Transannular Cyclisation of Cyclo-olefinic *N*-Chloro-amines. Synthesis of Azabicyclic Compounds

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N-Chloro-*N*-methylcyclo-oct-4-enamine and *N*-chloro-*N*-methylcyclohept-4-enamine cyclise in the presence of various catalysts and solvents to give 2-substituted, nitrogen-bridged bicyclic compounds. The structures and stereochemistry of these products have been determined; several experiments with the eight-membered *N*-chloro-amine demonstrating the radical chain nature of the cyclisations are described.

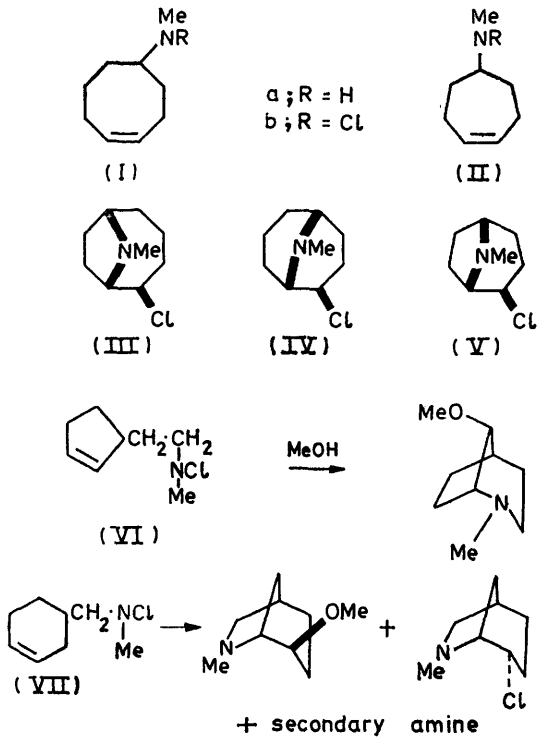
EDWARDS and his colleagues [1] have shown that saturated medium-sized ring *N*-chloro-amines can be converted into bicyclic tertiary amines under mild conditions by catalysis with silver salts in aqueous dioxan. Their suggestion that these reactions, in contrast to the Hofmann–Löffler–Freytag cyclisations, proceeded *via* nitrenium ions, prompted us to examine the feasibility of a nitrogen counterpart to the so-called 'π-route' to bicyclic compounds involving transannular cationic addition to an olefinic bond.

Our preliminary report [2] on the silver ion-catalysed conversion of the *N*-chloro-amines (Ib) and (IIb) into the bicyclic chlorides (III)—(V), and the description of analogous cyclisations of compounds (VI) and (VII) by Gassman and his co-workers [3] have been followed by several reports [4] illustrating the synthetic utility of intramolecular *N*-chloro-amine–olefin reactions. Some of these are clearly radical processes, initiated photochemically or by redox transfer, but some cyclisations appear to proceed simply on heating in neutral protic media, being also greatly accelerated by silver ion catalysis.[3] To explain such reactions, nitrenium ions have again been invoked,[3] largely on the basis of analogy with the behaviour of other *N*-chloro-amines, heterolysis of which to give cationic intermediates has been demonstrated in several cases.[5]

We now report our studies in greater detail, together with observations which indicate that the cyclisation of the *N*-chloro-amine (Ib) under a variety of conditions, including 'solvolysis' in methanol, proceeds *via* a radical chain mechanism.

[1] O. E. Edwards, D. Vocelle, and J. W. ApSimon, *J. Amer. Chem. Soc.*, 1965, **87**, 678.
[2] J. D. Hobson and W. D. Riddell, *Chem. Comm.*, 1968, 1178.
[3] P. G. Gassman, F. Hoyda, and J. Dygos, *J. Amer. Chem. Soc.*, 1968, **90**, 2716; P. G. Gassman and J. Dygos, *Tetrahedron Letters*, 1970, 4745.
[4] (*a*) J. M. Surzur, L. Stella, and P. Tordo, *Tetrahedron Letters*, 1970, 3107; *Bull. Soc. chim. France*, 1970, 111, 115; J. M. Surzur, L. Stella, and R. Nouguier, *Tetrahedron Letters*, 1971, 903; (*b*) K. Heusler, *ibid.*, 1970, 97; G. Esposito, R. Furstoss, and B. Waegell, *ibid.*, 1971, 895, 899.
[5] P. G. Gassman, *Accounts Chem. Res.*, 1970, **3**, 26, and references therein.

Preparation of N-*Chloro-amines*.—Previously described routes to the required starting materials, *N*-methylcyclooct-4-enamine (Ia) [6] and the seven-membered ring

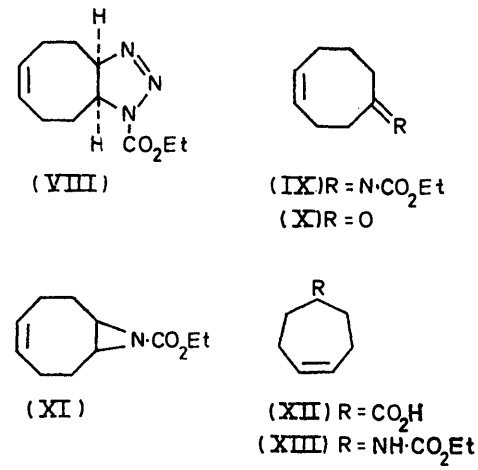


analogue (IIa),[7] appeared to be unsatisfactory, producing mixed products in poor yield. The eight-membered ring compound (Ia) was rendered readily accessible by the observation that thermolysis of ethyl azidoformate in an excess of cyclo-octa-1,5-diene at 100° gave high yields of the carbamate (IX). We were unable to isolate the undoubted intermediate in this reaction,[8] the triazoline (VIII), nor could we detect any of the alternative thermolysis product, the *N*-ethoxycarbonylaziridine (XI). The apparent exclusive formation of the carbamate (IX) has a probable steric cause, in analogy with the reactions of the cyclo-octenes with phenyl azide, in which the *cis*-isomer affords largely the corresponding anil, and the *trans*-isomer the *N*-phenylaziridine.[9] The carbamate (IX), characterised by spectroscopy and by acid-catalysed hydrolysis to cyclooct-4-enone (X), was reduced quantitatively to the amine (Ia).

For the preparation of the lower homologue (IIa), the carboxylic acid (XII), available *via* the method developed by Stork and Landesmann,[10] was converted through the acid chloride and azide into the urethane (XIII), which was then reduced.

The *N*-chloro-amines were obtained in virtually quantitative yield by reactions of the secondary amines with *N*-chlorosuccinimide in dichloromethane.[11]

Results.—In our preliminary experiments [2] reactions of the two *N*-chloro-amines, (Ib) and (IIb), with silver perchlorate were studied with acetone as solvent, in which an initially homogeneous solution of reactants was obtainable. No reaction was observed in the cold, but on heating there separated a dark precipitate which appeared to contain metallic silver as well as silver chloride and polymeric organic material. Products remaining in solution were partitioned into neutral and basic fractions with mineral acid; the former afforded small amounts of ketonic material, evidently arising by hydrolysis of *N*-methyliminocycloalkene. Liberation and extraction of the basic products gave only the parent secondary amines, together with the corresponding bicyclic chlorides (III) and (IV), and (V).

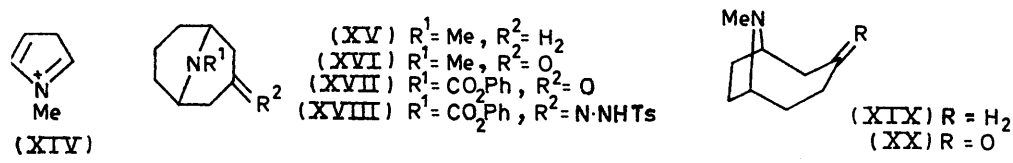


Compounds encountered in this work having the isomeric 9-azabicyclononane skeletons of (III) and (IV) were readily distinguished by mass spectrometry through the appearance of a major peak at *m/e* 82, attributable to the cation (XIV), generally found in the spectra of azabicyclic compounds containing an *N*-methylpyrrolidine ring.[12] Confirmation was provided by reductive dehalogenation to give the parent saturated heterocycles, which were identified by comparison with authentic materials. Tropane was obtained by known methods,[13] and to obtain the higher homologue (XV), the bicyclic ketone (XVI) was converted by treatment with phenyl chloroformate [14] into the phenyl *N*-carboxylate (XVII) and thence into its toluene-*p*-

[6] K. Ziegler, H. Sauer, L. Bruns, H. Froitzheim-Kühlhorn, and J. Schneider, *Annalen*, 1954, **589**, 122.
[7] M. Ehrenstein and I. Margraff, *Chem. Ber.*, 1934, **67B**, 486.
[8] G. L'Abbé, *Chem. Rev.*, 1969, **69**, 345.
[9] K. R. Henery-Logan and R. A. Clark, *Tetrahedron Letters*, 1968, 801.
[10] G. Stork and H. K. Landesmann, *J. Amer. Chem. Soc.*, 1956, **78**, 5129.
[11] G. P. Kovacic, M. K. Lowery, and K. W. Field, *Chem. Rev.*, 1970, **70**, 639.
[12] E. C. Blossey, H. Budzikiewicz, M. Ohashi, G. Fodor, and C. Djerassi, *Tetrahedron*, 1964, **20**, 585; W. M. Bryant, H. O. House, C. G. Pitt, and B. A. Tefertiller, *J. Org. Chem.*, 1966, **31**, 3120.
[13] R. Willstätter, and E. Waser, *Ber.*, 1910, **43**, 1182.
[14] J. D. Hobson and J. G. McCluskey, *J. Chem. Soc.* (*C*), 1967, 2015.

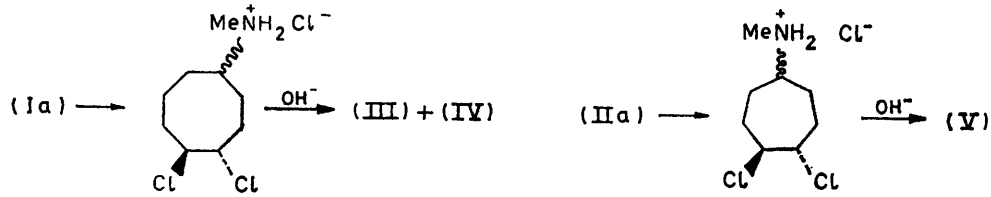
sulphonylhydrazone (XVIII). Attempts to reduce this with lithium aluminium hydride directly [15] to the saturated heterocycle gave instead the *N*-methyl-2-ene,[16] hydrogenation of which afforded compound (XV). The isomeric azabicyclo[4,2,1]nonane (XIX) was formed directly by catalytic reduction in acid solution [17] of the chlorides resulted in intramolecular displacement to give the 2β-chloro-azabicyclic compounds.

The apparent *cis*-addition of the *N*-chloro-amine function to the olefinic bond observed in our preliminary studies with silver ion catalysis, together with the formation of the corresponding secondary amine,



ketone (XX), itself available *via* ring expansion of tropan-3-one.[18]

Evidence for the β-configuration * of the 2-chloro-substituent in compounds (III)—(V) was provided by the observation that solvolysis in aqueous media gave totally rearranged products,[19] and also by the n.m.r. spectra of compounds (IV) and (V). The broad singlets presented some mechanistic problems, and further experiments were carried out with the more readily available *N*-chloro-amine (Ib). The results in Table 1 show that this compound (Ib), though relatively stable in cyclohexane at 60°, slowly decomposed in acetonitrile at this temperature or in refluxing acetone, giving largely the amine (Ia) and only traces of bicyclic products.



SCHEME 1

TABLE 1

Reactions of *N*-chloro-*N*-methylcyclo-oct-4-enamine (Ib) [a]

Solvent and temp. (°C)	Reagent (mol. equiv.)	Reaction time (h) [b]	Basic products (%) [c] Amine (Ia)	Chlorides (III)	Chlorides (IV)	Ethers (XXIII)	Ethers (XXIV)
Cyclohexane, 60	AIBN * (0·05)	60	9	25	16		
Cyclohexane + methanol,[d] 60	AIBN (0·05)	60	12	30	17	4	12
Acetone, 56		6	64	Tr. [e]	Tr.		
Acetone, 56	$AgClO_4$ (1·0)	0·5	Tr.	25	11		
Acetone + methanol,[d] 56	$AgClO_4$ (1·0)	1·0	4	16	4	4	12
Acetone/O_2 + methanol,[d] 56	$AgClO_4$ (1·0)	4	33	Tr.	2	2	2
Acetonitrile, 60		16	35	2	Tr.		
Acetonitrile, 81	$AgClO_4$ (1·0)	3	4	32	8		
Acetonitrile + methanol,[d] 81	$AgClO_4$ (1·0)	3	3	21	9	4	2

* Azobisisobutyronitrile.

[a] *ca.* 0·4M-solutions; under N_2 unless otherwise specified. [b] Approx. time required for complete disappearance of *N*-chloro-amine as measured iodometrically. [c] Yields based on *N*-chloro-amine. [d] Methanol added following disappearance of (Ib). [e] Trace, *i.e.* <2%.

due to the 2-protons in these compounds had a half-height width of only 8 Hz, characteristic of an equatorial orientation in a six-membered chair ring.[20] Further proof of structures was provided by stereospecific synthesis (Scheme 1). Chlorination of the hydrochlorides of (Ia) and (IIa) resulted in exclusive *trans*-addition, and basification of the dichloride hydro-

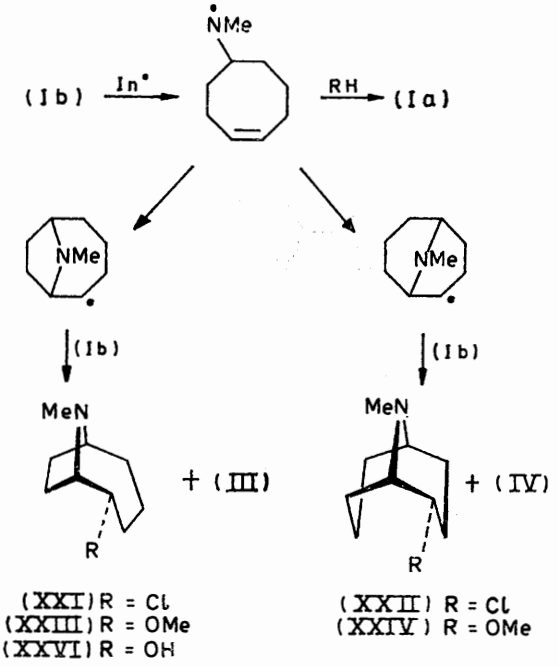
In contrast, addition of a small amount of the common radical initiator, azobisisobutyronitrile (AIBN) to the cyclohexane solution at 60° resulted in the formation of appreciable amounts of the bicyclic chlorides (III) and (IV) as well as the amine (Ia).

The initial failure to isolate 2α-substituted products from this reaction, and also from the silver perchlorate-catalysed reactions described earlier,[2] was traced to

* The symbols α and β are used here to denote substituents *trans* and *cis*, respectively, to the bridging nitrogen atom.

[15] L. Caglioti, *Tetrahedron*, 1966, **22**, 487.
[16] M. Fischer, Z. Pelah, D. H. Williams, and C. Djerassi, *Chem. Ber.*, 1965, **98**, 3236.
[17] L. P. Reiff and H. S. Aaron, *Tetrahedron Letters*, 1967, 2329.
[18] A. C. Cope, H. R. Nace, and L. L. Estes, *J. Amer. Chem. Soc.*, 1950, **72**, 1123.
[19] J. D. Hobson and W. D. Riddell, *Chem. Comm.*, 1968, 1180.
[20] A. C. Cope, D. L. Nealy, P. Scheiner, and G. Wood, *J. Amer. Chem. Soc.*, 1965, **87**, 3130; K. H. Baggaley, J. R. Dixon, J. M. Evans, and S. H. Graham, *Tetrahedron*, 1967, **23**, 299.

difficulties in the work-up. Addition of methanol to reaction mixtures immediately after complete disappearance of the *N*-chloro-amine, followed by a brief period of reflux, led to the isolation of two additional bicyclic products, shown (see later) to be the 2α-methoxy-9-methyl-9-azabicyclononanes (XXIII) and (XXIV). Since solvolysis of the 2β-chloro-derivatives (III) and (IV) has been shown to give totally rearranged products,[19] the 2α-methoxy-9-azabicyclononanes must have originated from the 2α-chloro-derivatives (XXI) and (XXII), which would be expected to have the high reactivity associated with β-aminoalkyl halides [21] and to undergo solvolysis with retention of configuration *via* the intermediate aziridinium ion (XXV).[22] Formation and inefficient extraction of highly water-soluble alcohols derived from (XXV) must account for our initial failure to isolate 2α-substituted products.



SCHEME 2

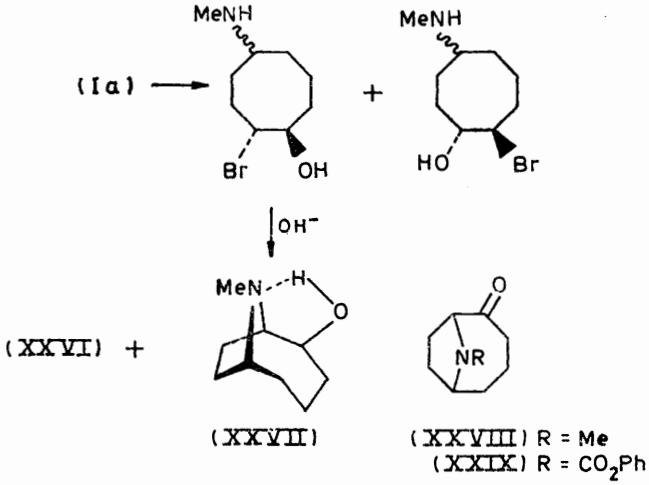
(XXV)

The bicyclic skeleton of the ether (XXIII) was again readily distinguished by the presence of a prominent peak at *m/e* 82 in its mass spectrum, and the 2α-configuration of the substituent was established by synthesis.

* Direct intramolecular displacement of bromide ion by the amino-group in the *trans*-1-bromohydrins would be expected to lead only to 2β-alcohols; the epimeric 2α-alcohols could conceivably arise through the intermediacy of the *trans*-5-methylamino-*cis*-1,2-epoxide.

Addition of hypobromous acid to the amine (Ia) followed by treatment of the crude products with base and continuous extraction with ether gave a 60% yield of an oily product, shown by g.l.c. to contain three components in the ratio 10 : 6 : 1. Surprisingly, the two major products, separated by preparative g.l.c., were found to be the epimeric 9-methyl-9-azabicyclo[4,2,1]-nonan-2-ols (XXVI) and (XXVII).* Their mass spectra showed the characteristic peak at *m/e* 82, and oxidation with chromic acid converted both into the same oily ketone (XXVIII), which was fully characterised by conversion [14] into the crystalline *N*-phenoxycarbonyl derivative (XXIX). The configurations of the alcohols were assigned on the basis of their i.r. spectra in analogy with observations on the tropan-2-ols.[23] The spectrum of the major component showed a single OH peak at 3520 cm^{-1}, the relative intensity of which was unaffected by dilution, indicating the presence of an intramolecular hydrogen bond only possible in the 2β-isomer (XXVII). The spectrum of the epimeric alcohol showed bands at 3625 and 3380 cm^{-1}, characteristic of free and associated OH groups, the relative intensity of the second absorption increasing with concentration.

Methylation of the alcohols by treatment with sodium hydride in hexamethylphosphoramide followed by methyl iodide, and comparison of the methyl ethers with those obtained from the *N*-chloro-amine cyclisation



confirmed that one of the latter was indeed the 2α-methoxy-compound (XXIII). The structure and stereochemistry of the second isomer (XXIV) were apparent from its spectra, in particular the presence of a broad signal at τ 6·2—6·6 characterising the axial 2-proton.

The total reaction sequence of the AIBN-initiated reaction can thus be represented as a conventional

[21] P. D. Bartlett, S. D. Ross, and C. G. Swain, *J. Amer. Chem. Soc.*, 1947, **69**, 2971.
[22] *Cf.* S. Archer, T. R. Lewis, M. R. Bell, and J. W. Schulenberg, *J. Amer. Chem. Soc.*, 1961, **83**, 2386.
[23] H. S. Aaron, C. Parker-Ferguson, and C. P. Rader, *J. Amer. Chem. Soc.*, 1967, **86**, 1431.

radical chain process (Scheme 2) in which the bicyclic chlorides are formed non-stereospecifically.†

The close correspondence between the nature and proportions of products obtained in this process and in the silver perchlorate-catalysed reactions in acetone or acetonitrile suggested a similarity of mechanism. The intermediacy of radicals in these cyclisations was demonstrated by the observation that only traces of bicyclic products were formed in the presence of oxygen (see Table 1). Though ineffective for trapping nitrogen radicals [4a,26] the chain-propagating bicyclic carbon radicals were evidently efficiently scavenged by oxygen, and the consequent suppression of the chain allowed slow formation of the secondary amine to supervene.

terms of nitrenium ion intermediates.[5] Similar rearrangements have been observed with leaving groups other than chloride ion,[27] and it has been pointed out that such cations, being isoelectronic with carbenes, could show analogous triplet reactivity and thus account for the generation of the parent secondary amine as a significant product in many of these reactions.[5] Cyclisations of the cyclo-olefinic *N*-chloro-amines (VI) and (VII) occurring in methanol, with or without catalysis by added silver salts, were similarly considered to involve heterolysis to nitrenium intermediates.[3]

Nevertheless, the results described for the *N*-chloro-amine (Ib) suggest that for this compound, and perhaps those substrates lacking any features which especially

TABLE 2

Reactions of the *N*-chloro-amine (Ib) in methanol [a]

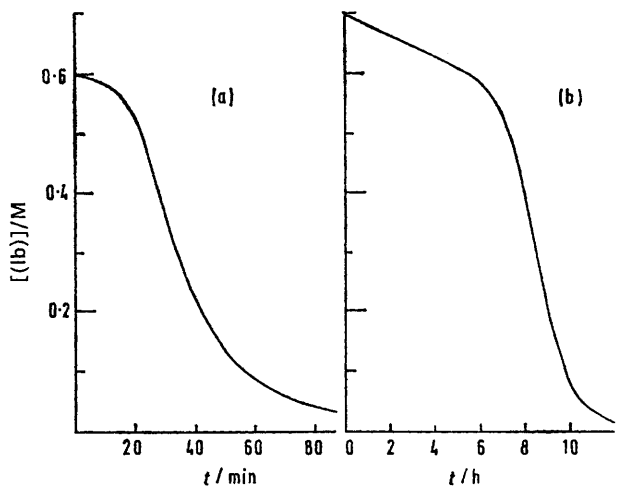
		Basic products (%)				
			Chlorides		Ethers	
Reagent (mol. equiv.)	Reaction time (h) [b]	Amine (Ia)	(III)	(IV)	(XXIII)	(XXIV)
—	2	19	25	10	11	14
DPPH * (0·075)	18 [c]	64	1	2		Tr.[d]
O_2	30	44	1	Tr.		
$AgClO_4$ (1·0) [e]	1	4	25	7	7	22
$AgClO_4$ (1·0) [e] + O_2	4	32	3	1		3

* *NN*-Diphenylpicrylhydrazyl. [a] *ca.* 0·4M-solutions, kept at 60° under N_2 unless otherwise specified. [b] Time required for complete consumption of (Ib). [c] Estimated. [d] Trace, *i.e.* <1%. [e] Reaction temp. 50°.

Of the various other solvents used for the cyclisation of the *N*-chloro-amine (Ib), methanol was of most interest in view of the hypothesis that reactions of olefinic *N*-chloro-amines in this medium proceeded *via* heterolysis to nitrenium ion intermediates.[3]

The results (Table 2) show that in methanol alone at 60° compound (Ib) was converted in relatively high yield into the bicyclic β-chlorides and α-ethers; the reaction was preceded by a short induction period (see Figure) but was complete within 2 h. Addition of silver perchlorate caused substantial acceleration but with little variation in the proportions of products. However, in the presence of oxygen or *NN*-diphenylpicrylhydrazyl the formation of bicyclic products in methanol alone was again almost completely suppressed. The same result was observed in reactions catalysed by silver perchlorate carried out under oxygen; the major product in these experiments was again the amine (Ia).

Discussion.—In their studies on the solvolytic reactivity of *N*-chloro-amines Gassman and his co-workers have observed rearrangements closely simulating carbonium ion behaviour, which they have interpreted in favour cation formation ‡ a radical mechanism can intrude, even under those conditions normally expected



Plots of concentration of the *N*-chloro-amine (Ib) against time (a) in methanol at 60°; (b) in acetone at 50°

to induce heterolysis of the N–Cl bond. Neutral aminyl radicals, rather than the electron-deficient, triplet nitrenium species, seem the most probable intermediates in spite of their frequently observed lack of

† The literature contains numerous examples of radical chain additions of *N*-chloro-amines to olefins in acid solution *via* ammoniumyl radicals,[11,24] but comparatively few studies have been reported of additions involving neutral aminyl radicals.[4a,25]

‡ A case clearly involving heretolysis of a bicyclic *N*-chloro-amine anchimerically assisted by a non-adjacent olefinic bond has been described by Rautenstrauch.[28]

[24] *Inter alia*, R. S. Neale, *J. Org. Chem.*, 1967, **32**, 3263; R. S. Neale and N. L. Marcus, *ibid.*, p. 3273; *J. Org. Chem.*, 1968, **33**, 3457; and references therein; F. Minisci, R. Galli, *Tetrahedron Letters*, 1965, 1679; F. Minisci, G. P. Gardini, and F. Bertini, *Canad. J. Chem.*, 1970, **48**, 544, and references therein.

[25] D. Mackay and W. A. Waters, *J. Chem. Soc.* (*C*), 1966, 813; R. E. Jacobson, K. M. Kohnston, and G. H. Williams, *Chem. and Ind.*, 1967, 157; F. Minisci, R. Galli, and G. Pollina, *Chimica e Industria*, 1965, **47**, 736.

[26] F. Minisci and R. Galli, *Tetrahedron Letters*, 1964, **43**, 3197.

[27] J. P. Fleury, J. M. Bichler, and M. Desbois, *Tetrahedron Letters*, 1969, 4091; P. G. Gassman, and K. Shudo, *J. Amer. Chem. Soc.*, 1971, **93**, 5899.

[28] V. Rautenstrauch, *Chem. Comm.*, 1969, 1122.

reactivity towards mono-olefins.[25] The special opportunity for transannular addition provided by (Ib), and to a lesser extent (IIb), with the consequent formation of a carbon radical, thus allows a chain process to be sustained. For the Ag^+-catalysed reactions, the identity of the initiator for the radical chain process is suggested by recent work carried out by Edwards and his colleagues [29] clarifying the mechanism of their transannular cyclisations of medium-sized ring *N*-chloro-amines. The presence of traces of amine, known [30] to be capable of reducing Ag^+, in the *N*-chloro-amine–silver salt reaction mixtures evidently resulted in the generation of sufficient metallic silver to initiate the radical chain: $R_2NCl + Ag^0 \longrightarrow AgCl + R_2\dot{N}$. The operation of a similar initiation mechanism for the silver ion-catalysed reactions described in the present work seems probable, and is consistent with the observation of a distinct induction period, presumably required for the accumulation of products capable of reducing Ag^+.

In the absence of silver salts a marked distinction was apparent between the thermal decompositions of compound (Ib) in methanol compared with reactions in acetone or acetonitrile. In methanol the results again indicate a radical chain reaction; the nature of the initiator remains obscure, although one possibility is the thermally unstable methyl hypochlorite [31] which is a potential trace ingredient formed *via* the equilibrium: [32] $>NCl + MeOH \rightleftharpoons >NH + MeOCl$.

The virtual absence of bicyclic products from the relatively slow decompositions in acetone or acetonitrile implies that if neutral aminyl radicals are generated in these solvents, intermolecular hydrogen abstraction prevails over intramolecular addition. Chlorination of solvent by a heterolytic mechanism, perhaps catalysed by hydrogen chloride slowly liberated from the accompanying elimination reaction, represents an alternative possibility, which could also account for the lengthy induction period (Figure).

In conclusion, at least three pathways are available to *N*-chloro-amines reacting in neutral protic solvents, leading variously to the formation of aminyl radicals or cationic intermediates, or the elimination of hydrogen chloride. The balance among these possibilities favoured by a particular *N*-chloro-amine is clearly dependent upon its structure, but, as in the case of alkyl hypobromites,[33] there appears to be considerable predisposition towards homolysis, even in reactions catalysed by silver salts.

EXPERIMENTAL

I.r. spectra were recorded with Unicam SP 200G and Perkin-Elmer 257 instruments, and a Perkin-Elmer R14 spectrometer was used to obtain 100 MHz n.m.r. spectra of solutions in deuteriochloroform, with tetramethylsilane as internal reference. G.l.c. analyses were carried out on 7 ft × 3/16 in columns packed with 10% neopentyl glycol succinate or 20% Carbowax 20M on 100—120 mesh silanised Supasorb.

Ethyl N-*Cyclo-oct-4-enylidenecarbamate* (IX).—A solution of ethyl azidoformate (35 g) in redistilled cyclo-octa-1,5-diene (330 g) was heated for 16 h on a steam-bath. The excess of diene was removed *in vacuo* and the residual oil distilled (Vigreux fractionating column); the *carbamate* was obtained as a viscous oil (45·7 g, 82%), b.p. 94—102° at 0·08 mmHg, $\nu_{max.}$ (film) 3020 (:CH), 2940, 2865, 1720 (CO_2Et), 1666 (C:C and C:N), 1230, and 725 cm^{-1} (Found: C, 67·4; H, 8·6; N, 7·1. $C_{11}H_{17}NO_2$ requires C, 67·7; H, 8·8; N, 7·2%), τ (CCl_4) 4·3—4·7 (2H, complex m, CH:CH), 5·95 (2H, q, *J* 8·5 Hz, $CH_2{\cdot}CH_3$), 7·5—8·2 (8H, complex m, 4 × CH_2), and 8·75 (3H, t, *J* 8·5 Hz, $CH_2{\cdot}CH_3$).

A solution of the carbamate (130 mg) in ethanol (10 ml) and water (2 ml) containing sulphuric acid (3 drops) was kept for 18 h at room temperature and then poured into water. The oily product, isolated with ether, was identical with an authentic sample of cyclo-oct-4-enone (i.r. and g.l.c. data).

N-*Methylcyclo-oct-4-enamine* (Ia).—A solution of the carbamate (IX) (40 g) in dry ether (150 ml) was added slowly with vigorous stirring to a suspension of lithium aluminium hydride (11·7 g) in dry ether (250 ml). The mixture was heated under reflux for 3 h, cooled, and carefully decomposed with saturated aqueous potassium sodium tartrate. Isolation with ether and distillation *in vacuo* gave the amine as an oil (21·5 g), b.p. 84—85° at 8 mmHg. Further purification was effected *via* the crystalline carbamate, isolated by saturation of a solution of the base in n-pentane with dry carbon dioxide; the amine was regenerated by warming. The picrate crystallised from ethanol as needles, m.p. 138—140° (lit.,[6] 135—136°).

Ethyl N-*Cyclohept-4-enylcarbamate* (XIII).—Cyclohept-4-enecarboxylic acid [10] was converted into its acid chloride by the procedure of Doering *et al.*[34] with the slight modification that a temperature of 60° was used, leading to an improved (90%) yield.

A solution of the acid chloride (9·0 g) in ether (50 ml) was added to an ice-cold, stirred solution of sodium azide (6·5 g) in water (50 ml). After 3 h the organic layer was separated, washed with aqueous sodium hydrogen carbonate and with water, dried, and evaporated to afford cyclohept-4-enecarbonyl azide (8·65 g, 93%) as an oil, $\nu_{max.}$ (film) 3018 (:CH), 2260 and 2135 (N_3), 1710 (CO), and 1650 cm^{-1} (C:C).

The crude azide (8·65 g) in ethanol (100 ml) was refluxed for 14 h. Removal of the solvent left the *ester* (XIII) (9·2 g, 96%); crystallisation from light petroleum (b.p. 60—80°) gave needles, m.p. 69—71° (Found: C, 65·8; H, 9·3; N, 7·6. $C_{10}H_{17}NO_2$ requires C, 65·5; H, 9·3; N, 7·6%).

N-*Methylcyclohept-4-enamine* (IIa).—A solution of the crude carbamate (XIII) (8·53 g) in dry ether (100 ml) was slowly added to a stirred suspension of lithium aluminium hydride (2·7 g) in dry ether (50 ml). After 12 h, the cooled mixture was decomposed with saturated aqueous potassium sodium tartrate and the product isolated with ether. Distillation *in vacuo* gave the amine (4·1 g, 66%) as an oil, b.p. 55—57° at 16 mmHg, $\nu_{max.}$ (film) 3280 (NH), 3010

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(:CH), and 1650 cm^{-1} (C:C). Treatment of the amine with phenyl isocyanate in light petroleum gave the N-*phenylurea*, obtained from ethanol as needles, m.p. 186—187° (Found: C, 72·9; H, 8·4; N, 11·6. $C_{15}H_{20}N_2O$ requires C, 72·4; H, 8·7; N, 12·1%).

Preparation of N-*Chloro-amines*.—A solution of the secondary amine (0·02 mol) in anhydrous dichloromethane (30 ml) cooled to 5° was treated with a cold 0·4M-solution of *N*-chlorosuccinimide (50 ml) in dry dichloromethane. After 30 min at 5°, and a further 1 h at room temperature, the solvent was removed *in vacuo*, leaving a pasty residue which was extracted with n-pentane (3 × 30 ml). The combined extracts were filtered through a short column of Celite and the solvent was removed at room temperature *in vacuo* giving the *N*-chloro-amines as pale yellow oils, which were generally 98% pure (by iodometric titration) though too unstable to permit further purification by distillation.

N-Chloro-*N*-methylcyclo-oct-4-enamine (Ib) showed $\nu_{max.}$ (film) 3010 (:CH) and 1650 (C:C) cm^{-1}, τ (CCl_4) 4·5 (2H, t, HC:CH), 7·3 (3H, s, NMe), 7·4 (1H, m, CH:N), and 7·5—8·8 (10H, m, 5 × CH_2); $\lambda_{max.}$ (cyclohexane) 280 nm (ε 400).

Reaction of N-*Chloro*-N-*methylcyclohept-4-enamine* (IIb) *with Silver Perchlorate in Acetone*.—A solution of silver perchlorate (0·41 g) and the *N*-chloro-amine (0·31 g) in dry acetone (10 ml) was refluxed under nitrogen for 45 min, after which the presence of *N*-chloro-amine could no longer be detected iodometrically. The cooled mixture was filtered, the greyish brown precipitate was washed thoroughly with hot acetone, and the filtrate was evaporated *in vacuo*. The brown residue was digested with cold N-hydrochloric acid, the precipitated silver chloride was removed by filtration through Celite and washed successively with N-hydrochloric acid, water, and ether. Neutral organic material (20 mg) was removed by extraction with ether of the filtrate, which was then made strongly basic with aqueous sodium hydroxide, and the products were isolated by continuous extraction with ether for 24 h. G.l.c. of the resulting brown oil (107 mg) showed that it contained two volatile components. Chromatography on alumina (20 g; Woelm, activity III) and elution with light petroleum (b.p. 40—60°) containing 3% ether afforded 2β-*chloro*-8-*methyl*-8-*azabicyclo*[3,2,1]*octane* (V) (23 mg, 7·5%). Sublimation at 50° and 10 mmHg gave crystals, m.p. 30—32°, $\nu_{max.}$ (film) 2940br, 2800, and 2765 cm^{-1} (NMe) (Found: C, 60·2; H, 8·8; Cl, 22·0. $C_8H_{14}ClN$ requires C, 60·1; H, 8·8; Cl, 22·2%); τ 6·00 (CHCl, $W_{\frac{1}{2}}$ 8 Hz), 6·82br (s, bridgehead protons), 7·75 (s, NMe), and 7·5—8·9 (m, methylenes) (intensity ratio 1 : 2 : 3 : 8); *m/e* 159 (M^+), 124, 96, 82 (base peak), and 42.

The *picrate* crystallised from ethanol as yellow needles, m.p. 241—243° (decomp.) (Found: C, 43·3; H, 4·4; Cl, 8·9; N, 14·6. $C_{14}H_{17}ClN_4O_7$ requires C, 43·2; H, 4·4; Cl, 9·1; N, 14·4%).

Further elution of the column with ether afforded *N*-methylcyclohept-4-enamine (35 mg, 14%), identified by comparison (spectra and g.l.c. retention times) with an authentic sample.

Hydrogenolysis of 2β-*Chloro*-8-*methyl*-8-*azabicyclo*[3,2,1]-*octane* (V).—Finely chopped sodium (0·8 g) was added during 15 min to a stirred solution of the chloride (136 mg) in anhydrous t-butyl alcohol (2 ml) and anhydrous tetrahydrofuran (8 ml). The mixture was stirred under nitrogen for 0·5 h at room temperature and then for 6 h under reflux. The excess of sodium was destroyed by addition of methanol to the cooled mixture, and after dilution with water the product was isolated with ether. Distillation at 50 mmHg gave tropane (90 mg, 85%), identical with an authentic sample in i.r. and n.m.r. spectra, g.l.c. retention times, and the m.p. and mixed m.p. of their picrates, m.p. 286—288° (decomp.) [lit.,[13] 284—285° (decomp.)].

Synthesis of the 2β-*Chloroazabicyclo-octane* (V).—A solution of *N*-methylcyclohept-4-enamine (50 mg) in dry ether (10 ml) was saturated with dry hydrogen chloride; the resulting hydrochloride was collected, washed with ether, and dissolved in dry dichloromethane (5 ml). The solution was cooled to 10° and treated with dry chlorine until a faint yellow colour persisted. Solvent and excess of chlorine were removed *in vacuo* leaving a colourless gum, trituration of which with ether afforded the *trans*-dichloride hydrochloride (68 mg, 83%) as crystals, m.p. 145—151°, $\nu_{max.}$ (Nujol) 2480 and 2440 (NH_2^+), and 1600 cm^{-1} (NH_2^+). A solution of the hydrochloride (54 mg) in water (5 ml) was made strongly alkaline by addition of 20% sodium hydroxide; isolation with ether afforded a colourless oil (32 mg) shown by g.l.c. to contain only one volatile product. Preparative g.l.c. followed by recrystallisation from n-pentane at −60° gave the 2β-chloroazabicyclo-octane (V), m.p. 29—31°, identical with the sample obtained as described previously.

Reactions of N-*Chloro*-N-*methylcyclo-oct-4-enamine* (Ib).—Reactions were carried out on freshly prepared compound (*ca.* 1 g) dissolved (0·4M-solutions) in the dry, redistilled solvent (*ca.* 15 ml). Solutions were deoxygenated and protected from light and reactions were carried out under nitrogen. The concentration of unchanged *N*-chloro-amine in 0·2 ml samples was determined by addition to a mixture of propan-2-ol (0·5 ml), glacial acetic acid (0·5 ml), and aqueous 25% potassium iodide (1 ml); liberated iodine was titrated with 0·02M-sodium thiosulphate. Quantitative g.l.c. analyses of the crude products were carried out with isopentyl benzoate as internal standard; substance-specific correction factors were determined by use of the appropriate pure compounds.

Results are given in Tables 1 and 2; the following general procedures were used:

(a) *In acetone*. A solution of the *N*-chloro-amine in acetone was kept at 50°; decomposition was complete in 12 h. The basic products contained one major product, *N*-methylcyclo-oct-4-enamine (52%) with only traces (<2%) of the 2β-chloroazabicyclononanes (III) and (IV).

Reaction of the *N*-chloro-amine (0·7 g) with silver perchlorate (0·83 g) in refluxing acetone (10 ml) was complete after 0·5 h. The mixture was cooled and worked up as described for the lower homologue; the neutral fraction (40 mg) was identical (g.l.c.) with cyclo-oct-4-enone. The basic fraction, containing three volatile components (ratio 1 : 12 : 5), was separated by preparative g.l.c. (20 ft × 3/8 in of 25% Carbowax 6000 on 60—80 mesh Supasorb at 150°) or by chromatography on alumina and elution with 3% ether–light petroleum (b.p. 40—60°). In addition to the minor product, *N*-methylcyclo-oct-4-enamine (Ia), 2β-*chloro*-9-*methyl*-9-*azabicyclo*[4,2,1]*nonane* (III) was obtained as a colourless oil, $\nu_{max.}$ (film) 2930, 2810, 2770, 1472, and 1448 cm^{-1}; τ 5·7br (1H, $W_{\frac{1}{2}}$ 8 Hz, C*H*Cl), 7·1br (m, bridgehead protons), 7·40 (s, NMe), and 7·5—9·0 (m, methylenes); *m/e* 173 (M^+), 138, 110, 96 (base peak), 83, 82, and 42; the *picrate* crystallised from water as needles, m.p. 230—231° (Found: C, 44·5; H, 4·5; Cl, 9·2; N, 13·9. $C_{15}H_{19}ClN_4O_7$

requires C, 44·7; H, 4·7; Cl, 8·8; N, 13·9%). 2β-*Chloro-9-methyl-9-azabicyclo*[3,3,1]*nonane* (IV) was obtained as colourless needles, which after sublimation had m.p. 44—46°, $\nu_{max.}$ (Nujol) 2805, 2770 (NMe), 1481 and 893 cm^{-1}; τ 5·7br (1H, $W_{\frac{1}{2}}$ 8 Hz, CHCl), 7·1br (2H, m, bridgehead protons), 7·40 (s, NMe), and 7·5—9·0 (m, methylenes); *m/e* 173 (M^+), 138, 110, 96 (base peak), 57, and 42 (Found: C, 62·1; H, 9·1; Cl, 20·7; N, 8·1. $C_9H_{16}ClN$ requires C, 62·2; H, 9·3; Cl, 20·4; N, 8·1%). The *picrate* crystallised from water as needles, m.p. 256—258° (decomp.) (Found: C, 45·0; H, 4·7; Cl, 9·0; N, 13·7. $C_{15}H_{19}ClN_4O_7$ requires C, 44·7; H, 4·7; Cl, 8·8; N, 13·9%).

In a similar experiment, after complete disappearance of the *N*-chloro-amine, dry methanol was added and the mixture was heated under reflux for 30 min. Quantitative g.l.c. examination of the basic products, isolated as already described, showed the presence of secondary amine, the two chlorides described before, and 2α-methoxy-9-methyl-9-azabicyclo-[4,2,1]- and -[3,3,1]-nonane (see later) in the amounts tabulated.

The two chlorides (III) and (IV) were recovered unchanged after being kept in methanolic solution at 60° for 12 h.

(b) *In acetonitrile.* Reactions were carried out at 60° and followed iodometrically; products were isolated and analysed as already described.

(c) *In cyclohexane.* A solution of the *N*-chloro-amine (1·05 g) in cyclohexane (15 ml) was kept in a thermostat at 60°; the concentration was virtually unaltered after 6 days. Azobisisobutyronitrile (67 mg, 0·05 mol. equiv.) was added; the decomposition of the substrate was found to be complete after 60 h. The solvent was removed and the residue was partitioned between 4N-hydrochloric acid (25 ml) and ether. The aqueous layer was washed with ether, basified with aqueous 30% sodium hydroxide, and extracted continuously with ether, giving a crude basic product (535 mg) containing secondary amine and the chlorides (III) and (IV) in the amounts tabulated.

In a similar experiment, after the *N*-chloro-amine had disappeared methanol (15 ml) was added and the mixture was maintained at 60° for 6 h; the basic fraction contained the five products in the amounts tabulated.

(d) *In methanol.* A solution of the *N*-chloro-amine (2·3 g) in methanol (30 ml) was kept at 60°; the reaction was followed iodometrically (Figure) and was found to be complete in 2 h. The mixture was worked up as previously described giving a neutral fraction (90 mg) shown by g.l.c. and i.r. spectroscopy to consist chiefly of cyclo-oct-4-enone. The basic fraction (720 mg) was distilled at 110° (bath temp.) and 0·5 mmHg giving a colourless oil (540 mg), shown by g.l.c. to contain five major components, three of which were identified by their retention times as the amine (Ia), and the 2β-chloroazabicyclononanes (III) and (IV). The mixture was separated by a combination of preparative g.l.c. (30 ft × 3/8 in column of 10% E30 on silanised Supasorb at 150°) and chromatography on alumina, with mixtures of ether and light petroleum (b.p. 40—60°) as eluants. In addition to the three compounds mentioned, 2α-methoxy-9-methyl-9-azabicyclo[4,2,1]nonane (XXIII), identical with the sample synthesised as described later, was isolated, together with 2α-*methoxy-9-methyl-9-azabicyclo*[3,3,1]*nonane* (XXIV), $\nu_{max.}$ 2980, 2815, 2770, 1487, 1180, 1106, and 893 cm^{-1}; τ 6·2—6·6 (1H, m, C*H*·OMe), 6·67 (3H, s, OMe), 7·1 (2H, m, bridgehead protons), 7·45 (3H, s, NMe), and 7·8—8·8 (10H, m, methylenes); *m/e* 169 (M^+), 154, 138, 110, 96 (base peak), 70, 57, and 42. The *picrate* crystallised from aqueous methanol as needles, m.p. 157—159° (Found: C, 48·4; H, 5·8. $C_{16}H_{22}N_4O_8$ requires C, 48·2; H, 5·6%).

Experiments on the decomposition of the *N*-chloro-amine in methanolic solution in the presence of silver perchlorate (1 mol. equiv.), oxygen, diphenyldipicrylhydrazyl (0·075 mol. equiv.), and silver perchlorate (1 mol. equiv.), and oxygen, were also carried out (results in Table 2).

9-Methyl-9-azabicyclo[3,3,1]*nonane* (XV).—(a) *Hydrogenolysis of* 2β-*Chloro-9-methyl-9-azabicyclo*[3,3,1]*nonane* (IV). The chloride (250 mg), dissolved in a mixture of t-butyl alcohol (4 ml) and tetrahydrofuran (15 ml) was reduced with metallic sodium (1·5 g), and the product was isolated as described for the lower homologue. Distillation at 50 mmHg afforded 9-methyl-9-azabicyclo[3,3,1]nonane (140 mg, 70%) as an oil, identical in i.r. spectrum, g.l.c. retention time, and picrate [m.p. and mixed m.p. 298—300° (decomp.)] [lit.,[35] 300° (decomp.)] with the sample prepared as described in (b).

(b) *From 9-methyl-9-azabicyclo*[3,3,1]*nonan-3-one* (XVI). A solution of phenyl chloroformate (0·79 g) in dry dichloromethane (5 ml) was slowly added to a solution of the ketone (XVI) (0·85 mg) in dry dichloromethane (5 ml) cooled to 5°. After 24 h at room temperature the solution was washed successively with 4N-sodium hydroxide, N-hydrochloric acid, and water, dried, and evaporated; extraction of the crude product with boiling light petroleum (b.p. 60—80°) gave, on concentration and cooling, *phenyl 3-oxo-9-azabicyclo*-[3,3,1]*nonane-9-carboxylate* (XVII) (1·18 g, 91%) as plates, m.p. 121—122°, $\nu_{max.}$ (CCl_4) 1717 cm^{-1} (CO and CO_2Ph); τ 2·3—2·8 (m, Ph), 5·05br (s, bridgehead protons), 7·2—7·6 (m, CH_2·CO), and 8·0—8·5 (methylenes) (intensity ratio 5 : 2 : 4 : 6) (Found: C, 69·5; H, 6·7; N, 5·5. $C_{15}H_{17}NO_3$ requires C, 69·5; H, 6·6; N, 5·4%).

The keto-ester (0·98 g) was refluxed with *p*-tolylsulphonylhydrazine (1·42 g) in methanol (20 ml) for 3 h; the mixture was stored overnight at 0° and *phenyl* 3-p-*tolylsulphonylhydrazono-9-azabicyclo*[3,3,1]*nonane-9-carboxylate* (XVIII) (1·08 g, 63%) was collected. Recrystallisation from methanol gave needles, m.p. 202—204°, $\nu_{max.}$ (Nujol) 3120 (NH), 1690 (CO_2Ph), and 1627 cm^{-1} (C:N) (Found: C, 61·9; H, 6·1; S, 7·4. $C_{22}H_{25}N_3O_4S$ requires C, 61·8; H, 5·9; S, 7·5%).

The *p*-tolylsulphonylhydrazone (0·97 g) was added to a stirred suspension of lithium aluminium hydride (1·50 g) in dry tetrahydrofuran (50 ml); the mixture was refluxed for 6 h and excess of reagent was destroyed by careful addition of saturated aqueous sodium potassium tartrate (75 ml). The organic layer was separated, the aqueous layer was extracted with ether, and the combined extracts were washed successively with 4N-sodium hydroxide and brine, and then dried. Removal of the solvents and distillation of the residual oil at 50 mmHg gave 9-methyl-9-azabicyclo-[3,3,1]non-2-ene (197 mg, 63%) as an oil, $\nu_{max.}$ (film) 3015 (:CH), 2800, 2770, 1643 (C:C), and 710 cm^{-1}, characterised as its picrate, m.p. 282—285° (decomp.) [lit.,[36] 286° (decomp.)].

Hydrogenation of the olefin (180 mg) in acetic acid (50 ml) over Adams catalyst (50 mg) gave pure 9-methyl-9-azabicyclo[3,3,1]nonane as an oil, $\nu_{max.}$ 2900br, 2800, and 2765 cm^{-1}.

9-Methyl-9-azabicyclo[4,2,1]*nonane* (XIX).—(*a*) 9-Methyl-

[35] A. Piccinini, *Gazzetta*, 1902, **32**, 260.
[36] A. C. Cope and C. G. Overberger, *J. Amer. Chem. Soc.*, 1948, **70**, 1433.

9-azabicyclo[4,2,1]nonan-3-one (XX), prepared[18] from tropan-3-one and purified by preparative g.l.c. (30 ft × 3/8 in column of 10% SE 30 on 60—80 mesh Celite at 150°) was obtained as an oil, $\nu_{max.}$ (film) 2940, 2790, 2765, 1700, 1472, and 1450 cm^{-1}; *m/e* 153 (M^+), 97, 96, 83, 82 (base peak), and 42; the *picrate* crystallised from ethanol as needles, m.p. 191—193° (decomp.) (Found: C, 46·9; H, 4·7; N, 14·7. $C_{15}H_{18}N_4O_8$ requires C, 47·1; H, 4·7; N, 14·6%).

A solution of this ketone (280 mg) in 4N-hydrochloric acid (50 ml) was hydrogenated for 14 h over Adams catalyst (200 mg) at 4 atm. The product contained two volatile components (ratio 3 : 1), which were separated by preparative g.l.c. (5 ft × 1/4 in SE 30 on 80—100 mesh Celite at 130°). The major component was an alcohol, $\nu_{max.}$ (film) 3370br (OH), 1473 (CH_2), 1092, and 1050 cm^{-1} (C–O), characterised as its picrate, obtained from water as needles, m.p. 285—290° (decomp.) [lit.,[18] 275—280° (previous sintering)]. The minor product, 9-methyl-9-azabicyclo-[4,2,1]nonane, was obtained as an oil, *m/e* 139 (M^+), 110, 96 (base peak), 83, 82, and 42; $\nu_{max.}$ (film) 2800, 2775, 2760, and 1472 cm^{-1}, also characterised as its picrate, m.p. 270—273° (decomp.) (lit.,[18] 272—273°).

(*b*) A solution of 2β-chloro-9-methyl-9-azabicyclo[4,2,1]-nonane (III) (250 mg) in t-butyl alcohol (2·0 ml) and dry tetrahydrofuran (8 ml) was treated with sodium (1·1 g) as previously described. Distillation of the product at 50 mmHg afforded the base, identical with the material prepared in (*a*).

9-Methyl-9-azabicyclo[4,2,1]*nonan-2α- and -2β-ol* [(XXVI) *and* (XXVII)].—A solution of *N*-bromosuccinimide (13·9 g) in 10% aqueous 1,2-dimethoxyethane (50 ml) was added during 15 min to a stirred solution of *N*-methylcyclo-oct-4-enamine (10·7 g) and 60% (w/v) perchloric acid (40 ml) in water (100 ml) cooled to 5—10°. After 1 h, basification with aqueous sodium hydroxide was followed by continuous extraction with ether for 24 h. The oily residue remaining after removal of the solvent was triturated with light petroleum (b.p. 40—60°; 70 ml). Filtration from precipitated succinimide, evaporation, and distillation at 70—100° (bath temp.) and 0·9 mmHg gave a colourless oil (7·2 g, 60%), shown by g.l.c. to contain three volatile components in the ratio 10 : 6 : 1. Separation was accomplished by preparative g.l.c. (20 ft × 3/8 in column of 10% neopentyl glycol succinate on Supasorb at 200°).

9-Methyl-9-azabicyclo[4,2,1]*nonan-2β-ol* (XXVII) had m.p. 37—39°, $\nu_{max.}$ (film) 3380br (OH), 2810, 2775, and 1475 cm^{-1}, τ 5·83 (s, OH), 6·37 (t, C*H*·OH), 6·80br (bridgehead protons), 7·50 (s, NMe), and 7·4—8·8 (m, methylenes) (intensity ratio 1 : 1 : 2 : 3 : 10); *m/e* 155 (M^+), 138, 126, 110, 96, 83, 82 (base peak), 57, and 42. The *picrate* crystallised from ethanol as needles, m.p. 257—260° (decomp.) (Found: C, 46·7; H, 5·5; N, 14·4. $C_{15}H_{20}N_4O_8$ requires C, 46·9; H, 5·3; N, 14·6%).

The second component to emerge from the column was the epimeric *2α-alcohol*, obtained as an oil, $\nu_{max.}$ (film) 3450br (OH), 2805, and 1480 cm^{-1}; τ 5·55 (s, OH), 6·02br (s, C*H*·OH), 6·73br (m, bridgehead protons), 7·53 (s, NMe), and 7·6—8·7 (m, methylenes) (intensity ratio 1 : 1 : 2 : 3 : 10); *m/e* 155 (M^+), 96, 83, 82 (base peak), 57, and 42. The *picrate* crystallised from ethanol as needles, m.p. 244—248° (decomp.) (Found: C, 45·6; H, 5·7; N, 14·4. $C_{15}H_{20}N_4O_8$ requires C, 46·9; H, 5·3; N, 14·6%).

The i.r. spectrum of each alcohol was also recorded on a Perkin-Elmer 125 spectrophotometer. A solution of the alcohol (40 mg) in pure dry carbon tetrachloride (0·5 ml) was contained in a variable path length cell; spectra were recorded at four path lengths in the range 0·2—6·0 mm. Solvent was added to maintain a constant level, giving concentrations in the range 0·5—0·015M.

Oxidation of 9-Methyl-9-azabicyclo[4,2,1]*nonan-2-ols.*—A solution of the alcohol (100 mg) in N-sulphuric acid (2 ml) was added to sodium dichromate (60 mg) in N-sulphuric acid (2 ml). The resulting solution was heated for 1 h on a steam-bath, cooled, and basified, and the product was isolated with ether. From either alcohol, 9-methyl-9-azabicyclo[4,2,1]nonan-2-one was obtained as a colourless oil, $\nu_{max.}$ (film) 2800, 2770 (NMe), and 1700 (CO) cm^{-1}, slightly contaminated with unoxidised material as shown by g.l.c. and a weak i.r. absorption at 3430 cm^{-1}. A solution of the crude ketone (174 mg) and phenyl chloroformate (178 mg) in dichloromethane (10 ml) was kept at room temperature for 48 h. The solution was washed successively with 2N-sodium hydroxide (10 ml), 4N-hydrochloric acid (10 ml), and water (2 × 20 ml), dried, and evaporated. The residue (200 mg) crystallised from ether–light petroleum (b.p. 40—60°) giving *phenyl 2-oxo-9-azabicyclo*[4,2,1]*nonane-9-carboxylate* (XXIX) as crystals, m.p. 93°, $\nu_{max.}$ (CCl_4) 3055, 3080 (arom. CH), 1730 (CO), and 1600 cm^{-1} (C:C); τ 2·70 (m, aromatic protons), 5·35 (m, bridgehead protons), and 7·0—8·4 (m, methylenes) (intensity ratio 5 : 2 : 10) (Found: C, 69·7; H, 5·6; N, 6·5. $C_{15}H_{17}NO_2$ requires C, 69·5; H, 5·4; N, 6·6%).

Reduction of 9-Methyl-9-azabicyclo[4,2,1]*nonan-2-one.*—A solution of the ketone (170 mg) in dry ether (5 ml) containing lithium aluminium hydride (60 mg) was stirred at room temperature for 16 h. Saturated aqueous sodium tartrate was carefully added, and isolation with ether gave an oil shown by g.l.c. (7 ft × 3/16 in column of 10% neopentyl glycol succinate on Supasorb at 150°) to consist of a mixture of 9-methyl-9-azabicyclo[4,2,1]nonan-2β- and -2α-ols in the ratio 2 : 1.

2β- and 2α-Methoxy-9-methyl-9-azabicyclo[4,2,1]*nonanes.*—A solution of each pure alcohol (180 mg) in hexamethylphosphoramide (10 ml) was stirred with sodium hydride (50% oil dispersion; 550 mg) at room temperature for 18 h under nitrogen. Methyl iodide (165 mg) was added and the mixture was stirred for a further 8 h, then poured into water (60 ml). The oily products were isolated with ether. Chromatography on alumina (Woelm, activity III) and elution with ether–light petroleum (b.p. 40—60°) gave the pure ethers.

2α-Methoxy-9-methyl-9-azabicyclo[4,2,1]*nonane* (XXIII) was obtained as an oil (31 mg), $\nu_{max.}$ (film) 2770, 2820 (NMe), 1473, 1160, and 1105 cm^{-1}; *m/e* 169 (M^+), 154 (base peak), 138, 110, 96, 83, 82, and 42; τ 6·67 (3H, s, OMe), 6·4—7·0 (3H, m, bridgehead protons and C*H*·OMe), 7·55 (3H, s, NMe), and 7·6—8·8 (10H, m, methylenes). The *picrate* crystallised from aqueous methanol as needles, m.p. 163—165° (Found: C, 48·5; H, 5·6; N, 14·1. $C_{16}H_{22}N_4O_8$ requires C, 48·2; H, 5·6; N, 14·1%).

2β-Methoxy-9-methyl-9-azabicyclo[4,2,1]*nonane* was also an oil, $\nu_{max.}$ (film) 2815, 2775, and 1103 cm^{-1}, τ 6·63 (s, OMe), 6·60—6·95 (m, *CH*·OMe and bridgehead protons), 7·53 (s, NMe), and 7·60—8·90 (m, methylenes) (intensity ratio 3 : 3 : 3 : 10); *m/e* 169 (M^+), 154, 96, 82, and 42. The *picrate* had m.p. 168—170° (from ether–methanol) (Found: C, 48·2; H, 5·4; N, 14·2. $C_{16}H_{22}N_4O_8$ requires C, 48·2; H, 5·6; N, 14·1%).

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