Tetrahedron. Vol. 30, pp. 39 to 45. Pergamon Press 1974. Printed in Great Britain

ASYMMETRICAL NONBRIDGEHEAD NITROGEN—IV[1]

CHIROPTICAL PROPERTIES OF THE AMINES, N-CHLOROAMINES AND CYANAMIDES

R. G. KOSTYANOVSKY,* I. M. GELLA, V. I. MARKOV and Z. E. SAMOJLOVA
Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow, USSR

(*Received in the UK* 11 *January* 1973; *Accepted for publication* 27 *July* 1973)

Abstract—The ORD and CD spectra of 2-methyl-aziridine, azetidine, pyrrolidine, piperidine, their N-Me, N-Hal, N-CN derivatives as well as those of camphidine, N-methyl- and N-cyano-camphidine have been investigated. The possibility of application of the quadrant rule for N-chloroamines is discussed. A similar rule is proposed for the N-CN chromophore.

Chiroptical properties of the aliphatic amines have been studied using 2-substituted piperidines[2-7] and some steroidal alkaloids and amines with the tertiary amine chromophore.[8] In the case of dithiocarbamates,[9] dithiourethanes,[10] chiral pyrrolidines and piperidines, a quadrant rule can be applied while a sector rule is valid for N-nitrososubstituted 4-, 5- and 6-membered cyclic amines and aminoacids.[11,12] For N-chloropiperidines[13] only the substituent increments were established on the ground of their additive contributions to the Cotton effects.

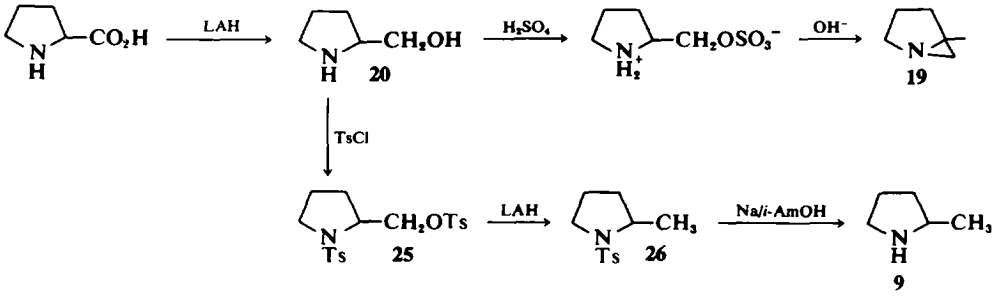
We have investigated the chiroptical properties of N-H, N-Me, N-Hal and N-CN chromophores in 2-methyl-substituted heterocycles:

$CH_3—\underbrace{CH—(CH_2)_n—N}—R$

n = 1 R = H(1), Cl(2), Br(3)
n = 2 R = H(4), Me(5), Cl(6), Br(7), CN(8)
n = 3 R = H(9), Me(10), Cl(11), CN(12)
n = 4 R = H(13), Me(14), CN(15)

and azabicyles: camphidine (**16**), N-methylcamphidine (**17**), N-cyanocamphidine (**18**), 1-azabicyclo[3.1.0]hexane (**19**) and L-prolinole (**20**).

Configuration of these products is defined by means of the synthesis of (1) from the L-alanine,[14] **16** from the (+)-camphoric acid[15,16] and **9** and **19** from the L-proline according to the scheme:



(+)-α-Pipecoline was prepared by resolution of *dl*-base with dibensoyltartaric acid. Its *S*-configuration was proved by Ripperger.[17] The *S*-configuration of (+)-2-methylazetidine (**4**) resolved as dibenzoyltartrate was proved in the following way. (+)-(3*S*)-N-(α-phenylethyl)aminobutyric acid (**21**)[18] prepared from optically pure (−)-α-phenylethylamine was converted into (*S*)-4-methylazetidinone-2 (**22**)[19] whose configuration was proved independently by X-ray analysis.[20] The PMR spectrum of the intermediate N-(α-phenylethyl)-4*S*-methylazetidinone-2 (**23**) proved it to be diastereomeric pure (Fig 1). Therefore we may consider the (*S*)-4-methylazetidinone-2 (**22**) to be optically pure.

Compound **22** was reduced with LAH to (*S*)-2-methylazetidine. The latter was tosylated without isolation to give dextrorotatory (*S*)-1-tosyl-2-methylazetidine (**24a**). The tosylation of (+)-2-methylazetidine (**4**) gave dextrorotatory 1-tosylate (**24b**) which proves the *S*-configuration of **4**, the specific rotation of **24b** being 79% of rotation of **24a** which can be assumed optically pure on the basis of previously listed data. Hence our previous assignment of the *R*-configuration to (+)-2-methylazetidine based on ORD data[1] is not correct.

The aliphatic amines have several superimposed absorption bands in the region 190–240 nm.[21,22] Dis-

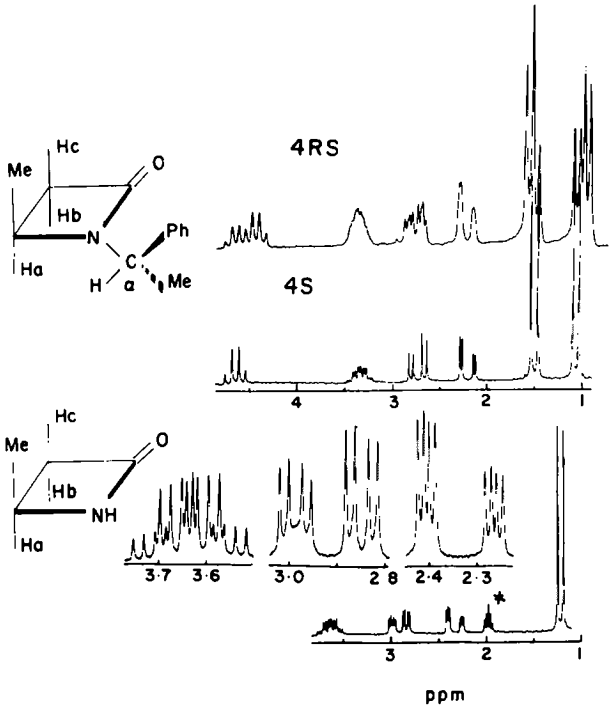


Fig 1. PMR spectra of (*S*)-4-methylazetidinone-2, N[(−)-α-phenylethyl]-4S-methylazetidinone-2 and N[(−)-α-phenylethyl]-4RS-methylazetidinone-2 (* — signal from uncomplete deuterated acetone).

appearance of these bands on the protonation of the amines shows that electron transitions of the nitrogen lone pair have taken place. Often only one maximum is observed in the UV spectra of amines, but the complex nature of the absorption region is evident from the CD spectra where one can see two Cotton effects with the opposite signs in the region 210–230 nm and below 205 nm. The blue shift of the absorption maximum results in observing only one shoulder of Cotton effect in the CD spectrum of **1**.

The sign of the Cotton effect and the smooth part of the ORD curve for 2-alkylpiperidines[2-6] depends on the absolute configuration of the asymmetrical center. The same dependence is observed for 2-substituted aziridines, azetidines and pyrrolidines: with amines of the *S*-series the ORD curve is positive, while it is negative with the *R*-series (Fig 2).

It should be noted that appreciable differences exist between ORD and CD spectra of the 4–5-membered cyclic amines and those of the substituted piperidines. In the first case the character of the ORD curve is determined by a longwave Cotton effect with a max at 215–218 nm in the CD spectra (Fig 3). In the CD spectra of *d*-camphidine (Fig 3), (*S*)-(+)-coniine,[23] (−)-sedridine and (+)-allosedridine[4] the longwave Cotton effect has a low intensity. In each case the sign of the ORD curve is defined by a Cotton effect which is lower than

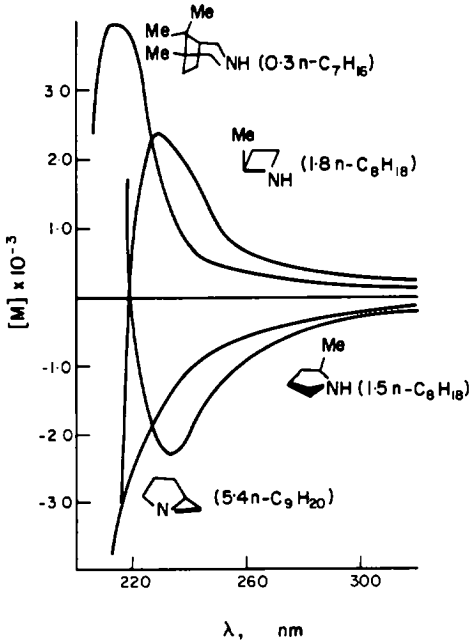


Fig 2. ORD spectra of d-camphidine, S-2-methylazetidine R-2-methylpyrrolidine and 5S-1-azabicyclo[3.1.0]-hexane.

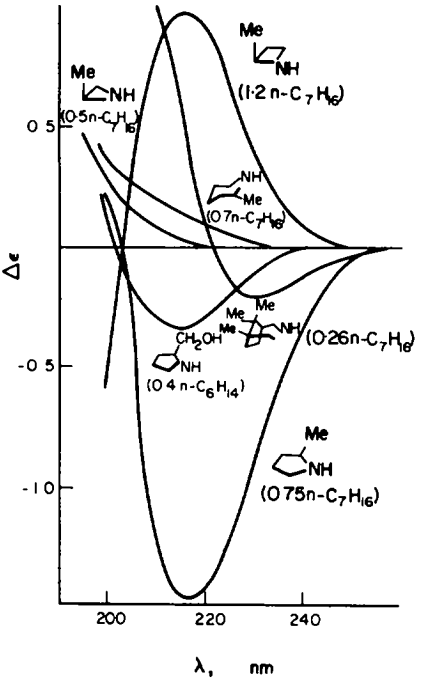


Fig 3. CD spectra of S-2-methylaziridine, S-2-methylazetidine, R-2-methylpyrrolidine, 4-prolinole S-2-methylpiperidine and d-camphidine.

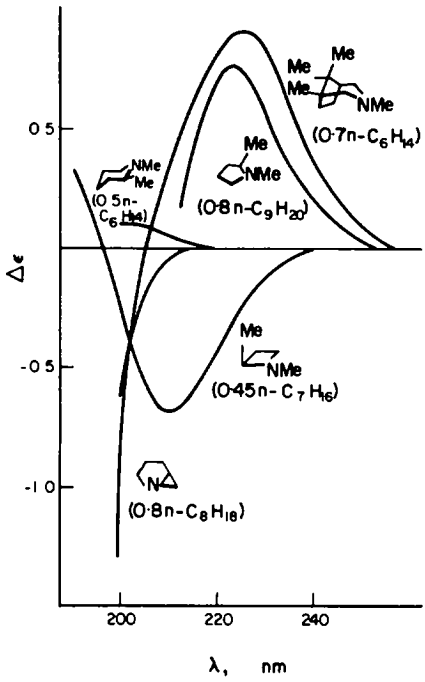


Fig 4. CD spectra of S-1,2-dimethylazetidine, R-1,2-dimethylpyrrolidine, 5S-1-azabicyclohexane, S-1,2-dimethylpiperidine and 1-methyl-d-camphidine.

200 nm. The Cotton effect is completely absent in the CD spectra of (*S*)-α-pipecoline (Fig 3).

A positive Cotton effect is observed for the *R*-Me groups in 1,2-dimethylpyrrolidine (Fig 4) and heteroconanine[8] whereas it is negative for the *S*-Me groups in 1,2-dimethylazetidine (Fig 4) and conanine[8] with maxima at 210–225 nm. A weak Cotton effect at 225 nm ($\Delta\epsilon + 0{\cdot}013$) is observed in the CD spectrum of 5S-1-azabicyclo[3.1.0]hexane (**19**), where configuration of the C-2 center is the same as for **9**. Probably, 2-substituted piperidines are the exception since methylation does not change the character of ORD curve in the case of sedridine and allosedridine[7] or the CD curve in the case of (*S*)-2-methylpiperidine (Figs 3, 4).

The interpretation of the electron transitions of the aliphatic amines presents problems. Therefore we need to introduce into the molecule a chromophore with a known geometry of the optically active transition in order to rationalize a Cotton effect from the point of view of the regional rule.

The N-Cl chromophore stands out sharply against the other well known chromophores because of its internal symmetry. It gives an optically active absorption band of the $n \rightarrow \sigma^*$ transition in the region of 260–280 nm (ϵ 320 ÷ 560).[13] The N-substituent is fixed in *cis*- and *trans*-1-chloro-2-methylaziridine due to the high inversion barrier of the N atom. We have suggested that the N-Cl axis is significant for the application of a quadrant rule to determine the Cotton effect sign. This rule in the case of **6** and **7** with preferred *trans*-orientation of 1,2-substituents predicts a weak negative Cotton effect; however a positive effect is observed in the CD spectrum of **6** and no effect is observed in the case of **7** (Fig 5).

Thus, this prediction is valid only if the value of the out of plane angle of N-Hal bond in **6** and **7** does not appreciably differ from the value of this angle in **2**.[24] Decreasing the out of plane angle can lead to the reverse Cotton effect sign. On the other hand the Cotton effect may be influenced by an increase in the conformational mobility of the chromophore resulting from a low inversion barrier of the N atom in 1-haloazetidines.

The described rule gives the right prediction of the Cotton effect sign in (*R*)-1-chloro-2-methylpyrrolidine (**11**); a study of Dreiding's molecular models shows the identical sign contribution of *cis*- and *trans*-epimers for pseudoequatorial orientation of Me groups. The quadrant rule cannot in practice be applied to 1-chloropiperidines, as all the possible conformers cannot be taken into consideration.

In contrast to N-haloamines the C-hal chromophore has a rigid configuration and in the latter case such a quadrant rule is applied more widely. In the 2-haloalkanes series[25] and in numerous iodosteroids[26] it was established that the Cotton effect in the region of the $n \rightarrow \sigma^*$ transition of the

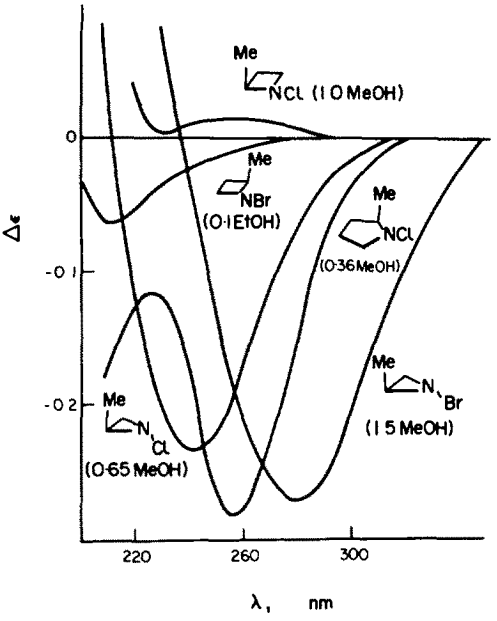


Fig 5. CD spectra of S-N-chloro-2-methylaziridine, S-N-bromo-2-methylaziridine, S-N-chloro-2-methylazetidine, R-N-chloro-2-methylpyrrolidine, R-N-bromo-2-methylazetidine.

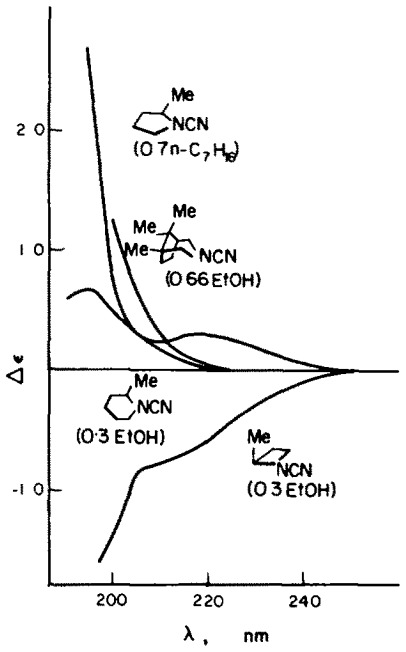


Fig 6. CD spectra of S-1-cyano-2-methylazetidine, R-1-cyano-2-piperidine, 1-cyano-d-camphidine, and 1-cyano-2-methylpirrolidine.

C-hal chromophore is determined by the absolute configuration of the secondary C atom of the chromophore. In all these cases the Cotton effect sign may be predicted by means of a quadrant rule similar to N-chloroamine, but with the reverse sign.

The above arguments prompted us to investigate the symmetrical cyanamide chromophore. In the CD spectra (Fig 6) of (*S*)-1-cyano-2-methylazetidine (**8**) and (*R*)-1-cyano-2-methylpyrrolidine (**12**) this is a complex Cotton effect which consists of two superimposed dichroic absorption bands of the same sign, but in 1-cyano-α-pipecoline (**15**) and 1-cyano-(+)-camphidine (**18**) only one CD band is observed. The first CD band is related to the UV absorption max in the region 200–210 nm whereas the second Cotton effect depends upon an absorption band below 180 nm; the shoulder of this band is observed in the UV spectra of **8** and **12** in aqueous solutions (Fig 7).

The shift of UV absorption band as a function of the solvent used and HMO calculation of cyanamide and dimethylcyanamide,[27] the absorption bands can be assigned to transitions of electrons of an amine nitrogen lone pair occupying the three-center non-bonding orbitals π^*_z to the antibonding π^*_y and π^*_z orbitals.

The Cotton effect sign may be unambiguously correlated with the absolute configuration of the asymmetrical center. The quadrant rule must be the common regional rule which is controlled by the symmetry properties[28] of the N-CN chromophore

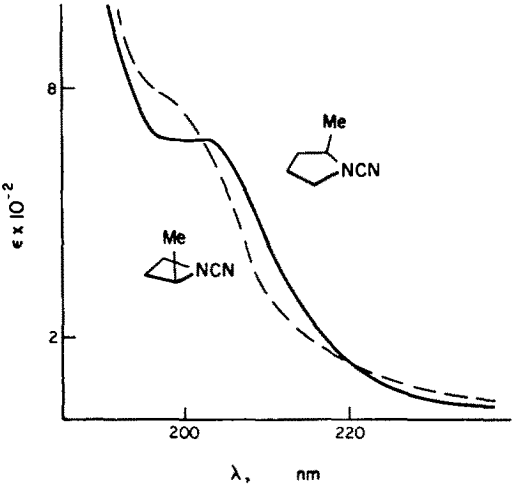
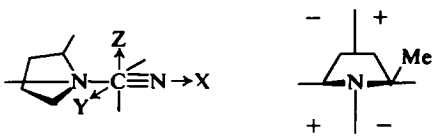


Fig 7. UV spectra of S-1-cyano-2-methylazetidine and R-1-cyano-2-methylpyrrolidine in aqueous solution.

under the assumption of planarity of the chromophore. From the microwave data it is known that the out of plane angle in cyanamide is equal to 38°58'[29] and in dimethylcyanamide it is nearly the same.[30] With such geometry of the chromophore, the equatorial group in **15** is arranged near the nodal surface. Presumably, because of this the shoulder of longwave Cotton effect is absent in the CD spectra (Fig 6). By analogy with azide[31] and

thiocyanate[32] chromophores, it is believed that the cyanamide chromophore should also follow the octant rule. One can see from the CD spectra of **8** and **12** that the N-CN chromophore is governed by the same sign rule as the azide and thiocyanate chromophore (Fig 6).

In compound **12**, for example, projection along NCN axis and the corresponding quadrant signs may be represented as follows:



EXPERIMENTAL

PMR spectra were obtained with Varian HA-100 spectrometer, chemical shifts were measured from HMDS internal standard. The specific rotation was measured with polarimeter Perkin-Elmer, ORD spectra were obtained with JASCO-ORD/UV-5 spectropolarimeter, CD spectra were obtained with Roussel-Jouan dichrograph, model CD-185. UV-spectra were measured with UV-Spicord spectrophotometer. Mass spectra of compounds **4**, **6**, **7** were published elsewhere[33] and mass spectra of **8–18** are to be published.

S(−)-2-*Methylaziridine* (**1**). To a suspension of LAH (33·5 g) in 500 ml THF, 22·5 g of L-alanine was added on cooling and stirring with heating at 75° for 50 h. After cooling the mixture was carefully treated with 50 ml water. The ppt was filtered off and washed with portions of THF. The combined filtrates were evaporated and azeotropically dried with benzene. The residue was distilled to give 13 g (63·2%) of L-alaninol, b.p. 80–82°/18 mm, n_D^{20} 1·4480 (lit.[14] b.p. 84°/23 mm, n_D^{29} 1·4493).

A mixture of conc H_2SO_4 (20 g) and 20 ml water was added to a soln of L-alaninol (12·8 g) in 12 ml water with cooling. The bath temp was gradually increased to 180°, and the water was distilled from the reaction mixture *in vacuo*. After cooling the residue, a soln of NaOH (20 g) in 100 ml water was added, 60 ml of liquid was distilled and saturated with pellets of KOH. The separated amine was dried over pellets of KOH and distilled over Na to yield 2·8 g (29%) of **1**, b.p. 65–65·5°, $[\alpha]_D^{20}$ −8·1° (*c* 3·0 in nonane); n_D^{20} 1·4120 (lit.[14] b.p. 66–67°, $[\alpha]_D^{20}$ −12·8° (0·227 g in 10 ml EtOH); $n_D^{27.5}$ 1·4156).

S(+)-1-*Bromo*-2-*methylaziridine* (**3**). To a soln of NaOH (1·6 g) in 8 ml water, Br_2 (3·2 g) was added at 0° with stirring and 1 g of **1** was slowly added in a dropwise manner. The organic layer was separated and washed with water. Drying over $MgSO_4$ and distillation *in vacuo* yielded 0·97 g (41%) of **3**, b.p. 31–32°/35 mm, UV: λ_{max} 293 nm (in nonane); CD: λ_{max} 280 nm, $\Delta\epsilon = 0·269$.

S(+)-2-*Methylazetidine* (**4**). The *dl*-base was prepared by reduction of 1-tosyl-2-methylazetidine with sodium in isoamyl alcohol according to the Vaughan procedure.[34] *dl*-2-Methylazetidine (25·8 g) was mixed with a soln of dibenzoyltartaric acid (100 g) in MeOH. Four-fold crystallisation of the resulting salt gave 43·7 g of dibenzoyltartrate of **4** (m.p. 161°). This salt was treated with excess NaOH aq. The amine was steam-distilled, saturated with pellets of KOH and after drying over KOH was distilled to yield 5·3 g (42% per one enantiomer) of *S*(+)-2-methylazetidine, b.p. 71–72°, $[\alpha]_D^{20}$ + 11·6° (*c* 1·0, in hexane); UV: λ_{max} 198 nm, $\epsilon = 1540$ (in hexane); CD: λ_{max} 215 nm, $\Delta\epsilon = 0·98$ (1.2, in heptane); n_D^{20} 1·4208 (lit[34] b.p. 72–76°).

S(+)-1,2-*Dimethylazetidine* (**5**). 2·6 g of **4** ($[\alpha]_D^{20}$ + 13·2°, *c* 1·0 in heptane) was added to a mixture of 10 ml aqueous formaldehyde and 10 ml formic acid and heated for 4 h on a boiling water bath. 3 ml conc HCl was added and the water was removed *in vacuo*. The residue was treated with conc KOH aq and the amine layer was separated. Drying over pellets of KOH and distillation resulted in 1·0 g (32·2%) of **5**, b.p. 61°, n_D^{20} 1·400, $[\alpha]_D^{20}$ + 43·5° (*c* 1·0 in heptane). CD: $\lambda_{max} = 210$ nm, $\Delta\epsilon$ 0·69 (Found: N, 16·35, $C_5H_{11}N$ requires: N, 16·46%).

S(+)-1-*Chloro*-2-*methylazetidine* (**6**). To a suspension of N-chlorosuccinimide (5·4 g) in 8 ml anhyd ether, 2·1 g of **4** ($[\alpha]_D^{20}$ 3·05, *c* 3·7 in nonane) in 2 ml ether was added with stirring. After stirring for 1 h the ppt was filtered off. The ether was removed and the residue was distilled to give 0·9 g (28·5%) of **6**, b.p. 32–33°/48 mm, $[\alpha]_D^{20}$ 21·5° (*c* 3·0 in MeOH) n_D^{20} 1·441; UV: λ_{max} 264 nm; CD: λ_{max} 257·5 nm, $\Delta\epsilon = 0·016$.

R(−)-1-*Bromo*-2-*methylazetidine* (**7**). To a suspension of N-bromosuccinimide (5 g) in 25 ml anhyd ether 2·1 g of *R*(−)-2-methylazetidine (isolated from mother liquor from resolution of *dl*-2-methylazetidine, $[\alpha]_D^{20}$ −6·4°; *c* 1·0, in heptane) in 5 ml ether was added and the mixture was stirring for 1 h. The ppt was filtered off and the ether was removed. Repeated filtration and distillation at a bath temp up to 60° yielded 1·23 g (27%) of **7**, b.p. 40·5–41·5°/40 mm, $[\alpha]_D^{20}$ −47° (*c* 1·0 in heptane); UV: λ_{max} 302 nm, $\epsilon = 320$; CD: λ_{max} 210 nm, $\Delta\epsilon = 0·064$ (lit[33] b.p. 41°/37 mm).

S(+)-1-*Cyano*-2-*methylazetidine* (**8**). Cyanochloride (3 g) was passed through a soln of **4** (3·55 g) ($[\alpha]_D^{20}$ + 11·6, *c* 1·0 in hexane) and triethylamine (4·85 g) in 50 ml anhyd ether. After 0·5 h, the ppt was filtered off and ether was removed. Distillation of the residue gave 2·55 g (53%) of **8**, b.p. 95–96°/25 mm, n_D^{20} 1·4482, $[\alpha]_D^{20}$ 69·4° (*c* 1·0 in hexane), UV: λ_{max} 202·8 nm, ϵ 475 (in EtOH) and λ_{max} 207 nm, ϵ 390 (in hexane). (Found: N, 29·19, $C_5H_8N_2$ requires: 29·13%).

S(+)-1-*Tosyl*-2-*methylazetidine* (**24b**). To a soln of *p*-toluenesulfochloride (0·3 g) in 15 ml hexane **4** (0·4 g) ($[\alpha]_D^{20}$ + 11·6°, *c* 1·0, in hexane) was added. The mixture was heated to dissolve the product. The ppt was separated and mother liquor was allowed to crystallize, 0·4 g (80%) of **24b** was obtained, m.p. 84–85°, $[\alpha]_D^{20}$ + 69° (*c* 1·3 in methanol). (Found: N, 6·13; $C_{11}H_{15}NO_2S$ requires: N, 6·21%).

N(−)-1(α-*Phenylethyl*)-4S-*methylazetidinone*-2 (**23**). To (+)3*S*-N-(α-phenylethyl)aminobutyric acid (8·6 g), 20 ml of $SOCl_2$ was added and the mixture was allowed to stand over night. The excess of $SOCl_2$ was removed *in vacuo*. To the solid residue, 20 ml anhyd benzene was added and the latter was removed. A suspension of 3*S*-N-(α-phenylethyl)-aminobutyrochloride hydrochloride in 50 ml benzene was slowly added to a boiling mixture of 15 ml dimethylaniline and 150 ml benzene and the mixture was stirred for 3 h. After cooling, the mixture was subsequently washed with 50 ml water, 3% HCl aq, sat $NaHCO_3$ aq and water.

Benzene was removed and the residue was distilled to yield 6·2 g (48%) of **23**, b.p. 111–112°/0·2 mm, n_D^{20} 1·5308, $[\alpha]_D^{20}$ −36·8° (*c* 1·2 in CH_2Cl_2); PMR (CCl_4): ν_a 4·65, ν_A 3·35, ν_B 2·74, ν_C 2·21, ν_{CH_3} 1·49, $\nu_{a\text{-}CH_3}$ 2·06, J_{AB} 5·0 Hz, J_{AC} 2·5 Hz, $J_{A\text{-}Me}$ 6·0 Hz, J_{BC} 14·2 Hz, $J_{Ha\text{-}Me}$ 7·0 Hz (Fig 1). (Lit[18] $[\alpha]_D^{20}$ −40·6°, *c* 1·17 in CH_2Cl_2).

S(+)-1-*Tosyl*-2-*methylazetidine* (**24a**). Compound **23** (2·4 g) was added to 100 ml of liquid ammonia and Na was added in small portions with stirring until a steady blue colour was observed. The excess of Na was decomposed by addition of NH_4Cl (5 g). After vaporisation of the ammonia, the dry residue was extracted with anhyd ether. Removal of the ether yielded 1·2 g of **22** identified by PMR (CD_3COCD_3): ν_A 3·64, ν_B 2·92, ν_C 2·33, ν_{CH_3} 1·21, J_{AB} 4·6 Hz, J_{AC} 2·3 Hz, $J_{A\text{-}Me}$ 6 Hz, J_{BC} 14 Hz, $J_{B\text{-}NH}$ 1·9 Hz, $J_{C\text{-}NH}$ 1·3 Hz (Fig 1).

Compound **22** (1·2 g) in 15 ml dry ether was added to a suspension of LAH (2 g) in 50 ml anhydrous ether and boiled for 3 h. After cooling, the mixture was decomposed with water, the ether layer was removed and 20 ml of the product was steam-distilled from the water layer. The distilled product was combined with the ether layer and treated with excess *p*-toluenesulphochloride and KOH aq. After the ether removal, the solid residue was filtered off, dried and recrystallized from hexane to yield 1 g (35%) of **24a**; m.p. 88–89°, $[\alpha]_D^{20}$ +87·4° (*c* 1·0 in MeOH). (Found: N, 6·12, $C_{11}H_{15}NO_2S$ requires: N, 6·21%).

L-*Prolinole* (**20**). L-proline (40 g) was added to LAH (40 g) in 800 ml THF with stirring and cooling. The mixture was heated to 75° and stirred for 120 h. After cooling, the mixture was treated with 140 ml water, the residue was filtered off and washed with several portions of THF. The solvent was removed from the combined filtrate and the residue was dried by azeotropic distillation with benzene and distilled *in vacuo*. The yield was 20·1 g (57·5%) of L-prolinole (**20**), b.p. 81–85° (4 mm) (lit[35] b.p. 69–72°/2 mm); $[\alpha]_D^{20}$ +3·38° (*c* 5·4 in MeOH), CD: λ_{max} = 215 nm, $\Delta\epsilon$ = +0·34.

(–)O,N-*Ditosyl*-L-*prolinole* (**25**). *p*-Toluenesulphochloride (86 g) was added with cooling to a soln of **20** (20·1 g) in 200 ml pyridine distilled over BaO. After 2 days, the mixture was carefully diluted with water, the ppt was filtered off, washed with water and dried. The product was purified by column chromatography on Al_2O_3 with a mixture of benzene and chlorophorm (10:1). After removal of solvent, the eluate yielded 64·5 g (79%) of **25**, m.p. 94–95° (from benzene–hexane mixture); $[\alpha]_D^{20}$ –123·2° (*c* 1·4 in benzene). (Found: N, 3·36, $C_{19}H_{23}NO_5S_2$ requires: N, 3·42%).

R(–)-1-*Tosyl*-2-*methylpyrrolidine* (**26**). Compound **25** (64·5 g) in 200 ml dry THF was added with stirring and cooling to a suspension of LAH (18 g) in 800 ml ether. The mixture was boiled for 7 h until complete disappearance of the starting material. After the reaction was complete the mixture was treated with water and acidified with HCl. The ether layer was removed and the water layer was repeatedly extracted with benzene. After the solvent had evaporated, the solid product was obtained from the combined extracts, and was purified by column chromatography on SiO_2 with benzene. The yield was 27·7 g (72%) of **26**; m.p. 69·5–70° (from hexane); $[\alpha]_D^{20}$ –62·5° (*c* 5·5 in benzene). (Found: N, 5·68, $C_{12}H_{17}NO_2S$ requires: N, 5·85%).

R(–)-2-*Methylpyrrolidine* (**9**). Compound **9** (5·7 g; 67%) was prepared by reduction of 23·9 g of **26** with Na in isoamyl alcohol according to the Vaughan procedure,[34] b.p. 95–97°, $[\alpha]_D^{20}$ –18·8° (*c* 13 in MeOH), $[\alpha]_D^{20}$ –31·2° (*c* 1·0 in hexane) (lit[36] b.p. 95·5–96·5°/744 mm).

R(–)-1,2-*Dimethylpyrrolidine* (**10**). Compound **9** (1·0 g) was added to a mixture of aqueous formaldehyde (3 ml) and formic acid (3 ml) and heated for 4 h on a boiling water bath. Conc HCl (3 ml) was added and the water was removed *in vacuo*. The residue was treated with conc KOH, the amine layer was removed, dried over KOH and distilled over Na. The yield was 0·42 g (37%) of **10**, b.p. 88–89°; $[\alpha]_D^{20}$ –63·4° (*c* 1·0 in hexane) (lit[37] b.p. 92–94°).

R(–)-1-*Chloro*-2-*methylpyrrolidine* (**11**). A soln of **9** (1·28 g) in 5 ml dry ether was slowly added with stirring to a suspension of N-chlorosuccinimide (2·6 g) in 30 ml dry ether. One h later, the mixture was filtered, the ether was removed, and the residue was distilled *in vacuo* (the bath temp up to 70°). The yield was 0·75 g (41·6%) of **11**, b.p. 40–41° (28 mm), n_D^{20} 1·4598, $[\alpha]_D^{20}$ –94·8° (*c* 0·36 in MeOH); UV: λ_{max} 270 nm, ϵ 360; CD: λ_{max} 256 nm, $\Delta\epsilon$ = –0·285 (in MeOH).

R(–)-1-*Cyano*-2-*methylpyrrolidine* (**12**). Cyanochloride (1·4 g) was passed through a soln of **9** (1·1 g) and triethylamine (2 g) in 50 ml dry ether. The ppt was filtered off 0·5 h later, the ether was removed from the filtrate and the residue was distilled *in vacuo*. The yield was 0·7 g (50%) of **12**, b.p. 111–112°/23 mm, n_D^{20} 1·4614, $[\alpha]_D^{20}$ –85° (*c* 1·0 in hexane). (Found: N, 25·54, $C_6H_{10}N_2$ requires: N, 25·42%).

S(+)-2-*Methylpiperidine* (**13**). α-Pipecoline (9·9 g) was treated with dibenzoyltartaric acid (36 g) in methanol–acetone mixture (1:4). The free base was isolated from the resulting pipecoline dibenzoyltartrate by analogy with **4**. The yield was 1·35 g (27·2% per one enantiomer), b.p. 118–119°; n_D^{20} 1·4510; $[\alpha]_D^{20}$ +15° (*c* 1·0, in hexane). Lit.[38]: b.p. 117–118°; n_D^{15} 1·44983; $[\alpha]_D^{15}$ +36° (neat).

S(+)-1,2-*Dimethylpiperidine* (**14**). Compound **13** (0·45 g) was methylated in the same way as **4**. The yield was 0·3 g (59%); b.p. 127–128°; n_D^{20} 1·4445; $[\alpha]_D^{20}$ +23·8° (*c* 1·0, in hexane). Picrate, m.p. 239·5–240°, Lit[38]: b.p. 127°; n_D^{15} 1·44306; $[\alpha]_D^{15}$ +68·8° (neat); picrate, m.p. 240°.

S(+)-1-*Cyano*-2-*methylpiperidine* (**15**). Bromocyanide (1·5 g) in 10 ml ether was added to a soln of **13** (0·7 g) in 20 ml dry ether in a dropwise manner with stirring and cooling. 0·5 h later, the ppt was separated, the solvent was removed and the residue was distilled *in vacuo*. The yield was 0·32 g (37%) of **15**; b.p. 74–76°/3 mm; n_D^{20} 1·4698; $[\alpha]_D^{20}$ +7·2° (*c* 1·0, in hexane).

d-*Camphidine* (**16**). *d*-Camphorimide (12·4 g) in 250 ml THF was added with stirring to LAH (6 g) in 200 ml THF, and the mixture was heated to 75° for 24 h. After cooling, the mixture was treated with a calculated volume of water, and the ppt was filtered off and washed with several portions of THF. The combined filtrate was dried with $MgSO_4$ and saturated with dry HCl, after this solvent had been removed. The ppt was recrystallized from the ether–ethanol mixture, treated with conc KOH and the product was extracted with ether. The extract was dried over CaH_2, the ether was removed, and the solid product was sublimated *in vacuo* (1 mm). The yield was 3·5 g (34·3% of *d*-camphidine (**16**), m.p. 166–168°; $[\alpha]_D^{20}$ +19·8° (*c* 1, in MeOH), and $[\alpha]_D^{20}$ 31° (*c* 0·4 in hexane) (lit[16] m.p. 168°, $[\alpha]_D^{20}$ +12·7° (*c* 2·99 in 50% EtOH).

1-*Methyl*-d-*camphidine* (**17**). Compound **16** (0·4 g) was methylated in the same way as **4**. 0·23 g (53%) of **17** was obtained; b.p. 188–190°; n_D^{20} 1·4579; $[\alpha]_D^{20}$ +33° (*c* 1·0, in hexane); picrate, m.p. 235·5–236°. Lit[39,40] b.p. 68°/10 mm; n_D^{25} 1·4776; picrate, m.p. 236°.

(+)1-*Cyano*-d-*camphidine* (**18**). Cyanochloride (0·5 g) in 10 ml dry ether was added to a soln of **16** (0·76 g) and triethylamine (0·6 g) in 50 ml dry ether. After 0·5 h, the ppt was filtered off and the ether was removed. The residue was purified by column chromatography on SiO_2 with CH_2Cl_2. The yield was 0·65 g (82%) of **18** after sublimation *in vacuo*, m.p. 117–118°, $[\alpha]_D^{20}$ +44·5° (*c* 1·0 in hexane).

(Found: N, 15·5, $C_{11}H_{18}N_2$ requires: N, 15·66%).

5S-1-*Azabicyclo*[3.1.0]*hexane* (**19**). This was prepared from **20** (27·7 g) by the Gassman procedure.[35]

The yield was 8·6 g (37%) of **19**, b.p. 107–108°, n_D^{20} 1·4575, $[\alpha]_D^{20}$ −17·8° (*c* 5·4 n-C_9H_{20}). Lit[35] b.p. 107–110°, $[\alpha]_D^{28}$ −19° (neat).

REFERENCES

[1]R. G. Kostyanovsky, V. I. Markov and I. M. Gella, *Tetrahedron Letters* 1301 (1972)*

[2]J. C. Craig and S. K. Roy, *Tetrahedron* **21**, 401 (1965)

[3]J. C. Craig. *Some Newer Physical Methods in Structural Chemistry* (Edited by R. Bonnet) London, p. 170 (1967)

[4]H. C. Beyerman, L. Maat, J. P. Visser, J. C. Craig and Chan R. P. K., *Rec. Trav. Chim.* **88**, 1012 (1969)

[5]G. Fodor, E. Bauerschmidt and J. C. Craig, *Canad. J. Chem.* **47**, 4393 (1969)

[6]H. C. Beyerman, S. van den Bosch and J. H. Brenker, *Rec. Trav. Chim.* **90**, 755 (1971)

[7]H. C. Beyerman, B. S. L. Bordes, L. Maat and F. M. Varnaar, *Ibid.* **91**, 1441 (1972)

[8]J. Parello and F. Picot, *Tetrahedron Letters* 5083 (1968)

[9]H. Ripperger, *Tetrahedron* **25**, 725 (1969)

[10]H. Ripperger, *Angew. Chem.* **79**, 721 (1967)

[11]G. Snatzke, H. Ripperger, Chr. Horstmann and K. Schreiber, *Tetrahedron* **22**, 3103 (1966)

[12]W. Gaffield, L. Keeter and W. Lijinsky, *Tetrahedron Letters* 779 (1972)

[13]H. Ripperger and K. Schreiber, *J. Prakt. Chem.* **313**, 825 (1971)

[14]Y. Minoura, M. Takebayashi and C. Price, *J. Am. Chem. Soc.* **81**, 4689 (1959)

[15]W. R. Hertler and E. J. Corey, *J. Org. Chem.* **24**, 572 (1959)

[16]H. Ripperger and K. Schreiber, *Tetrahedron* **23**, 1841 (1967)

[17]H. Ripperger and K. Schreiber, *Ibid.* **21**, 1485 (1965)

[18]A. P. Terent'ev, R. A. Gracheva and T. F. Dedenko, *Dokl Akad. Nauk SSSR* **163**, 386 (1968)

[19]Ger. Offen. 1807496 (K.-D. Klaus, June (1970) Appl. Nov. (1968)

[20]E. F. Paulus, D. Kobelt and H. Jensen, *Angew. Chem.* **81**, 1048 (1969)

[21]E. Tannenbaum, E. M. Coffin and H. Harrison, *J. Chem. Phys.* **21**, 311 (1953)

[22]L. W. Pickett, M. E. Corning, G. M. Wieder, D. A. Semenow and J. M. Buckley, *J. Am. Chem. Soc.* **75**, 1618 (1953)

[23]J. C. Craig, unpublished data, see Ref 9 in [4], Ref 13 in [5]

[24]O. C. Dermer and G. E. Ham, *Ethylenimine and other aziridines* p. 103. Academic Press (1969)

[25]B. A. Shaudri, D. G. Goodwin, H. R. Hudson, L. Barlett and P. M. Scopes, *J. Chem. Soc.* (C), 1329 (1970)

[26]R. C. Cookson and J. M. Coxon, *Ibid.* (C), 1466 (1971)

[27]H. F. Henneike and R. S. Drago, *J. Am. Chem. Soc.* **90**, 5112 (1968)

[28]J. A. Schellman, *J. Chem. Phys.* **44**, 55 (1966)

[29]J. K. Tyller and J. Shevidan, *J. Mol. Spectr.* **43**, 248 (1972)

[30]L. S. Khaikin, L. V. Vilkov, private communication

[31]C. Djerassi, A. Moscowitz, K. Ponsold and G. Steiner, *J. Am. Chem. Soc.* **89**, 347 (1967)

[32]K. Takeda, T. Komeno and K. Kuriyama, *Tetrahedron* **24**, 6913 (1968)

[33]R. G. Kostyanovsky, V. I. Markov, I. M. Gella, Kh. Khafizov and V. G. Plekhanov, *Org. Mass Spectrom.* **6**, 661 (1972)

[34]W. R. Vaughan, R. S. Klonovsky, R. S. McElhinney and B. B. Milward, *J. Org. Chem.* **26**, 138 (1961)

[35]P. G. Gassman and A. Fentiman, *Ibid.*, **32**, 2388 (1967)

[36]J. V. Braun, *Ber. Dtsch Chem. Ges* **43**, 2864 (1910)

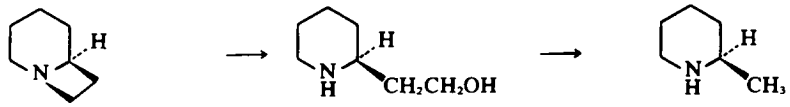
[37]A. P. Terent'ev, M. A. Volodina and V. G. Mishina, *Zh. Obshchej Khimii* **28**, 223 (1958)

[38]W. Leithe, *Ber. Dtsch. Chem. Ges* **63**, 805 (1930)

[39]L. M. Rice and Ch. H. Grogan, *J. Org. Chem.* **22**, 185 (1957)

[40]J. McKenna, J. M. McKenna, A. Tulley and J. White, *J. Chem. Soc.* 1711 (1965)

*Incorrect assignment of the absolute configuration of the (+)-2-methylazetidine is associated with our erroneous assignment of the (+)-conidine configuration. S-Configuration of the latter may be actually proved on the basis of the following transformations:



(S) (S) (R)