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N-Cyanoammonium Salts as Intermediates in the von Braun Cyanogen Bromide Reaction

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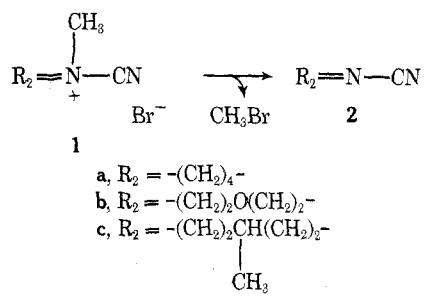
Cyanogen bromide was treated in a 1:1 ratio with a variety of tertiary amines (*e.g.*, *N*-methylpiperidine, *N*-methyl-*trans*-decahydroquinoline) to give *N*-cyanoammonium bromides (**1**), which have been trapped at temperatures of −50 to −10° for the first time, in crystalline form, and analyzed. Spontaneous decomposition of the bromides (**1**) led to methyl bromide and a secondary cyanamide (**2**). A low-temperature nmr kinetic study of step **1** → **2** in a variety of solvents yielded first-order rate constants. This two-step, low-temperature technique gave *sec*-cyanamides and, in turn, amines in yields superior to previous ones. In addition, no protection of hydroxyl groups is needed. Replacement of bromide by nonnucleophilic anions gave a number of stable cyanoammonium salts. N diastereoisomers (92:8) of *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium fluoroborate (**3b** and **4b**) have been separated and their configurations determined by combined pmr, ^{13}C nmr, and X-ray crystallographic studies, whereby equatorial preference of N-cyanation was established. These stable cyanoammonium salts were then reconverted into the epimeric bromides (**3a** and **4a**), and relative reaction rates of axial cyano *vs.* equatorial cyano epimers in the step **1** → **2** were determined. Furthermore, the decomposition of the chiral intermediate, (*S*)-(+)-*N*-cyano-*N*-*sec*-butyl-4-methylpiperidinium bromide (**15a**), gave (*R*)-(−)-*sec*-butyl bromide (**16**) with inversion. Some synthetic aspects of the cyanoammonium salt intermediates are outlined.

The von Braun cyanogen bromide reaction[1] (illustrated in Scheme I) has been extensively applied[2] over the past 70 years, but no mechanistic study has been undertaken, except some early unsuccessful approaches based on analogies with triphenylphosphine–cyanogen bromide[3] or with arsines.[4] The first circumstantial evidence for the mechanism was presented by Harper, *et al.*,[5] and Casy, *et al.*,[6] respectively. Methadone, a tertiary amine containing a carbonyl group, gave with cyanogen bromide no incorporation of bromide ion, but an unexpected cyclic, nitrogen-free compound: a tetrahydrofuran derivative. Therefore, an *N*-cyanoammonium salt structure was suggested for the first time as a possible intermediate, which underwent cleavage by carbonyl oxygen as an internal nucleophile. Along similar lines Albright and Goldman[7] recently succeeded in converting different alkaloids into cyclic ethoxy cyanamides with cyanogen bromide, using ethanol as a protic solvent. The incorporation of ethoxide instead of bromide occurred, and the overall steric course was one of inversion. This is further circumstantial evidence for the same type of intermediate, with no carbon–bromide bond; displacement by alkoxide ion should have otherwise resulted in a double inversion, equaling overall retention.

Preparation of *N*-Cyanoammonium Salts. We have undertaken a different study[8a,b] with the aim of finding direct evidence by trapping the postulated cyanoammonium salts for the first time. The present paper gives a full account of the experiments we have done in this field during the last 3 years. As a preliminary approach a stable cyanoammonium salt was sought, because any nucleophilic ion would very easily result in the breaking of the rather weakened *N*-methyl or other *N*-alkyl carbon bond.

Scheme I



There was no reagent known that would contain a cyanium cation compensated by any of the known nonnucleophilic anions, such as fluoroborate. However, a complex salt of cyanogen chloride and antimony pentachloride, described by Woolf[9] in the 1950's, gave cyanogen at the cathode upon electrolysis. It thus seemed an appropriate cyanium cation donor. In the meantime ^{13}C nmr studies were undertaken[10] on this complex salt, which showed that it is certainly not a cyanium hexachloroantimonate, but has the antimony coordinated with the nitrogen, not the chlorine, of cyanogen chloride. Nonetheless, the crystalline complex salt still held the promise of being a potential CN cation donor.

Therefore, we treated $CNCl \cdot SbCl_5$ with triethylamine in nitromethane; the ir spectrum of the product showed a strong C≡N stretch around 2200 cm^{-1}. The nmr spectrum indicated a strong downfield shift (by 0.8 ppm) of the methylene protons adjacent to nitrogen, indicative of the conversion of the amine nitrogen into a quaternary

Table I
Cyanoammonium Salts and Related Compounds

Registry no.	*N*-Cyanoammonium ion	Anion	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Calcd, % X	Found, % C	Found, % H	Found, % N	Found, % X
51075-32-2	*N*-Methylpiperidinium	Chloroantimonate	78–80	$C_7H_{13}Cl_6N_2Sb$	18.2	2.9	5.4	46.5[b]	18.07	3.31	5.19	44.86[b]
51075-33-3	*N*-Methylpiperidinium	Bromide	0 dec	$C_7H_{13}BrN_2$	40.97	6.34	13.65	39.04[a]	41.10	6.32	13.81	
51075-34-4	*N*-Methylpiperidinium	Methanesulfonate	78–80	$C_8H_{16}N_2O_3S$	43.63	7.30	12.72	14.54[c]	44.24	7.43	12.50	15.07[c]
51075-36-6	*N*-Ethylpiperidinium	Methanesulfonate	74–75	$C_9H_{18}N_2O_3S$	46.05	7.69	11.96	13.67[c]	44.86	8.28	11.50	13.17[c]
51157-32-5	*N*-Methylmorpholinium	Methanesulfonate	92.5	$C_7H_{14}N_2O_4S$				14.50[c]				15.54[c]
51075-37-7	4-Hydroxypiperidine		Liquid	$C_6H_{10}N_2O$	57.14	7.93	22.22		56.91	8.06	22.26	
51075-39-9	3-β-Hydroxytropanium	Fluoroborate	142	$C_9H_{15}BF_4N_2O$	42.55	5.91	11.02		42.22	6.00	10.80	
51075-41-3	3-Oxotropanium	Fluoroborate	158–159	$C_9H_{13}BF_4N_2O$	42.86	5.16	11.11		43.09	5.12	11.04	
51075-42-4	3-Oxotropanium	Bromide	5 dec	$C_8H_{10}BrN_2O$	44.08	5.31	11.42		44.42	5.37	11.69	
51075-44-6	1-Hydroxymethylquinolizidinium	Fluoroborate	162–163	$C_{11}N_{19}BF_4N_2O$	46.81	6.74	9.98		46.91	6.65	10.11	
51153-93-6	*N*-Methyl-*trans*-decahydroquinolinium	Bromide	20 dec	$C_{11}N_{19}BrN_2$	50.96	7.34	10.81	30.89[a]	51.25	7.26	11.08	
51153-95-8	*N*-Methyl-*trans*-decahydroquinolinium	Chloroantimonate	175–180	$C_{11}N_{19}Cl_6N_2Sb$			5.45				5.45	
	N-Methyl-*trans*-decahydroquinolinium	Fluoroborate epimers		$C_{11}N_{19}BF_4N_2$	49.66	7.14	10.54	28.59[d]	49.53	7.05	10.76	28.42[d]
51075-45-7	*N*-Methyl-*trans*-decahydroquinolinium	Fluoroborate CN equatorial	135–136	$C_{11}H_{19}BF_4N_2$	49.66	7.14	10.54	28.59[d]	49.75	7.15	10.52	28.53[d]
51075-46-8	*N*-Methyl-*trans*-decahydroquinolinium	Fluoroborate CN axial	148–152	$C_{11}H_{19}BF_4N_2$	49.66	7.14	10.54	28.59[d]	49.95	7.40	10.47	
51075-47-9	*N*-Cyano-*trans*-decahydroquinoline			$C_{10}H_{16}N_2$	73.17	9.75			73.30	9.59		
51075-48-0	*N*-*sec*-Butyl-4-methylpiperidine		Bp 82 (22 mm)	$C_{10}H_{21}N$	77.42	13.54			77.24	13.53		

[a] Bromine. [b] Chlorine. [c] Sulfur. [d] Fluorine.

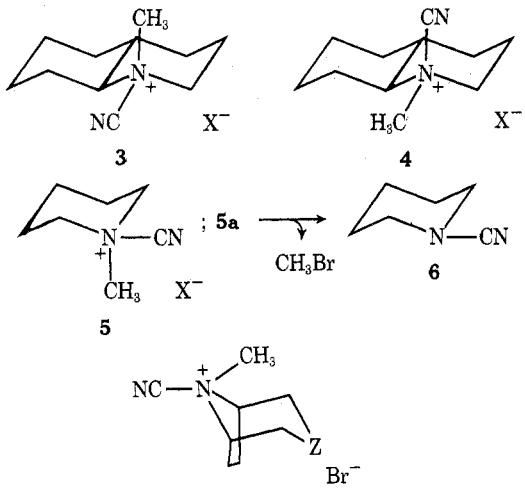
Table II
Significant Spectral Data of Cyanoammonium Salts, Cyanamides, and Some Related Compounds

Registry no.	*N*-Cyanoammonium ion	Anion	Ir, cm^{-1} (C≡N)	$^+NCH_3$ or $^+N(CN)CH_3$	$^+NCH_2$ or ^+NCH	Remote CH_2 and CH	Other protons
51075-49-1	Triethylammonium	Hexachloroantimonate	2200[a]	3.35 (t)	1.42 (q)		
51075-50-4	Triethylammonium	Bromide		2.86[e]	3.35[e] (q)	2.00[e]	
				3.08[b]	3.22[b] (q)	2.10[b]	
	N-Methylpiperidinium	Hexachloroantimonate	2200[j,k]	3.05 (s)	3.81,[c] 3.68	2.15[c]	
				3.22[b] (s)	3.95, 3.76 (m)	1.93[b]	
				3.15[b] (s)			
51075-51-5	*N*-Methylpiperidinium	Hexafluoroantimonate	2200[m]	3.14 (broad, s)	3.65 (m)	2.00	
	N-Methylpiperidinium	Methanesulfonate	2278[i]	2.88[b]	3.68	3.10 (CH_3SO_3)	
				2.90[c]	3.55[c]	3.18[c]	
				2.85[d]	3.55[d]	3.10[d]	

1530-87-6	Piperidine[h]		2205[l]		3.18[c,e]	1.62[c,e]	
	N-Ethylpiperidinium	Methanesulfonate	2200[i]	2.72[d]	3.7–3.4 3.10	1.42 (CH_2CH_3)	3.10 (CH_3SO_3)
51075-53-7	*N*-2,6-Trimethylpiperidinium	Methanesulfonate	2200[i]	3.02[c] (eq) 2.86[c] (ax)	3.2[c] (broad)	1.70[c]	3.30[c] (CH_3SO_3) 1.55 (d, J = 7 Hz, CCH_3)
51075-54-8	*N*-2,6-Trimethylpiperidinium[f]	*p*-Toluenesulfonate	2275[i]	2.93[c] (major) 2.60 (minor)	3.55[c] (broad)	1.82[c]	2.50[c] Ar–CH_3 major 1.47 (d, J = 6 Hz, CCH_3) 1.35 (d, J = 6 Hz, CCH_3)
	N-Methylmorpholinium	Methanesulfonate	2200[i]	2.78[d]	3.45[d]	4.15[d] (OCH_2)	
51157-34-7	*N*-Methyl-4-hydroxypiperidinium	Methanesulfonate	2220[i]	2.67[c]	3.48[c]	2.2	2.97 (CH_3SO_3)
51157-35-8	*N*-Methyl-4-hydroxypiperidinium	*p*-Toluenesulfonate	2215[i]	2.90[d]	3.42[d]	4.15 (CHOH)	2.52[d] ($ArCH_3$)
1530-89-8	Morpholine[h]		2215[l]		3.26[d] (NCH_2)	3.75[d] (OCH_2)	
	3β-Hydroxytropanium	Fluoroborate	2280[i]	3.68[d] (s)	4.82[d] (H-1,5)	1.95[d] (H-2,3,6,7)	4.0 (CHOH) 2.70 (OH)
	3-Oxotropanium	Fluoroborate	2280[i]	4.01[d]	5.1[d] (H-1,5)	2.0[d]	2.8 (CH_2CO)
	N-Methyl-*trans*-decahydroquinolinium	Hexachloroantimonate	2220[i]	3.10[b,f] (eq, major) 3.02 (ax, minor)	3.85[b,f] (H-2 eq) 3.68 (H-2 ax) 2.9 (H-9)	1.9[b,f]	
51153-96-9	*N*-Methyl-*trans*-decahydroquinolinium	Methanesulfonate	2280[i]	2.56[b,f]	3.55[b,f] (H-2,9) (broad)	1.72	3.20 3.10 (CH_3SO_3)
	N-Methyl-*trans*-decahydroquinolinium	Fluoroborate (CN eq)	2280[i]	3.63[d] 4.00[e]	4.34[d] (H-2 eq) 4.25 (H-2 ax) 4.13 (H-9)	1.70[d]	
	N-Methyl-*trans*-decahydroquinolinium	Fluoroborate (CN axial)	2280[i]	3.74[d]	4.36 (H-2 eq) 3.96 (H-2 ax) 3.87 (H-9)	1.70[d]	
51157-36-9	*N*-*sec*-Butyl-2-(3-bromopropyl)-cyclohexylamine[h]		2200[i]		3.48 (q, J = 7.1 Hz, CH_3CH)	1.65	1.21 (J = 7.1 Hz, CH_3CH) 0.95 (J = 6 Hz, CH_3CH_2)
51075-56-0	*N*-*sec*-Butyl-4-methylpiperidinium	Fluoroborate	2220[i]		3.50[e] (CH_2) 4.80[e] (CH)	1.72[e]	1.05 (CH_2CH_3) ($CHCH_3$) 1.35 (4-CH_3)
20696-86-0	4-Methylpiperidine[h]		2200[l]		2.8[g]	1.1[k]	0.68 (d, CCH_3)
51075-57-1	*N*-*sec*-Butyl-4-methylpiperidine[g]	Fluoroborate			3.2[e] 2.8	1.75[e]	0.95 (CH_2CH_3, $CHCH_3$) 1.35 (4-CH_3) 4.2 (NH)
51075-58-2	*N*-*sec*-Butyl-4-methylpiperidine[g]	Hydrobromide			3.3[e] 2.75	2.00[e]	1.08 (2 d, s, CH_2CH_3, $CHCH_3$) 1.45 (4-CH_3)
	1-Hydroxymethylquinolizidinium	Fluoroborate	2275[m]		4.7–4.0[d] (m, s, H-4,5,10)	2.00 (m, 12 H) 2.58 (H-1)	3.45 (CH_2O) 2.75 (OH)
10159-79-2	1-Hydroxymethylquinolizidine[g]				2.80[d] (H-4,5 eq)	2.0[d] 1.6	3.57 (CH_2O) 4.0 (OH)
51075-60-6	Methylpyrrolidinium	Fluoroborate	2200[i]	3.80[d]	4.40[d]	2.00[d]	
51075-61-7	*N*-Methyl-4-bromobutanamine[h]			2.82			
51075-62-8	*N*-4-(*N'*-methyl)piperidinium *N*-methylbutanamine bromide[h]			3.40[e] 2.80 $CH_3N(CN)$	3.70[e] (6 H)	1.80	

[a] Nitromethane. [b] DMSO-d_6. [c] Acetone-d_6. [d] Acetonitrile-d_3. [e] Chloroform-d. [f] Mixture of chloroform-d and acetonitrile-d_3. [g] Not a cyano compound. [h] Cyanamide. [i] Film. [j] Nitromethane. [k] Nujol. [l] Dimethylformamide. [m] Dinethyl sulfoxide.

Scheme II



3 **4**

5 **6**

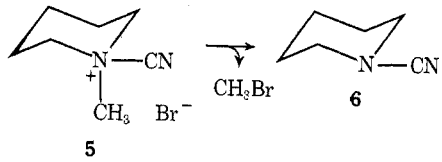
7

a, X = Br^-
b, X = BF_4^-
c, X = $O_3SCH_3^-$
d, X = $O_3S\text{-}C_6H_4CH_3\text{-}p^-$
e, X = $SbCl_6^-$

a, Z = CO
b, Z = CH(OH) ax
c, Z = CH(OH)eq

ammonium ion. Similarly, the chemical shift of the *N*-methyl signal of *N*-methylpiperidine, in its addition compound with the $CNCl\cdot SbCl_5$ complex, moved downfield by 0.82 ppm. Those shifts were of the same order of magnitude as those in the general quaternization of tertiary nitrogen into an ammonium ion center.[12c] Thus, we have indeed isolated *N*-cyanoammonium salts, *e.g.*, **5e** (Scheme II).

Although a variety of cyanoammonium hexachloroantimonates have now been prepared and analyzed (Tables I and II), these stabilized salts were not suitable for further study on any nucleophilic displacements of cyanoammonium salts because of solubility reasons. Therefore, as the next step, we intended to isolate the actual intermediates of the cyanogen bromide reaction. In ethereal solution at temperatures ranging from −10 to −50° we succeeded in isolating a white precipitate[8a,b] which could be filtered and dried. These cyanoammonium bromides were white, crystalline solids that have been kept for several days under vacuum at −16°. However, depending on their alkyl group, they decomposed between −10 and 10° and gave the cyanamides in very high yields. Thus, they proved to be the real intermediates in the von Braun reaction. They were immediately analyzed. Elemental analyses gave carbon, hydrogen, and nitrogen values close to the calculated ones for these unstable cyanoammonium bromides (Table I). On the other hand, *N*-cyano-*N*-methylpiperidinium bromide (**5a**) gave only the final displacement products, *N*-cyanopiperidine (**6**) and methyl bromide, the latter of which was trapped and quantitatively analyzed as *N*-ethylpiperidine methobromide. The cyanoammonium bro-



5

mides, although sensitive, could be converted at −20° into "stabilized" salts, by ion exchange with silver methanesulfonate, *p*-toluenesulfonate, hexafluoroantimonate, or fluoroborate. Shortly after these experiments[8a] a different and independent approach was published in a communication by Paukstelis and Kim,[11] who converted the reaction mixtures of a few tertiary amines with cyanogen bromide into *N*-cyanoammonium fluoroborates with triethyloxonium fluoroborate, *i.e.*, the Meerwein salt.

The cyanoammonium bromides, *e.g.*, **1a–c, 3a, 4a, 5a, 7a–c,** etc., we have prepared were derived from *N*-methyl- and *N*-ethylpiperidine, 4-hydroxy-*N*-methylpiperidine, *N*-methylmorpholine, tropine, pseudotropine, tropinone, lupinine, *N*-methyl-*trans*-decahydroquinoline, 1,4-diazabicyclo[2.2.2]octane, and quinine. Most of these bromides were converted into the stable salts *via* ion exchange.

Table I indicates most physical and analytical properties of a number of both unstable and stabilized cyanoammonium salts. Table II contains the spectral data. Infrared spectra are consistent with their structure, the C≡N bond appearing as a sharp, medium-intensity band between 2200 and 2280 cm^{-1}.

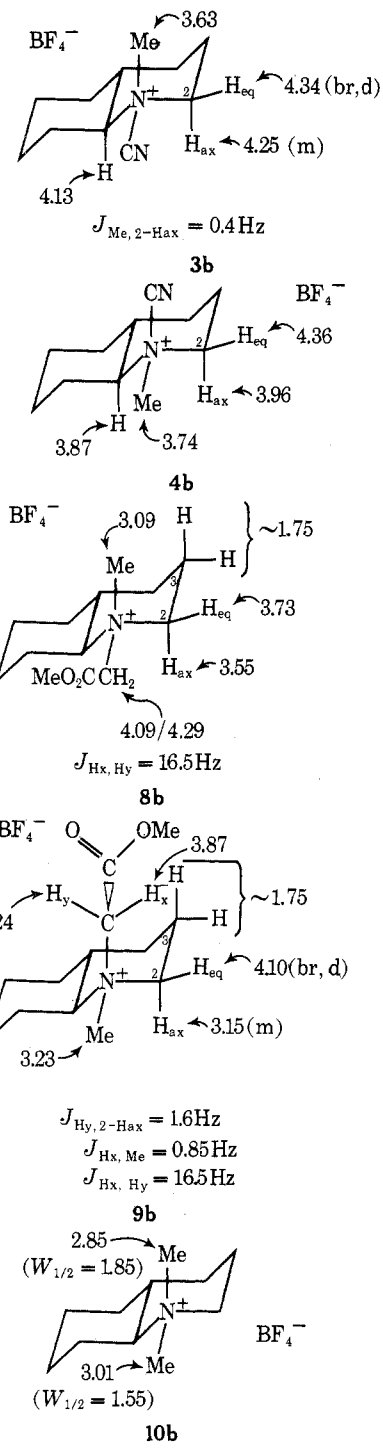
Structure and Stereochemistry. Our technique of low-temperature precipitation of the cyanoammonium bromide with subsequent conversion into the *stabilized* cyanoammonium salt gave near-quantitative yields of the latter. With these stable salts we were in the position to determine the preferred steric course of cyanation. The model we have used was (±)-*N*-methyl-*trans*-decahydroquinoline because of its configurational and conformational rigidity. Cyanation thereof by cyanogen bromide (addition of cyanide ion is now known as cyanylation[13]) was immeasurably fast and nearly quantitative. No traces of the tertiary amine could be detected by spectral methods, at as low as −65°, in a variety of solvents (after adding 1 mol of cyanogen bromide per mole of the tertiary amine). Cyanation may be regarded as a special case of quaternizations of nitrogen. *N*-Methyl-*trans*-decahydroquinoline in ethereal solution gave a very high yield of a crystalline product, which, based upon integration of the two pmr methyl signals (at δ 3.63 and 3.74 ppm; see Table II and Scheme III), consisted of the two N-epimeric bromides **3a** and **4a** in a ratio of 92:8. Those were separated by fractional crystallization after conversion into the fluoroborates **3b** and **4b** (Scheme III).

The crude product melted at 127–130° after recrystallization. The purified major product had mp 156°. The *cT* diagram of mixtures of the pure isomers showed a eutectic point at 100° and 50% composition; thus they gave a *definite* mixture melting point depression.

These cyanoammonium fluoroborates could also be prepared *in situ* if the reactions were done in acetonitrile with subsequent addition of silver fluoroborate; removal of silver bromide and freeze drying (or vacuum evaporation at low temperature) afforded the mixture of the stereoisomeric fluoroborates **3b** and **4b.** The Meerwein salt technique did not allow isolation of the minor isomer. The individual isomers, as well as their mixture, gave correct elemental analysis data (Table I). Both have been subjected to detailed spectroscopic study. Moreover, the major stereoisomer was analyzed by X-ray crystallography.[12b]

Nuclear Magnetic Resonance Studies. Extensive pmr measurements at 250 and 100 MHz enabled unequivocal determination of relative configurations about the chiral nitrogen atom. Only the most important and pertinent data are given in Table II and Scheme III. The major stereoisomer (**3b**) showed three deshielded protons at δ 4.13, 4.25, and 4.34 ppm. The minor isomer (**4b**) contained the equivalent protons at δ 3.87, 3.96, and 4.36 ppm, respectively. The difference is striking regarding the first two chemical shifts. Therefore, the δ 4.13 and 4.25 ppm signals were assigned to H-9 and to H-2 axial, these protons being deshielded by an adjacent electronegative (*i.e.*, CN) group

Scheme III



in the major product. The signals at δ 3.87 and 3.96 ppm were assigned to H-9 and H-2 axial in the minor stereoisomer, these being shielded by the adjacent equatorial *N*-methyl group. The two low-field signals at δ 4.34 and 4.36 ppm, in practically the same position in the two epimers, were attributed to the less affected equatorial protons at C-2. This by itself is evidence that the cyano group is equatorial in the major product, hence it must be axial in the minor product. In addition a long-range *W* coupling (J = 0.4 Hz) between *N*-methyl and H-2 axial of the major isomer could be decoupled by double irradiation of either signal at δ 3.63 or 4.25 ppm. There was no appreciable coupling between NCH_3 and H-9 protons.

In addition, methoxycarbonylmethylation of the same amine resulted in a 4:1 ratio of two N stereoisomers (**8a** and **9a**). The fluoroborate of the major and the minor products, **8b** and **9b**, respectively, indicated two diastereotopic methylene signals of the methoxycarbonylmethyl group at δ 4.29 and 4.09 ppm (J = 16.5 Hz) and at δ 4.24 and 3.87 ppm (J = 16.5 Hz), respectively. Also in the minor product the protons at C-3 have been located at approximately δ 1.75 ppm, by decoupling of the H-2 signals at δ 4.10 and 3.15 ppm. Furthermore, ^{14}N decoupling resulted in significant change in signal shape about δ 1.75 ppm, in agreement with results that β protons are more strongly coupled[14] to ^{14}N than are other protons. Irradiation at δ 1.75 ppm resulted in a 10% nuclear Overhauser effect (NOE) in the δ 3.87 ppm signal, which we assigned as H_x. Therefore, the methoxycarbonylmethyl group is axial in the minor product. The two C-2 proton assignments were made on the basis of their splitting patterns. It should be noted that, in accordance with the configuration derived from the NOE, *W*-type couplings were observed on the one hand between H_y and H-2 axial, and on the other between H_x and *N*-methyl. The two couplings show that rotation of the axial methoxycarbonylmethyl group is restricted in **9**.

A further reference compound, *N,N*-dimethyl-*trans*-decahydroquinolinium fluoroborate (**10b**), showed a difference in chemical shift between the two methyl signals of δ 2.85 and 3.01 ppm, respectively, and there was a considerable difference in half-height peak width (1.85 and 1.55 Hz). The greater half-height width is due to the *W* coupling of the higher field protons with H-2 axial and H-9 axial, which can only be the case if that methyl group was itself axial. The chemical shifts of the axial methyl group and methylene protons appeared at higher field than those of their equatorial counterparts in a number of other *trans*-decahydroquinoline derivatives.[12b]

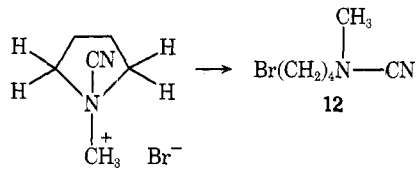
In conclusion, evidence based on pmr spectra point to the fact that cyanation of *N*-methyl-*trans*-decahydroquinoline took place preferentially in the equatorial position. In addition an extensive ^{13}C nmr spectroscopic study of compounds **3b**, **4b**, **8b**, **9b**, and **10b** was also undertaken. Details of that work will be published.[15] Wenkert, *et al.*[15] have shown that the *N*-methyl carbon atom of the major product of cyanation of the same base resonated at 8.7 ppm higher field than the one in the minor product. Furthermore, the C-3 and C-10 signals appeared at 3.4 and 4.1 ppm higher field than in the minor product, respectively. The conformational effect, in particular the 1,3-diaxial interaction of the two protons at C-10 and C-3 with axial *N*-methyl, would result in considerable shielding of carbons 10 and 3, while the axial cyano group in the major epimer does not as greatly affect those ^{13}C nmr shifts (similar to related cyclohexane derivatives[16]).

X-Ray Crystallography. X-Ray measurements were made at room temperature using a Picker four-circle diffractometer with Cu Kα radiation, proving structure **3b** for the major product of cyanation. Details of that X-ray crystallographic study will be published elsewhere.[17]

Thus, the combined pmr, ^{13}C nmr, and X-ray crystallographic studies[12b] have confirmed the complete geometry of the N-epimeric *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium fluoroborates, and are in complete agreement with other quaternization studies carried out with the same type of compound.

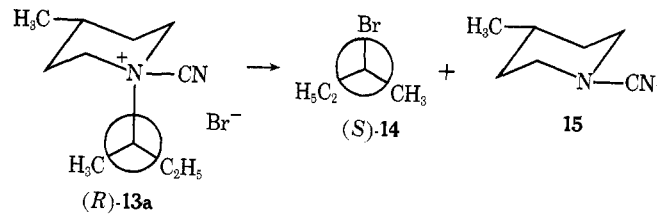
Reactions of *N*-Cyanoammonium Salts. Interionic Reaction. The reaction we studied most extensively is nucleophilic displacement of one of the alkyl groups from the chiral (or pseudo-chiral) nitrogen of the *N*-cyanoammonium salts. Two models in particular have been studied: *N*-methyl-*N*-cyanopiperidinium bromide (**5a**) and *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium bromide (**3a** and **4a**). In addition, preliminary studies have been undertaken with *N*-cyano-*N*-methylpyrrolidinium bromide

Scheme IV



11a

Scheme V



(R)-13a

(11a). For solubility reasons most of our kinetic studies were carried out with **3a** and **4a**. All *N*-cyanoammonium bromides we have isolated or prepared *in situ* are spontaneously decomposed at temperatures ≥0°. None were stable above 25° (see Kinetic Studies).

The bromides were attacked by other nucleophiles as well, such as alcohols or pyridine. The stable cyanoammonium methanesulfonates, *p*-toluenesulfonates, fluoroborates, or hexafluoroantimonates were decomposed in solution upon the addition of lithium bromide, whereby the bromide ion displaced the *N*-methyl group in most cases. With *N*-ethyl-*N*-cyanopiperidinium salts, however, ring cleavage occurred to a considerable extent concomitantly with ethylation. Similarly, *N*-methyl-*N*-cyanomorpholinium bromide (**1b**) also underwent ring cleavage. In the case of *N*-cyano-*N*-methylpyrrolidinium bromide (**11a**), the fluoroborate **11b** could be isolated. However, the major pathway was that of ring cleavage of the bromide **11a** (Scheme IV) into 4-(*N*-cyano-*N*-methylbutyl) bromide (**12**).[18] Most likely, in the cyanoammonium ion that forms in the course of the reaction, the strongly eclipsed C-2 and C-5 hydrogens interfered with the cis-positioned cyano or methyl groups attached to the ring nitrogen. Therefore, these additional nonbonded interactions may considerably weaken a ring C–N bond, ultimately resulting in ring cleavage. In addition, steric factors in the transition state may have a definite effect on the course of this reaction, but at present we are unable to assess their relative importance. *N*-Cyano-*N*-*sec*-butyl-4-methylpiperidinium bromide (**13a**) (Scheme V) prepared *in situ* was decomposed by mild heating into the expected cyanamide (**6**) and *sec*-butyl bromide (**14**). A mixture of 1- and 2-butenes and some *N*-*sec*-butyl-4-methylpiperidinium bromide were also isolated, as identified by their nmr spectra. The possible mechanism for olefin and amine salt formation could involve removal of a proton from the *sec*-butyl group of the cyanoammonium ion by the unchanged tertiary amine, *i.e.*, a Hofmann-type elimination instead of a nucleophilic attack of bromide upon the secondary butyl carbon atom.

Reactions with Other Nucleophiles. When the cyanoammonium bromide from either *N*-methylpiperidine or *N*-methyl-*trans*-decahydroquinoline was dissolved in acetone and sodium iodide was added, an instant coloration appeared, which upon titration showed that about 30% iodine had formed, by oxidation. Since the cyanoammonium cation cannot be an oxidizing agent, while cyanogen bromide is known to be, one reason[19] for this reaction was the dissociation of the cyanoammonium bromide into the tertiary amine and cyanogen bromide. The latter would then oxidize the iodide. One may object that there is no spectral evidence for any free base in the presence of cyanogen bromide. However, even if present in infinitesimally small amounts, rapid oxidation of iodide by cyanogen bromide could result in a shift of the equilibrium, in addition to the "normal" interionic reaction leading to the cyanamide and methyl bromide.

Reduction of the cyanoammonium salt **3b** with sodium borohydride (in methanol) at 0° leads to an 80% yield of *N*-methyl-*trans*-decahydroquinoline. No other product could be isolated. Solvolysis of a 92:8 mixture of **3b** and **4b** with methanol-d_4 at 26.5 and 28.5°, respectively, resulted in the formation of *N*-methyl-*trans*-decahydroquinoline, characterized by its nmr spectrum. It showed no infrared stretch in the 2200-cm^{-1} region. That reaction was also monitored by pmr kinetics.

Action of sodium methoxide [$\delta(CH_3)$ 3.2 ppm] upon the salt **3b** gave a product with a *N*-methyl signal at rather high field (δ 2.15, s) which can be assigned to *N*-methyl-*trans*-decahydroquinoline. However, no signal indicating the presence of dimethyl ether was detected. It is apparent that reduction of the cyanoammonium salt competed with alkylation. In spite of this, *N*-cyanotrialkylammonium salts can be used in synthesis as potential alkyl cation donors.

Reactions with Electrophiles. *N*-Cyano-*N*-methylpiperidinium fluoroborate reacts with trifluoroacetic acid. As shown by its pmr spectrum the N^+-methyl signal at δ 3.3 ppm slowly disappeared, giving rise to a new doublet of increasing intensity at δ 2.95 ppm. This product was identified as the trifluoroacetate of *N*-methylpiperidine. The fate of the CN group remains unclear. However, in the light of recently published experiments,[20] trifluoroacetic acid may react with the cyanoammonium salts to form $CF_3COOC{\equiv}N$ and/or $(CF_3CO)_2O$. The cyano group is thus removed, and the resulting tertiary base can subsequently form the salt with additional trifluoroacetic acid. A similar experiment with trifluoroacetic acid was carried out in acetonitrile-d_3. The major methyl signal appeared at δ 3.8 ppm. Upon addition of a drop of D_2O a doublet appeared in the δ 2.72 ppm region. The intensity of that signal increased while the one of the N^+-methyl signal decreased. At the end of addition of D_2O that signal became predominant. The doublet was again typical of the trifluoroacetate of the tertiary base. It is not easy to interpret that reaction; however, the product indicates an acidolytic or hydrolytic removal of the cyano group. Such a reaction would not be unexpected in the case of a cyanoammonium bromide, because dissociation thereof should lead to cyanogen bromide and the tertiary amine, the latter being protonated; hence the equilibrium slowly shifted. However, an analogous reaction with the fluoroborate leading to cyanium tetrafluoroborate was unlikely. The latter was not accessible from cyanogen bromide and silver fluoroborate.

Kinetic Studies. Kinetic data were obtained by measuring the decrease in intensity of the *N*-methyl signal in the pmr spectrum of the various cyanoammonium compounds under the appropriate reaction conditions. *N*-Cyano-*N*-methyl-*trans*-decahydroquinolinium bromide (**3a** + **4a**) was found to be reasonably soluble in chloroform-*d*, acetonitrile-d_3, and nitromethane-d_3, and, in addition, the *trans*-decahydroquinoline skeleton is conformationally more rigid than that of piperidine. Thus, the greater part of the kinetic measurements were carried out in the *trans*-decahydroquinoline series.[12a,b]

The kinetic studies were essentially in three parts: (A) on mixed axial and equatorial N stereoisomers (**3a** + **4a**) in the above three solvents (Figures 1 and 2); (B) on the separated N stereoisomers (**3b** or **4b**) in the same three sol-

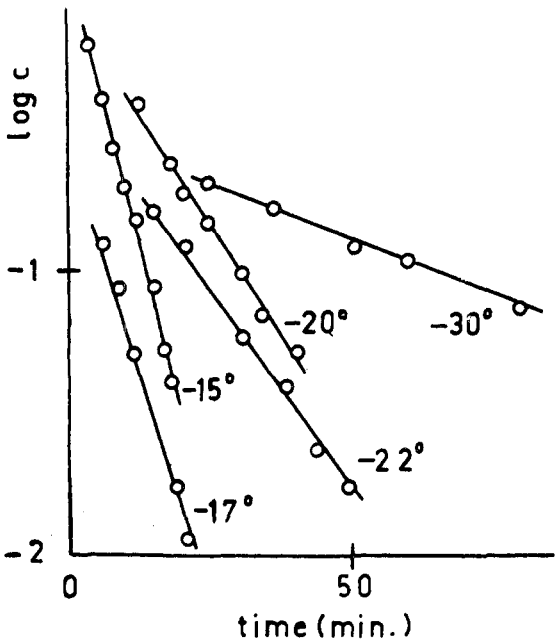


Figure 1. First-order plots for the decomposition of 3a + 4a in $CDCl_3$ at various temperatures.

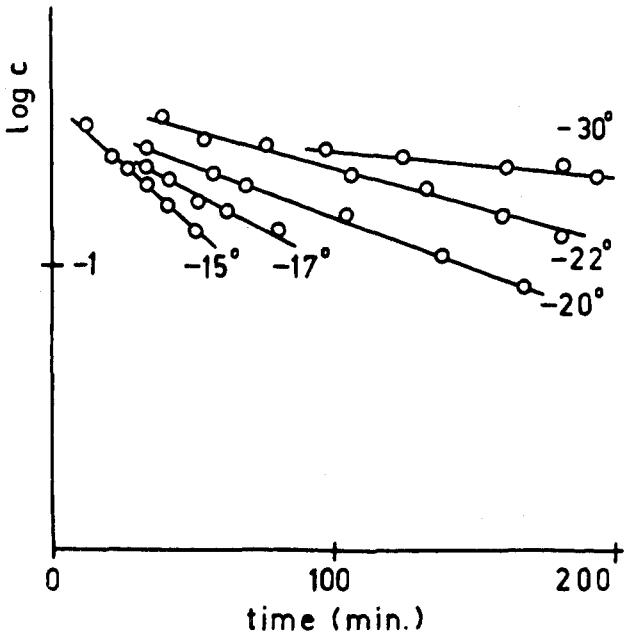


Figure 2. First-order plots for the decomposition of 3a + 4a in CD_3CN at various temperatures.

vents; and (C) on the separated N stereoisomers (3b or 4b) in CH_3OD. No difference was observed in the kinetic behavior whether the cyanation was carried out in one of these solvents or whether the cyanoammonium bromide (3a + 4a) was precipitated at −40 to −50° from ethereal solution and subsequently dissolved in the precooled reaction solvent. In addition to the molecularity of the reaction, these kinetic studies have allowed supporting conclusions to be drawn regarding the preferred steric course of the first step of cyanation, and of the configurational effect of substituents about the quaternary nitrogen upon the rate of decomposition of the cyanoammonium intermediate.

The decomposition rate of *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium bromide (3a + 4a) is ten times greater in chloroform-*d* than in acetonitrile-d_3 but only 2.5 times greater than in nitromethane-d_3. The decrease in rate tends to follow the order of increasing basicity and increasing *Z* value[21] (chloroform < nitromethane < acetonitrile) rather than an increase in the dipole moment (chloroform < acetonitrile < nitromethane).[22] The energies of activation are calculated to be 19 kcal mol^{-1} in chloroform and 22 kcal mol^{-1} in acetonitrile. Increase in the overall concentration of the salt or of the original cyanogen bromide did not affect the reaction rates. Added common ion (*e.g.*, from lithium bromide) to the acetonitrile solution only resulted in "salting out" the crystalline cyanoammonium bromide. However, the addition of 0.3 mol of lithium perchlorate per mole of cyanoammonium salt produced a considerable (*ca.* fivefold) rate attenuation, indicating a negative kinetic salt effect. These results can be explained by assuming a less polar transition state in the step 1 → 2, and that the reactant ions are solvated to a greater degree in acetonitrile.

The entropy of activation in chloroform-*d* was calculated to be +1.5 ± 3.0 eu, and in acetonitrile-d_3 it was +9.5 ± 3.0 eu (see Table III, Figures 1 and 2). The positive value in both of the above-mentioned cases is consistent with the above assumption of a transition state which is less polar (less strongly solvated) than the reactant ions in the step 1 → 2. In addition, the small positive ΔS^* in chloroform and the relatively larger value in acetonitrile suggests an intimate ion pair for the cyanoammonium bromide in chloroform, while in acetonitrile the more strongly solvated individual ions may give it a more "normal" salt structure. This conclusion is reached on the basis that an ion pair requires less reorganization of the solvent shell and loss of fewer solvent molecules in going from reactant to transition state than does a salt which is solvated as free, individual ions.

Conductance measurements taken at room temperature and at −42° in these solvents clearly show that there are a greater number of conducting species in the acetonitrile solution, there being a 1000-fold difference in conductivity between the two solvents; the conductivity is almost negligible in chloroform (Table IV).

We have followed Ross's analysis[23] in fitting the raw kinetic data to various rate laws. This analysis shows that, if the reacting salt is present in solution as all ion pairs, first-order kinetics will be observed; if free ions are present, second-order kinetics will be expected; if triple ions are present two-thirds-order kinetics will follow; and if quadruples are the predominant aggregates, one-half-order kinetics will be obtained. Intermediate reaction orders may indicate mixtures of species.

Our preliminary kinetic studies indicate that, in chloroform and in nitromethane at all temperatures investigated, first-order kinetics were followed. In acetonitrile at the relatively higher temperatures first-order kinetics were also observed, but both first-order and second-order plots became nonlinear below −20°. Taken together all of these physical data indicate that there is extensive ion pairing under the experimental conditions which we have used. However, the deviation from linearity below −20° in acetonitrile indicates that neither first- nor second-order kinetics are valid. Therefore, we interpret this as indicating in acetonitrile at these lower temperatures that the reacting species are most probably higher aggregates, *i.e.*, triple ions. We would suggest that the ion pair in chloroform is a tight ion pair and that in nitromethane and in acetonitrile it could be considered a solvent-separated ion pair.[24] The exact nature of the solvent cage about the ion aggregates is expected to be different in nitromethane and acetonitrile.

The influence of configuration about the ammonium nitrogen atom on reaction rates can be seen in the following data. The rate constant for the axial methyl derivative of *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium fluorobo-

Table III
First-Order Rate Constants[a] of the Decomposition of 3b and 4b into *N*-Cyano-*trans*-decahydroquinoline and Methyl Bromide at Different Temperatures

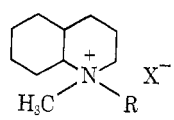
Solvent	−30°	−22°	−20°	−17°	−15°
Chloroform-*d*	3.0×10^{-4}	1.1×10^{-3}	1.2×10^{-3}	2.0×10^{-3}	3.0×10^{-3}
Acetonitrile-d_3	3.0×10^{-5}	1.0×10^{-4}	1.4×10^{-4}	2.0×10^{-4}	3.3×10^{-4}
Nitromethane-d_3			6.5×10^{-4}		1.2×10^{-3}

Calculated Activation Parameters

Solvent	E_a, kcal mol^{-1}	ΔG^* kcal mol^{-1}	ΔH^{*b} kcal mol^{-1}	ΔS^*, ev
Chloroform-*d*	19	18.1	18.5	+1.5
Acetonitrile-d_3	22	19.2	21.5	+9.5

[a] In reciprocal seconds. [b] ΔH^* calculated at −30 and −15°. For $CDCl_3$: 18.52 kcal mol^{-1} at −30°, 18.49 kcal mol^{-1} at −15°. For CD_3CN: 21.52 kcal mol^{-1} at −30°, 21.49 kcal mol^{-1} at −15°.

Table IV
Equivalent Conductance of Various *N*-Cyano-*trans*-decahydroquinoline Salts in Three Solvents



R	X	Solvent	Temp, °C	Δ, Mho/cm
CN	BF_4	CH_3CN	22.8	131.1
CN	BF_4	CH_3CN	−41.9	61.32
CN	Br	CH_3CN	−42.0	23.80
CN	BF_4	CH_3NO_2	22.7	78.17
CN	BF_4	$CHCl_3$	22.7	2.712×10^{-2}
CN	Br	$CHCl_3$	−42.0	"0"
C_2H_5[a]	Br	$CHCl_3$	22.7	14.07×10^{-2}
$(n\text{-Pr})_4{}^+NBr^-$[b]		$CHCl_3$	22.6	28.42×10^{-2}

[a] Registry no., 51075-63-9. [b] Registry no., 1941-30-6.

rate (reacts as the bromide) is 2.1×10^{-4} sec^{-1}, while that of the minor product, the equatorial *N*-methyl isomer, is 2.9×10^{-4} sec^{-1}; thus $k_{eq}/k_{ax} = 1.38$. This may be interpreted by assuming that the axial methyl group is somewhat hindered, or at least the equatorial methyl group is more easily attacked by the bromide ion.

Steric Course of the Decomposition of a Chiral Cyanoammonium Salt. Further insight into the mechanism of the interionic reaction was gained from the synthesis and decomposition of a cyanoammonium salt with a chiral *N*-alkyl group. 4-Methylpiperidine was butylated with (*S*)-(+)-2-butyl *p*-toluenesulfonate[25] of 59% optical purity to form (*R*)-(−)-*N*-*sec*-butyl-4-methylpiperidine, $[\alpha]^{20}_{4359}$ −26.97° (neat). This is similar to the preparation of (*R*)-(+)-*N*-*sec*-butylpiperidine.[25] The optical purity of this product could only be estimated at 27% [comparison with optically pure (*R*)-(+)-*N*-*sec*-butylpiperidine, $[\alpha]^{25}_{4359}$ +99° (neat)], since we have not yet completely resolved 4-methyl-*N*-*sec*-butylpiperidine. Reaction of the latter with cyanogen bromide led to isolation of the cyanoammonium bromide **13a**, which was characterized as the fluoroborate **13b**. Upon decomposition the chiral bromide **13a** gave rise to (*S*)-(+)-*sec*-butyl bromide (**14**), $[\alpha]^{20}_{4359}$ +7.3° (ether); optically pure (*S*)-(+)-butyl bromide[26,27] shows $[\alpha]^{20}_{4360}$ +70.5° (neat). On the other hand (*S*)-(+)-*sec*-butyl tosylate of 80% optical purity gave (*R*)-(−)-*sec*-butyl bromide, $[\alpha]^{20}_{4359}$ −58.2° (ether). That value was corrected to an optically pure bromide, $[\alpha]^{20}_{4359}$ −72.7°. Therefore, the optical purity of the bromide from **13a** was only 10%. The steric course of the N-debutylation, however, corresponds to 36% inversion, if the low optical purity of our *N*-*sec*-butyl-4-methylpiperidine is taken into account. This warrants the statement that the interionic dealkylation step leading to *sec*-butyl bromide occurred with inversion, which thus implies an SN2-type displacement of the nitrogen from the *sec*-butyl carbon 2.

The product of this reaction was the expected *N*-cyano-4-methylpiperidine (**15**) in high yield. In addition a mixture of 1- and 2-butenes, probably formed by the action of unchanged *N*-butylpiperidine upon the cyanoammonium bromide, *i.e.*, by Hofmann elimination, was detected. Furthermore, a 10% yield of *N*-*sec*-butyl-4-methylpiperidine hydrobromide (**16**) was isolated, in agreement with the elimination mechanism. Compound **16**, or rather its bromide ion, was responsible for considerable racemization of the (*S*)-(+)-*sec*-butyl bromide formed in the reaction **13a** → **14** + **15**. This was proven by distilling added optically pure *sec*-butyl bromide from the same salt in a control experiment, which resulted in complete racemization thereof. That undesirable process was somewhat minimized by precipitating the hydrobromide with ether immediately following the von Braun reaction of **13a** carried out at 10°, and subsequently distilling the (*S*)-(+)-*sec*-butyl bromide, now practically free of bromide ions.

Experimental Section

General. Nmr spectra were recorded on a Varian HA-60, HA-100, or T-60 spectrometer unless otherwise specified; chemical shifts are given in parts per million (δ) downfield from TMS as internal reference. Ir spectra were recorded on a Beckman IR-8 spectrophotometer. Melting points were taken on an Electrothermal Model 1A 6304 apparatus. Optical rotations were measured at 25° with a Perkin-Elmer Model 141 M electric polarimeter. Elemental analyses were partly carried out on F & M Model 185 C, H, N Analyser by Mr. R. Dulude, and partly by Galbraith Laboratories, Knoxville, Tenn.

All solvents employed in the preparation of *N*-cyanoammonium salts were carefully purified before use. Acetonitrile was dried over phosphorus pentoxide overnight and then distilled. Commercial anhydrous ether was refluxed with lithium aluminum hydride for 2 hr and then distilled directly into the reaction flask. Cyanogen bromide was distilled from calcium carbonate–magnesium oxide (1:1). Other liquid reagents were distilled and solid reagents were recrystallized to ensure purity.

General Procedure for the Preparation of Quaternary *N*-Cyanoammonium Bromides (for Details See Tables I and II). A solution of 1.9 g (0.018 mol) of cyanogen bromide in 15 ml of anhydrous ether was cooled to −50°, and 0.016 mol of the tertiary amine in 20 ml of anhydrous ether was added dropwise over a period of 30 min with efficient stirring. The reaction mixture was stirred for an additional 3 min, and the temperature was maintained between −50 and −60°. At the end of this period the voluminous precipitate was transferred as rapidly as possible to a sintered glass funnel equipped with an evacuated cooling jacket and suction filtered, first at the water aspirator and then with an oil pump. The yield of the dry solid was in the range of 95–98%. Attempts to dissolve either *N*-cyano-*N*-methylpiperidinium bromide (**5a**) or *N*-cyanotropinonium bromide (**7a**) in available nmr solvents at temperatures below −40° were unsuccessful. *N*-Cyano-

N-methyl-*trans*-decahydroquinolinium bromide (**3a** + **4a**), on the other hand, dissolved readily in chloroform-*d*, acetonitrile-d_3, or nitromethane-d_3. For physical and spectral data see Tables I and II.

General Procedure for the Thermal Decomposition of N-Cyanoammonium Bromides. All experiments were carried out under strictly anhydrous conditions. For example, 6.15 g (0.03 mol) of N-cyano-N-methylpiperidinium bromide, which had been kept at −80°, was placed in a 100-ml round-bottom flask being immersed in a Dry Ice–acetone bath. The flask was connected to a short-path distillation unit equipped with a cold finger condenser; the receiver was cooled in a Dry Ice–acetone bath. Upon warming gradually to room temperature, the solid mass began to appear deliquescent on the surface. When gentle heating was applied with a hot air gun, the solid disintegrated completely, yielding a gas, which was condensed into the cold receiver, and a liquid. The gas was identified as methyl bromide (2.47 g, 88%), a sample of which had superimposable nmr and ir spectra and identical chemical properties with authentic material. The liquid was distilled, yielding 3 g (92%) of N-cyanopiperidine: bp 104° (10 mm) [lit.[28] bp 102–104° (10 mm)]; ir 2200 cm^{-1} (s, C≡N); nmr spectrum was identical with that of an authentic sample. Thermal decomposition of N-cyanotropinonium bromide (**7a**) by the same method gave 85 and 86% yield of methyl bromide and N-cyanotropinone, respectively. Similarly N-cyano-N-methyl-*trans*-decahydroquinolinium bromide (**3a** + **4a**) was thermally decomposed to give methyl bromide (91%) and N-cyano-*trans*-decahydroquinoline (98%). The latter cyanamide boiled at 102–103° (0.09 mm) and showed no difference from the compound obtained by direct N-cyanation of *trans*-decahydroquinoline with cyanogen bromide.

General Procedure for the Preparation of Stabilized N-Cyanoammonium Salts. The N-cyanoammonium bromide was prepared by the method described above. To a very well stirred suspension of that salt in ether at −50° a solution of an equivalent amount of silver tetrafluoroborate (or silver *p*-toluenesulfonate) was slowly added in acetonitrile. The mixture was stirred at −50° for another 1 hr and then allowed to warm to room temperature. The solvents were evaporated at reduced pressure and room temperature; the remaining solid was then thoroughly triturated with acetonitrile. The silver bromide was removed by filtration, leaving behind a clear solution of the stable N-cyanoammonium salt. Reduced-pressure evaporation of the solvent at 10–20° afforded the crude product, which was analyzed by nmr. Recrystallization, usually from acetonitrile–ether, gave the pure N-cyanoammonium tetrafluoroborate (or *p*-toluenesulfonate). The yields and melting points of some products were as follows: N-cyano-N-methylpiperidinium methanesulfonate, 75%, mp 78–80°; N-cyano-N-ethylpiperidinium methanesulfonate, 64%, mp 75–75°; N-cyanopseudotropinium tetrafluoroborate, 95%, mp 142°; N-cyanotropinonium tetrafluoroborate, 90%, mp 158–159°; N-cyanolupininium tetrafluoroborate, 88%, mp 162–163°.

N-Cyano-N-methylpiperidinium Hexachloroantimonate (5e). The cyanogen chloride–antimony pentachloride complex salt was prepared according to the method of Woolf.[9] The pure crystalline material was obtained as colorless prisms by sublimation (10^{-3} mm) at room temperature: mp 124–125° dec; ir 2220 cm^{-1} (C≡N); λ_{max} (CH_3CN) 268 mμ. A solution of N-methylpiperidine (0.74 g, 7.5 mmol) in 5 ml of dry nitromethane was added dropwise to a cold, stirred solution (−10°) of the fresh sublimed complex salt (2.7 g, 7.5 mmol) in 10 ml of dry nitromethane. Freeze-drying of the reaction mixture left a solid product (3 g, 94%), mp 79–80°.

N-Methyl-*trans*-decahydroquinoline. The Eschweiler procedure was used as modified by Clarke, Gillespie, and Weisshaus.[29] *trans*-Decahydroquinoline (25 g, 0.18 mol) was heated[30a] to 95–100° with 45 ml of 91% formic acid and 45 ml of 37% aqueous formaldehyde for 10 hr. The cooled reaction solution was evaporated to dryness after addition of 100 ml of 4 *N* hydrochloric acid, and the tertiary amine was liberated by subsequent addition of a 20% potassium hydroxide solution. The crude product was purified by vacuum distillation. The yield of N-methyl-*trans*-decahydroquinoline was 21.4 g (78%); bp 73° (3 mm) [lit.[30b] bp 204° (721 mm)]; ir 2750 cm^{-1}; nmr ($CDCl_3$) δ 2.01 (NCH_3, 3 H, s).

Preparation and Separation of N Stereoisomers 3b and 4b, N-Cyano-N-methyl-*trans*-decahydroquinolinium Tetrafluoroborate. The crude cyanoammonium salt was obtained in 95% yield from the reaction of N-methyl-*trans*-decahydroquinoline with cyanogen bromide at −30° in ether or acetonitrile (see general procedure). Subsequent treatment of the resulting intermediates with silver tetrafluoroborate and integration of the $^+NCH_3$ nmr signals of the stabilized salt indicated a mixture consisting of 95% major product (**3b**) and 5% minor product (**4b**). The epimers were separated by fractional crystallization. Anhydrous ether was added gradually to a solution of 11 g of the crude product (**3b** and **4b**) in 150 ml of acetonitrile until the solution became faintly turbid and kept at 0–5° for a few hours. The CN-equatorial epimer (**3b**) had crystallized out as colorless needles (2.3 g, 21%), mp 135°.

Repeated recrystallization by the same procedure afforded two more crops of pure major compound **3b** from the mother liquor, yielding a total of 3.9 g (35.4%) of monoclinic crystals. The intermediate fractions contained mixtures (50:50 mixture, mp 100°) while the final two fractions contained a total of 0.2 g (1.8%) of the pure CN-axial epimer (**4b**). The latter melted at 156°.

Reaction of an N-Cyanoammonium Tetrafluoroborate with Lithium Bromide. Anhydrous lithium bromide (1.15 g, 0.013 mol) was dissolved in 25 ml of acetonitrile, and a solution of 2.44 g (0.0091 mol) of N-cyano-N-methyl-*trans*-decahydroquinolinium tetrafluoroborate (**3b**) in 10 ml of acetonitrile was added. A white precipitate formed immediately, the mixture was diluted with ether, and the precipitate was filtered and washed with ether. The filtrate and the ethereal solution were combined. Removal of the solvents followed by vacuum distillation yielded 1.33 g (89%) of N-cyano-*trans*-decahydroquinoline which was spectrally identical with an authentic specimen.

Optically Active 2-Butyl *p*-Toluenesulfonate. (*S*)-(+)-2-Butanol), $[\alpha]^{25}_{4359}$ +16.15°, was supplied by Professor J. L. Wolfhagen of the University of Maine. However, later a product of higher optical purity, $[\alpha]^{25}_{4359}$ +22.08°, was obtained from Norse Laboratories and used for most of our experiments. By a method reported elsewhere[25] the latter alcohol (15.33 g, 0.27 mol) was treated with *p*-toluenesulfonyl chloride (89.5 g, 0.4 mol) in 300 ml of pyridine at 0° to give 27.3 g (73%) of *sec*-butyl *p*-toluenesulfonate, $[\alpha]^{25}_{4359}$ +10.35° (neat). The (*S*)-(+)-2-butanol of lower rotation gave a tosyl ester: $[\alpha]^{25}_{4359}$ +7.76° (neat); bp 80° (0.01 mm) [lit.[25] bp 95° (0.1 mm)]; ir 668, 820, 910, 1190, 1360, 1605, 3000, 3050 cm^{-1}, Kenyon, Phillips, and Pittman[25] reported $[\alpha]^{20}_{4359}$ +12.98° (neat).

Optically Active N-*sec*-Butyl-4-methylpiperidine. A mixture of 33.66 g (0.34 mol) of freshly distilled 4-methylpiperidine and of (*S*)-(+)-*sec*-butyl *p*-toluenesulfonate, $[\alpha]^{25}_{4359}$ +7.76°, was stirred at 85° overnight. As the reaction proceeded, the clear solution separated gradually into two layers. At the end of the reaction, the bottom layer solidified upon cooling. The solid, 4-methylpiperidine hydrobromide, was separated by filtration, washed thoroughly with several portions of ether, dissolved in water, and finally treated with 20% aqueous KOH solution, and dried (K_2CO_3). The ether was evaporated on a rotary evaporator, and the residual oil was fractionally distilled to yield 20.2 g (77%) of (*R*)-(−)-N-*sec*-butyl-4-methylpiperidine, bp 82° (22 mm), $[\alpha]^{25}_{4359}$ −26.96° (neat). This was approximately 27% optically pure; ir and nmr spectra of this material matched perfectly those of the corresponding optically inactive compound which had been previously prepared. For analytical data see Table I.

Cyanogen Bromide Reaction of Optically Active N-*sec*-Butyl-4-methylpiperidine. A solution of 7.75 g (0.05 mol) of (*S*)-(+)-N-*sec*-butyl-4-methylpiperidine in 10 ml of anhydrous ether was added with constant stirring to a precooled solution (−60°) of 6.36 g (0.06 mol) of cyanogen bromide in 10 ml of anhydrous ether, similar to the general preparation of quaternary N-cyanoammonium bromides. After the NCH_3 signal in the pmr spectrum of the free tertiary amine had completely disappeared the reaction mixture was kept at −60° for 2 hr. The solution of **13a** was then allowed to warm to room temperature. After 30 min, 20 ml of dry ether was added to precipitate N-*sec*-butyl-4-methylpiperidine hydrobromide, mp 211° (4.7 g, 50.6%). Also isolated was 0.85 g (14.55%) of (*S*)-(+)-*sec*-butyl bromide (**16**), bp 90–92°, $[\alpha]^{25}_{4359}$ +7.3° (ether, *c* 0.85). The optical purity of the latter compound was 10% relative to the optically pure (*S*)-(+)-*sec*-butyl bromide, $[\alpha]^{25}_{4359}$ +7.05° (neat[27]), +72.9° (ether). A part of the butyl residue was detected by pmr as a mixture of 1- and 2-butene. The residue afforded 2.9 g (48%) of N-cyano-4-methylpiperidine (**15**), bp 75–76° (0.5 mm) [lit.[31] bp 78° (1 mm)]. The above experiment, when repeated with 15.5 g (0.1 mol) of (*R*)-(−)-N-*sec*-butyl-4-methylpiperidine and 10.6 g (0.1 mol) of cyanogen bromide in bromobenzene, gave 1.1 g (8%) of *sec*-butyl bromide, $[\alpha]^{27}_{4359}$ +1.22° (neat), corresponding to 1.74% optical purity, and about 6.4% inversion. The considerable loss of optical purity is due to secondary racemization by bromide ion as shown by the following control experiment.

Racemization of (*R*)-(−)-*sec*-Butyl Bromide by Bromide

Ion. Optically active (*R*)-(−)-*sec*-butyl bromide (1.37 g, 0.01 mol), $[\alpha]^{25}_{4359}$ −56° (neat), prepared[25] from (*S*)-(+)-*sec*-butyl tosylate, and 2.35 (0.01 mol) of racemic *N*-*sec*-butyl-4-methylpiperidine were dissolved in 30 ml of bromobenzene and then distilled to give 1 g (73%) of *sec*-butyl bromide, bp 90–91°, $[\alpha]^{25}_{4359}$ 0°, completely racemized.

Kinetic Measurements. Decomposition of *N*-Cyano-*N*-methyl-*trans*-decahydroquinolinium Bromide. All of the solutions for low-temperature nmr studies were 2 *M* concentration of the sample in chloroform-*d*, acetonitrile-d_3, or nitromethane-d_3. Sample temperatures were maintained by a Varian V-4340 low-temperature probe and were calibrated by recording the temperature as a function of the difference in chemical shifts of the hydroxyl proton and methyl protons of methanol. The rates of decomposition of the *N*-cyanoammonium bromide were measured at −30, −22, −20, −17, and −15 ± 0.05° by following changes in intensity of the $^+NCH_3$ signal at δ 4.0 ppm in chloroform-*d* (δ 3.67 ppm in acetonitrile-d_3, δ 3.86 ppm in nitromethane-d_3). In a typical run, solutions of *N*-methyl-*trans*-decahydroquinoline (0.122 g, 0.8 mmol) in 0.4 ml of the deuterated solvent and cyanogen bromide (0.085 g, 0.8 mmol) in 0.4 ml of the same solvent, in separate vials, were thermally equilibrated and then mixed in a thermally equilibrated nmr tube. The tube was then sealed with a torch. The mixture was analyzed by integration (mean of three runs) of the nmr signals in the $^+NCH_3$ region of the spectrum. The extent of reaction was normally followed to 90% completion.

Rate constants were obtained by standard procedures from the slopes of logarithmic plots. Activation parameters were also determined. All analyses were performed in duplicate and the data were reproducible within the limit of experimental error.

N Stereoisomers (3b and 4b) of *N*-Cyano-*N*-methyl-*trans*-decahydroquinolinium Tetrafluoroborate. The pure N stereoisomer (either the major or the minor product) of *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium tetrafluoroborate (0.093 g, 0.35 mmol) in 0.5 ml of CD_3CN at −9° was converted *in situ* into *N*-cyano-*N*-methyl-*trans*-decahydroquinolinium bromide (**3a** or **4a**) upon mixing, in a thermally equilibrated nmr tube, with an equivalent quantity of *N,N*-dimethyl-*trans*-decahydroquinolinium bromide in 0.5 ml of chloroform-*d* at −9°. The rate of decomposition of the isomeric *N*-cyanoammonium bromide at that temperature (−9°) was followed spectroscopically by nmr and the rate constant was computed as before. In cases of both the major and the minor isomer there was observed a good linear relationship between the logarithms of concentrations of the *N*-cyanoammonium bromide and the reaction times.

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Registry No.—*N*-Methylpiperidine, 626-67-5; *N*-ethylpiperidine, 766-09-6; *N*-methylmorpholine, 109-02-4; 4-hydroxypiperidine, 5382-16-1; 3-β-hydroxytropane, 135-97-7; 3-oxotropane, 5632-84-8; *N*-methyl-*trans*-decahydroquinoline, 875-63-8; triethylamine, 121-44-8; *N*,2,6-trimethylpiperidine, 669-81-8; *N*-methyl-4-hydroxypiperidine, 106-52-5; *N*-*sec*-butyl-4-methylpiperidine, 51075-48-0; methylpyrrolidine, 120-94-5; cyanogen bromide, 506-68-3; cyanogen chloride–antimony pentachloride complex, 24273-94-7; *trans*-decahydroquinoline, 767-92-0; lithium bromide, 7550-35-8; (*S*)-(+)-2-butanol, 4221-99-2; (*S*)-*sec*-butyl *p*-toluenesulfonate, 50896-54-3; (*R*)-(−)-*N*-*sec*-butyl-4-methylpiperidine, 51075-64-0; (*S*)-(+)-*N*-*sec*-butyl-4-methylpiperidine, 51075-65-1; (*S*)-(+)-*sec*-butyl bromide, 5787-32-6; (*R*)-(−)-*sec*-butyl bromide, 5787-33-7; racemic *N*-*sec*-butyl-4-methylpiperidine, 51153-97-0.

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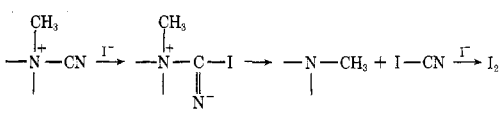
(19) Another might be expressed in the following mechanism, based on recent work,[20] as kindly suggested to us by referee II.



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