions are determined by the relevant rate-constant ratios. Interconversion of *N*-benzyl-*N*-methyl quaternary iodides can, however, be effected in hot chloroform; an additional procedure for determining configurations of diastereoisomers is thus available. The factors controlling the steric course of the quaternisation (Part I) and nucleophilic displacement (Part III) reactions are examined; a further check on configurations of the quaternary salts seems possible from a study of the effect on quaternisation stereospecificity of changing the relative size of the groups R and R′ in the reaction $\rangle NR + R'I \longrightarrow \rangle \overset{+}{N}RR'\bar{I}$.

In this Paper we present two additional procedures for determining the configuration of diastereoisomeric cyclic quaternary salts of the type discussed in Parts I—III, and we examine the factors controlling the steric course of the quaternisation (Part I) and nucleophilic displacement reactions (Part III), and of stereochemically analogous processes.

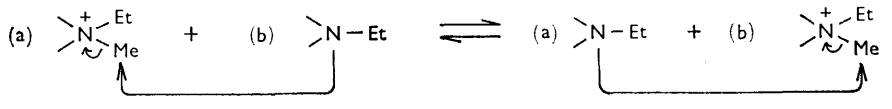
A point which must be strongly emphasised at the outset is that there is no necessary correspondence between the preferred orientation of an alkyl group R in a reduced cyclic tertiary base $\rangle NR$ and the preponderant configuration of this alkyl group in a derived quaternary salt mixture containing the diastereoisomers $\rangle \overset{+}{N}RR'\bar{X}$. In their excellent work [2] on quaternisations with tropine bases, Fodor and his co-workers at first overlooked [3] this critical point, and although Fodor has modified [4] his views recently, many other authors

[1] Part III, McKenna, Hutley, and White, preceding Paper.
[2] For reviews see Fodor, *Experentia*, 1955, **11**, 129; *Tetrahedron*, 1957, **1**, 87.
[3] Cf. Closs, *J. Amer. Chem. Soc.*, 1959, **81**, 5456.
[4] Fodor, *Chem. and Ind.*, 1961, 1500; Lecture to I.U.P.A.C. Congress, London, 1963.

continue [5] explicitly or implicitly to make the same assumption in discussions of quaternisations in various systems. There is no evidence, however, that rates of conformational inversion at nitrogen in cyclic tertiary bases >NR are in general much slower than rates of quaternisations (which is what the above supposition implies); indeed, the evidence so far as it goes [6] suggests that only with bases which are conformationally particularly rigid, like certain ethyleneimine derivatives, might the nitrogen inversion rate be comparable with the rate of a particularly fast quaternisation, *e.g.*, of a sterically unhindered amine with high concentrations of methyl or benzyl iodide. It may be calculated from the results of Roberts and his co-workers [6a] on 1,2,2-trimethylaziridine, for example, that the average lifetime of this molecule in methanol before conformational inversion at room temperature is of the order of a few tenths of a second. Clearly, there is need for additional evidence on the whole question, but at present we feel justified in discussing our quaternisation results in terms of the Curtin–Hammett hypothesis, *i.e.*, on the expectation that in all cases the ratio of quaternisation products is determined by the free-energy differences between the two competitive transition states: rate and rate-constant ratios for the competitive reactions in each quaternisation are expected to be the same.

It is first necessary to consider, however, if the observed product ratios of diastereoisomeric quaternary salts are determined essentially by the different rates of formation of the two salts or whether there has been an appreciable drift towards equilibrium under the reaction conditions. *A priori* the latter seems improbable for the quaternisations carried out at room temperature, and the question is more relevant for the slower reactions effected in refluxing solvents. Any progress towards equilibration would involve partial conversion of one diastereoisomeric quaternary salt into the other *via* an intermediate tertiary base which would be derived from the quaternary salt by nucleophilic displacement (by iodide or at a later stage, perhaps, by tertiary base: see suggested scheme for interconversion of pyrrolidine derivatives, below) at carbon α to N; *N*-benzyl or *N*-methyl groups would provide the best centres for such nucleophilic displacements. The detailed study with camphidinium salts recorded in summary in the Experimental section indicates that, under the conditions used for the quaternisations, these nucleophilic displacements (and associated equilibrations) are too slow to require consideration, although the displacements can take place quite smoothly under more forcing conditions, as shown by three separate pieces of experimental evidence: the recovery of *N*-n-propylcamphidine after treatment of *N*-methylcamphidine with n-propyl iodide at 102° (iodide attack on $^{+}$N–Me in the intermediate *N*-methyl-*N*-n-propylcamphidinium salt); the isolation of *N*-ethylcamphidine ethiodide following treatment of *N*-benzylcamphidine for a prolonged period in refluxing ethyl iodide (attack on $^{+}$N–CH_2Ph in the intermediate *N*-benzyl-*N*-ethylcamphidinium iodide, followed by reaction of the *N*-ethyl base so produced with ethyl iodide); and the failure of *N*-benzylcamphidine to yield an *N*-benzyl base benziodide (probably due to reversal of the quaternisation by iodide attack on $^{+}$N–CH_2Ph).

An examination of the stability of *trans*-*N*-methyldecahydroquinoline methiodide and the preparation of some quaternary salts of the general type $\overset{+}{\text{N}}R_2I^-$ required for the foregoing study are also recorded in the Experimental section, as is an unsatisfactory attempt to effect equilibrium between the *N*-ethyl-2,*N*-dimethylpyrrolidinium iodides by using the scheme



[5] *E.g.*, (*a*) Trojánek, Komrsová, Pospíšek, and Čekan, *Coll. Czech. Chem. Comm.*, 1961, **26**, 2921; (*b*) Ötvös, Dutka, and Tüdös, *Chem. and Ind.*, 1962, 818.

[6] (*a*) For summary see Loewenstein, Nuemer, and Roberts, *J. Amer. Chem. Soc.*, 1960, **82**, 3599; (*b*) Cf. also Saunders and Yamada, *ibid.*, 1963, **85**, 1882.

The expected fairly easy nucleophilic displacement at $^{+}N-CH_2Ph$, however, borne out by the limited experimental evidence quoted and by the known ease of racemisation of optically active ammonium salts containing benzyl (or allyl) attached to dissymmetric nitrogen * encouraged an examination of the possibility of interconversion of *N*-benzyl-*N*-methyl quaternary iodides, and we found that in all systems initially studied this could be done in hot chloroform at either reflux or higher temperatures. Since the benzyl group will be rather more space-demanding than methyl, we can thus with some assurance determine the configuration of the *N*-benzyl-*N*-methyl pairs, the diastereoisomers preponderating in the equilibria or near-equilibria established being written with the benzyl group attached in the less hindered of the two flanks at the ring nitrogen (*i.e.*, in an equatorial position for six-rings and *trans* to the 2-methyl group in 2-methylpyrrolidine salts). In all four systems studied (camphidine, 2-methylpyrrolidine, 2-methylpiperidine, *trans*-decahydroquinoline) the assigned configurations agreed with those determined by the other available methods described in the preceding Papers, so that confidence is increased in assignments for other salts in these base systems and for salts of other systems.

In considering the differential energetics of the competitive transition states in the quaternisations, one point to be emphasised is that, although some distortion of normal tetrahedral valency angles may take place in both transition states and final products, the disposition of groups around N^+ is in each case tetrahedral in general geometrical character. Furthermore, in the systems we have studied, which are devoid of other functional groups, the most important way in which the rest of the molecule can affect groups attached or partly attached to N^+ is by steric compression. Thus, the central relevant matter for consideration in quaternisations of the type we have studied is whether, in each system, a fully attached primary alkyl group will have more or less effective bulk at transition-state level than the partly attached primary alkyl group being introduced. The incoming alkyl group in the quaternisations is being attached to nitrogen *via* a carbon atom which, in the transition state, is pentaco-ordinate with bipyramidally disposed valencies; furthermore, solvation will be concentrated in the area between developing positive nitrogen and developing halide anion. Both factors in a quaternisation would make the partly attached group greater in bulk, but, on the other hand, the partial bond between nitrogen and incoming alkyl group will be longer and more deformable than the bond to the fully attached alkyl group originally present, and steric compressions can be relieved particularly easily by angular deformation especially in long bonds. Flexibility in the ring, particularly in the neighbourhood of the nitrogen atom, would probably increase the extent to which such an effect could operate. Of course, the difference in effective bulk between a fully attached alkyl group R and a partly attached alkyl group R′ will depend not only on the above considerations but also in the difference in *effective* bulks of R and R′ when these groups are in comparable structural circumstances, *e.g.*, each fully attached to a reduced cyclic ring system. For primary alkyl groups the latter type of difference is fairly small,[8] and it is clear from the overall picture of stereoselectivity in the quaternisations studied (Table 1; Part I) that the effective-bulk difference between *any* fully attached and *any* partly attached primary alkyl group is the more important consideration. Finally, the difference in the compressions introduced by other parts of the molecule at each of the two flanks of the cyclic nitrogen atom (where the alkyl groups are attached in the quaternary salt) must be a relevant consideration.

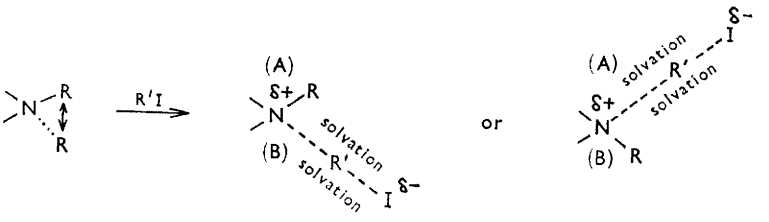
It would be premature to attempt too detailed a qualitative analysis of the data presented in Part I on the basis of the above considerations (which are summarised in the

* See, *e.g.*, ref. 7 for a summary. Many of the optically active quaternary salts examined in the early investigations also contained ^{+}N-aryl, and the resonance energy of the developing aromatic tertiary amines in the transition states was probably another factor aiding dissociation.

[7] Hückel, " Theoretical Principles of Organic Chemistry," (English edn.) Elsevier, London, 1955, Vol. 1, p. 517.

[8] See, *e.g.* (for methyl *vs.* ethyl), Eliel, " Stereochemistry of Organic Compounds," McGraw-Hill, 1962, p. 236.

Diagram), particularly in view of the variety of base systems examined. Except with tropane, the balance of factors where stereoselectivity is marked is evidently in favour of attack in the more compressed flank, so that a partly rather than a fully attached alkyl group must generally, in the examples studies, have a lower overall steric demand. Whilst we cannot be certain at present what particular relevant structural parameter causes a preferred equatorial attack in quaternisations in the tropane group, the most likely candidate appear to be ring-rigidity in the area of the nitrogen atom.



Competitive Transition States for Quaternisations

Factors controlling stereoselectivity of quaternisations of suitably unsymmetrical cyclic *N*-alkyl bases >NR by R'X, in absence of other functional groups:

(1) Differential compression by rest of molecule on flanks (A) and (B) of cyclic nitrogen atom.

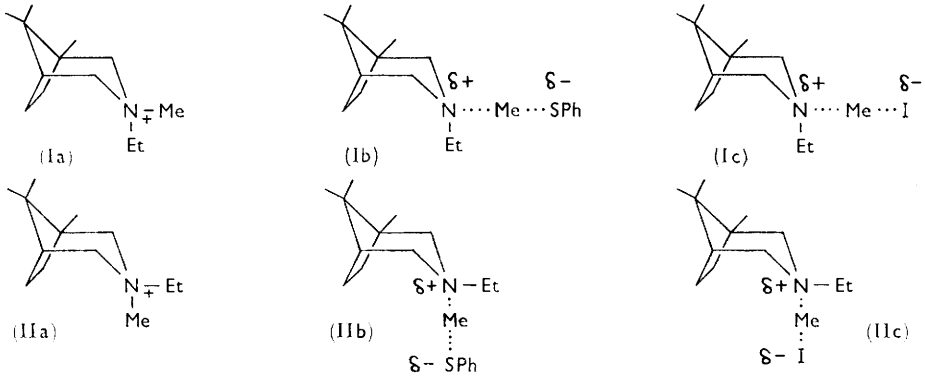
(2) Differential effective bulks of R and partly attached R' in transition states, compounded of (*a*) differential effective bulks of R and R' in comparable structural circumstances and (*b*) alteration in effective bulk of R' when incorporated in transition states shown arising from variation in (i) co-ordination, (ii) bonding, and (iii) solvation.

It is easier, especially initially, to detect and discuss stereoselectivity similarities or differences in quaternisations of fairly closely related base systems. Thus, the overall selectivity pictures for the *trans*-decahydroquinoline and the 2-methylpiperidine systems (each a 2-alkylpiperidine) are strikingly similar (and the picture for 2-methylpyrrolidine is not so very different), particularly in the way in which stereoselectivity is reduced when the cyclic *N*-methyl bases are alkylated with higher alkyl iodides, because of an increased tendency of the larger quaternising agents to attack equatorially. In work,[9] shortly to be described, on the 4-aza-5α-cholestane system (structurally analogous to *trans*-decahydroquinoline, but with an angular methyl group compressing the axial flank of the nitrogen atom) this tendency towards preferred equatorial entry, particularly with larger quaternising groups, is further increased, and alkylation of the *N*-methyl base is, in this system, more stereoselective than methylation of the *N*-alkyl base. The configurations of the steroidal quaternary salts have been independently established by interconversion of benziodides in chloroform.

We mention the results with the steroidal base system here, in advance of detailed publication, because they have given us confidence to state with some assurance another method which we believe should be frequently applicable in determining configurations of diastereoisomeric quaternary salts of the type we have been examining. Marked differences (if any) in the degrees of stereoselectivity observed in, on the one hand, methylating a cyclic *N*-alkyl base (*i.e.*, alkyl higher than methyl) and, on the other, alkylating the corresponding cyclic *N*-methyl base are examined. A higher stereoselectivity in reaction (*a*), >NR + MeI ⟶ quaternary salt mixture, than in reaction (*b*), >NMe + RI ⟶ quaternary salt mixture, indicates that, in the base system studied, marked stereoselectivity corresponds to attack by the quaternising agent on the more hindered nitrogen flank (*e.g.*, axial attack for a piperidine). On the other hand, a higher stereoselectivity in reaction (*b*) than in (*a*) indicates that marked stereoselectivity in quaternisations with that particular base system corresponds to attack on the less hindered flank (*e.g.*, equatorial attack).

[9] McKenna, McKenna, and Tulley, unpublished observations.

There are several examples of the first class quoted in Table 1, Part I, but until with the steroid base system we encountered an example of the second class we were not quite sure of the soundness of the suggested method for determining configuration: *a priori* it seemed reasonable, and gave results in agreement with those derived by the other methods described, but there remained the possibility, which we now feel safe in discounting, that other structural parameters than the different sizes of the relevant groups might be primarily responsible for the observed effects.



To examine the factors influencing the rates of the nucleophilic substitution processes with isomeric salts described in Part III, particularly the most thoroughly investigated reaction of sodium thiophenate with the epimeric *N*-ethyl-*N*-methylcamphidinium salts, we consider the epimeric reactants, (Ia) and (IIa), and the transition states for attack on $^{+}$N-methyl, (Ib) and (IIb); a corresponding discussion is of course possible for attack on *N*-ethyl. Transition states (Ic) and (IIc) are for the stereochemically corresponding quaternisations of *N*-ethyl base with methyl iodide. An immediate difficulty arises in that whereas for the quaternisations we have had to consider the free-energy differences between (Ic) and (IIc), respectively, and common reactant (the *N*-ethyl base, which is highly mobile conformationally at nitrogen), *i.e.*, the free-energy difference between (Ic) and (IIc), for the nucleophilic displacements we have to try to evaluate

$$[(\mathrm{Ib}) - (\mathrm{Ia})] - [(\mathrm{IIb}) - (\mathrm{IIa})] = [(\mathrm{Ib}) - (\mathrm{IIb})] - [(\mathrm{Ia}) - (\mathrm{IIa})]$$

i.e., we have four free-energies to consider rather than two. Experimentally this difficulty can be met by isotopic labelling (using *e.g.*, *N*-[^{14}C]methyl quaternary salts, the stereochemical homogeneity of which may be checked by nuclear magnetic resonance examination of the analogously made *N*-trideuteromethyl salts) and work of this type is in hand. In the meantime, however, if we make the assumption (which is, we believe, *a priori* a reasonable one from the available evidence, although difficult to argue in detail) that the free-energy difference between transition states, (Ib) — (IIb), is greater than that between reactants, (Ia) — (IIa), we arrive at the conclusion that it is the energetic preference of a partly attached group for the axial position in the camphidine system which determines the observed results in the nucleophilic displacement reaction as in the quaternisation, and the argument may be extended to other systems.

As indicated previously, transition states in the reactions of cyclic bases examined in these Papers are pictured as tetrahedral at nitrogen. In other reactions where there is a change between co-ordination numbers 3 and 4 at a ring atom this need not necessarily be so; for steric or other reasons (*e.g.*, conjugative forces in extended π-systems) the ring atom may be more nearly trigonal in the transition state, although tetrahedral in the product. The range of reactions covered in the general grouping indicated is very wide: protonation of ring carbanions, nucleophilic addition to cyclic ketones, reactions [10] of exocyclic enols,

[10] See, *e.g.*, Zimmerman and Thyogarajan, *J. Amer. Chem. Soc.*, 1958, **80**, 3060, and other Papers by Zimmerman and his collaborators.

alicyclic nitro-compounds, etc., and it should be emphasised that a centrally important consideration in discussion of the stereochemistry of these reactions is that of valency geometry at the relevant ring atom in the transition state. Some authors, *e.g.*, Zimmermann and his co-workers,[10] in discussion of particular reactions have been well aware of this, but in consideration of product ratios from reactions involving addition of nucleophiles to cyclic ketones the point does not seem previously to have been given the emphasis it deserves. The essential reason for the stereochemical differences between nucleophilic additions to highly hindered and to relatively unhindered cyclohexanones, for example, seems to be the nearly trigonal character of the carbonyl carbon atom in the former case as against its tetrahedral character in the latter. Thus, both oxygen (usually co-ordinated) and nucleophile can avoid the more highly hindered flank of the carbonyl group in the transition state for additions to highly hindered carbonyl groups, the nucleophile undergoing attachment on the less hindered flank. For less hindered ketones the transition state of lowest energy will be more nearly tetrahedral in character, the stereochemical outcome of the addition thus being determined by the differential compression on the two flanks of the ring-carbonyl group and by the different effective bulks of (possibly co-ordinated) fully bonded oxygen and partly attached nucleophile. More elaborate discussions have been given by Dauben and his collaborators [11] (particularly for reduction of cyclic ketones with complex hydrides) and by Kamernitskii and Akhrem in a useful review [12] of the whole field, but personally we prefer a simpler treatment directly developed from the considerations [13] indicated.

We have not been specially concerned with the question of preferred conformation of the tertiary bases used in the quaternisation studies, partly because this is not, for reasons stated, important in consideration of the preferred stereochemical course of the quaternisations. *N*-Alkyl groups are generally expected [14] to be more space-demanding than nitrogen lone-pairs, and the preferred conformation of the tertiary ring-bases should reflect this. An empirical rule [14b,15] is available correlating infrared (i.r.) bands in the 2600—2801 cm.$^{-1}$ region with presence of an axial lone-pair *trans* to and coplanar with at least two adjacent axial hydrogen atoms, and we have in general observed two or three bands in this region for bases expected to contain a preponderance of the conformation associated with the indicated structural unit.

Experimental

Quaternary Salts $>\overset{+}{\mathrm{N}}\mathrm{R}_2\overset{-}{\mathrm{I}}$.—These were prepared by the general procedure described in Part I at either reflux temperature (camphidine and *trans*-decahydroquinoline derivatives) or room temperature (2-methylpyrrolidine derivatives). Melting points and analyses are given in Table 1. No *N*-benzyl benziodide could be obtained in the camphidine series when the tertiary base and benzyl iodide were refluxed for 7 days in acetone at the usual reagent concentrations. The higher dialkiodides were formed much more slowly than the dimethiodides, particularly in the camphidine series, where the yield of the di-n-propiodide was only *ca.* 50% after 5 days' refluxing.

Stability of Some Quaternary Salts $>\overset{+}{\mathrm{N}}\mathrm{R}^1\mathrm{R}^2\overset{-}{\mathrm{I}}$.—The individual isomeric *N*-ethyl-*N*-methylcamphidinium iodides were recovered unchanged almost quantitatively after being refluxed in methanol, ethanol, chloroform, acetone, methyl iodide, or ethyl iodide, or various mixtures of these solvent for 2—3 days, sometimes in the presence of solid potassium carbonate. *N*-Methyldecahydroquinoline methiodide was likewise unaffected by refluxing ethyl iodide–ethanol. In illustration, a solution of the decahydroquinoline salt (148 mg.) in ethyl iodide (4 c.c.) and ethyl

[11] Dauben, Fonken, and Noyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2579.
[12] Kamernitskii and Akhrem, *Russ. Chem. Rev.*, 1961, **30**, 43.
[13] Cf. McKenna and White, *Tetrahedron Letters*, 1963, 1493; Lansbury and McLeay, *J. Org. Chem.*, 1963, **28**, 1940; Ritchie, *Tetrahedron Letters*, 1963, 2145.
[14] *Inter alia* (*a*) Pumphrey and Robinson, *Chem. and Ind.*, 1963, 1903; (*b*) Moynehan, Schofield, Jones, and Katritzky, *J.*, 1962, 2637; cf. however, (*c*) Aroney and Le Fèvre, *J.* 1958, 3002.
[15] Bohlman, *Chem. Ber.*, 1958, **91**, 2157; House, Wickham, and Muller, *J. Amer. Chem. Soc.*, 1962, **84**, 3139.

TABLE 1

Quaternary derivatives $>\overset{+}{N}R_2\bar{X}$

Compound	M. p. (lit. m. p. in brackets)	Cryst. from	Found (%) C	H	N	Formula	Reqd. (%) C	H	N
Derivatives of camphidine									
N-methyl methiodide	300° (272 [a]; 300 [b])	Me_2CO							
N-*methyl methopicrate*	266		52·3	6·4	13·6	$C_{18}H_{26}N_4O_7$	52·7	6·3	13·7
N-*ethyl ethiodide*	265 (252 [a])	Me_2CO–Et_2O	49·5	8·0	4·4	$C_{14}H_{28}IN$	49·8	8·3	4·2
N-*n-propyl n-propiodide*	170	Me_2CO–Et_2O	52·5	8·8	3·6	$C_{16}H_{32}IN$	52·6	8·8	3·8
Derivatives of 2-methylpyrrolidine									
N-*methyl methiodide*	354	EtOH–Et_2O			6·0	$C_7H_{16}IN$			5·8
N-*ethyl ethiodide*	306	Me_2CO	39·9	7·5	5·0	$C_9H_{20}IN$	40·1	7·4	5·2
N-*n-propyl n-propiodide*	263	EtOH	44·8	7·8	4·6	$C_{11}H_{24}IN$	44·5	8·1	4·7
N-*benzyl benziodide*	177	EtOH	58·2	6·4	3·3	$C_{19}H_{24}IN$	58·0	6·1	3·6
Derivatives of *trans*-decahydroquinoline									
N-*methyl methiodide*	282	Me_2CO	44·8	7·4	5·0	$C_{11}H_{22}IN$	44·8	7·5	4·7
N-*methyl methopicrolonate*	185	EtOH	57·9	6·8	16·1	$C_{21}H_{29}N_5O_5$	58·5	6·7	16·2
N-*ethyl ethiodide*	212	Me_2CO–$CHCl_3$	48·2	8·0	4·4	$C_{13}H_{26}IN$	48·3	8·1	4·3
N-*ethyl ethopicrate*	82	EtOH	53·6	6·7		$C_{19}H_{28}N_4O_7$	53·8	6·6	
N-*ethyl ethopicrolonate*	140	EtOH	60·0	7·4	15·3	$C_{23}H_{33}N_5O_5$	60·1	7·2	15·3
N-*n-propyl n-propiodide*	265	Me_2CO–$CHCl_3$	51·2	8·8	3·8	$C_{15}H_{30}IN$	51·3	8·6	4·0
N-*n-propyl n-propopicrate*	136	EtOH	55·9	7·0	12·6	$C_{21}H_{32}N_4O_7$	55·8	7·1	12·4

[a] Trojánek, Komrsová, Pospíšek, and Čekan, *Coll. Czech. Chem. Comm.*, 1961, **26**, 2921 [active compounds, m. p.s not strictly comparable with those of (±)-isomers]. [b] Rice and Grogan, *J. Org. Chem.*, 1957, **22**, 185.

alcohol (1 c.c.) was refluxed with finely ground potassium carbonate (1 g.) for 4 days and then evaporated and the residue extracted with chloroform. The extract (132 mg.) was completely insoluble in light petroleum, had m. p. 280—282° (from acetone), and was identical (mixed m. p. and i.r. spectrum) with the initial methiodide.

When the experiments with the *N*-ethyl-*N*-methylcamphidinium salts in non-halide solvents were repeated at 100° in sealed tubes, the yields of recovered quaternary salts were reduced, but no definite evidence of progress towards equilibration of isomers could be obtained. The same was true when the *N*-ethyl-*N*-methyl isomers derived from 2-methylpyrrolidine were heated at the same temperature with a mixture of acetone and 1-ethyl-2-methylpyrrolidine. When the dry camphidinium salts were heated at their melting points, some *N*-methyl base was formed, presumably by loss of ethylene.

Exchange of N-*Methyl* N-*Benzyl Groups during Quaternisations.*—When *N*-methylcamphidine was refluxed with n-propyl iodide (b. p. 102°: no other solvent added) for 3 days, the quaternary iodide mixture, isolated in 60% yield, had a similar composition to that indicated in Part I (preparation in refluxing acetone), but the recovered base was identified as *N*-n-propylcamphidine by i.r. spectrum and mixed m. p. of the picrate with an authentic specimen.

When *N*-benzylcamphidine and ethyl iodide were allowed to react for 7 days in refluxing acetone in presence of potassium carbonate, using the standard conditions indicated in Part I, the yield of quaternary salt was 20%; it was identified as *N*-ethylcamphidine ethiodide by m. p. (264° for all fractions from acetone), i.r. spectrum and analysis [Found: C, 49·3; H, 8·1. Calc. for $C_{19}H_{30}IN$ (*N*-benzylcamphidine ethiodide): C, 57·1; H, 7·5. Calc. for $C_{14}H_{28}IN$ (*N*-ethylcamphidine ethiodide): C, 49·8; H, 8·3%].

Interconversion of N-*Benzyl*-N-*Methyl Quaternary Salts in Hot Chloroform.*—The quaternary salts (50—100 mg.) in chloroform (5—10 c.c.) were refluxed or heated to a higher temperature in a glass-lined steel autoclave; details for individual reactions are given in Table 2. Recoveries of quaternary salt mixtures were of the order of 90—100%, little or no base or base hydroiodide being obtained under the conditions indicated in the Table, and only in odd cases a very slight odour of benzyl iodide: any loss resulted mainly from transfer operations. The composition of the crude recovered quaternary salts was estimated by i.r. and nuclear magnetic resonance

TABLE 2

Interconversion of *N*-benzyl-*N*-methyl quaternary iodides in chloroform

Base system	Conditions	Initial compound or major component of initial mixture of isomeric iodides [a]	Proportion [a] of *N*-benzyl base methiodide in isomerised mixture	Diagnostic bands i.r. ($cm.^{-1}$)	n.m.r. (τ) [b]	Further comments
Camphidine	62°; 96 hr.[c]	*N*-Benzyl base methiodide (pure)	++ or +++	Numerous bands in 850—1050 region	*ca.* 6·6, 6·30	[d]
	,,	*N*-Methyl base benziodide (pure)	++ or +++			
trans-Decahydroquinoline	62°; 96 hr.[c]	*N*-Benzyl base methiodide (0 ⟶ +)	+	870, 882	6·83, 6·77	[e]
	85°; 72 hr.	,,	+			
2-Methylpyrrolidine	85°; 72 hr.	*N*-Methyl base benziodide (+)	+	852, 865, 905	7·06, 6·77	[f]
	,,	*N*-Benzyl base methiodide (++)	+			
2-Methylpiperidine	85°; 48 hr.	*N*-Benzyl base methiodide (0 ⟶ +)	+	868, 878	6·91, 6·80	[g]
	85°; 96 hr.	,,	+			

[a] For nomenclature of salts see Part III; for meaning of indication of proportions of major components (+, ++, +++) see Part I. [b] N.m.r. bands quoted are the *N*-methyl signals (see Part II). Additional confirmation was sometimes possible from the $N\text{-}CH_2Ph$ signals. [c] Refluxing chloroform solutions. [d] Considerable decomposition to benzyl iodide and other compounds on being heated at 100° for 24 hr. [e] I.r. changes slight but definite. Proportions (n.m.r.) of *N*-benzyl base methiodide *ca.* 60% initially (peak ratio 1·5 : 1) rising to *ca.* 65—70% (ratio 2 : 1) after treatment at 62°, and to *ca.* 75—80% (ratio 3·5 : 1) after treatment at 85°. [f] Salts unaltered at 62° for 260 hr. [g] I.r. changes slight but definite. Proportions (n.m.r.) of *N*-benzyl base methiodide *ca.* 60% initially (peak ratio 1·5 : 1) rising to *ca.* 70% (ratio 2·5 : 1) after 48 hr. at 85°; ratio unchanged after a further 48 hr.

spectroscopy; for the latter both an A.E.I. R.S.2 and a Varian A60 instrument (both operating at 60 Mc./sec.) were employed.

In development work in the camphidine system, the *N*-benzyl base methiodide was isolated from the reaction mixture obtained from its isomer in refluxing chloroform, and was identified as the *N*-benzyl base methopicrate, m. p. 145°.

We thank the D.S.I.R. for a Maintenance Grant (to J. W.) and the University of Sheffield for research facilities (to J. M. McK.).

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, SHEFFIELD 10. [*Received, June 30th,* 1964.]