washed with chloroform. The washings, after removal of solvent at atmospheric pressure through a 10-cm Vigreux column, yielded a slightly colored oil (173 mg, 40%), $[\alpha]^{18}D$ −1.1° (c 2.3, methanol) [lit.[24] for optically pure ester, $[\alpha]^{27}D$ +21.1° (methanol)] whose nmr spectrum was consistent with methyl 2-methylbutyrate. The aqueous phase was made alkaline with ammonia and extracted 6–8 times with chloroform. Removal of the solvent left 1α-carbomethoxy-7α-hydroxy-8α-pyrrolizidine (**23**) as a colorless oil (493 mg, 71%) which did not crystallize. The nmr spectrum was indicative of one product only, there being one sharp singlet representing the methoxyl group. The hydrochloride formed needles from ethanol–ether: mp 134–135.5°; $[\alpha]^{20}D$ −18.5° (c 2.1, ethanol).

Anal. Calcd for $C_9H_{16}NO_3Cl$: C, 48.8; H, 7.2; N, 6.3. Found: C, 48.6; H, 7.3; N, 6.1.

(+)-**Hastanecine** (4).—A solution of **23** (352 mg) in THF (50 ml) was added to a suspension of lithium aluminium hydride (400 mg) in THF (30 ml). The reaction mixture was refluxed for 45 min and worked up as described above. (+)-Hastanecine crystallized as prisms from acetone: yield 246 mg (82%); mp 113–114°; $[\alpha]^{18}D$ +8.5° (c 2.2, ethanol), $[\alpha]^{18}D$ +8.2° (c 1.4, methanol) [lit. for (−)-hastanecine, mp 113–114°,[5] $[\alpha]^{20}D$ −10° (c 0.43, ethanol),[10] $[\alpha]D$ −9.1° (methanol)[3]]. A mixture melting point of (+)-hastanecine with (−)-hastanecine derived from hastacine was substantially depressed (to approximately 90°). The ir, nmr, and mass spectra were identical with those of (−)-hastanecine.

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.1; H, 9.6; N, 8.9; O, 20.4. Found: C, 61.4; H, 9.6; N, 8.9; O, 20.8.

The hydrochloride formed needles from ethanol–ether; it had mp 132–134°, and did not appear to be hygroscopic as reported by Konovalov and Men'shikov.[3] Excess hydrochloric acid was carefully removed under vacuum in the present work.

Anal. Calcd for $C_8H_{16}NO_2Cl$: C, 49.6; H, 8.3; N, 7.2. Found: C, 49.8; H, 8.5; N, 7.1.

Registry No.—**1**, 520-62-7; **2**, 21824-59-9; **3**, 21850-67-9; **4**, 21824-60-2; **6**, 21824-61-3; **19**, 6029-83-0; **20** (picrolonate), 21824-63-5; **22** (picrolonate), 21824-64-6; **23** (HCl), 21824-65-7; **24**, 21824-66-8; **24** (HCl), 21824-67-9; **25**, 20361-77-7; **26**, 480-86-4; platyphylline, 480-78-4; neoplatyphylline, 20361-76-6.

(24) A. S. Dreiding and J. A. Hartman, *J. Amer. Chem. Soc.*, **75**, 939 (1953); V. M. Micovic and M. Lj. Mihailovic, *Bull. Soc. Chim. Belgrade*, **19**, 329 (1954).

The Saturated Pyrrolizidinediols. II. The Total Synthesis and Stereochemistry of Macronecine

A. J. AASEN and C. C. J. CULVENOR

Division of Applied Chemistry, C.S.I.R.O., Melbourne, Australia

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Macronecine has been synthesised by a two-step reduction of 1-carbethoxy-2,3-dioxopyrrolizidine. The preparation and stereochemical definition of the other three diastereoisomers show that macronecine is 2β-hydroxy-1β-hydroxymethyl-8β-pyrrolizidine.

Macronecine is a dihydroxy amino alcohol obtained by hydrolysis of macrophylline, an alkaloid of the Caucasian species *Senecio macrophyllus*.[1] The degradation of macrophylline to laburnine (1β-hydroxymethyl-8β-pyrrolizidine)[2] established all structural features of macronecine other than the location of the second hydroxyl group. The relationship of macronecine to other saturated pyrrolizidinediols is discussed in the preceding communication,[3] in which it is shown from spectral evidence that macronecine is a 2-hydroxy compound, probably 2β-hydroxy-1β-hydroxymethyl-8β-pyrrolizidine (**1**). A synthesis[4] of **1** was undertaken to confirm this structure (Chart I).

The readily available (±)-1-carbethoxy-2,3-dioxopyrrolizidine (**2**)[5] was chosen as the starting point. This substance appears to exist almost entirely in the enol form (**2b**) rather than the keto form (**2a**). It is not extractable from alkaline solution and it is readily methylated with diazomethane.[5] Apart from the methyl signals, its nmr spectrum measured in deuteriochloroform has multiplets corresponding to only four protons at higher field than δ 3.0, leaving no signals attributable to a proton on C-1. Instead, there is a rounded multiplet at δ 8.9, exchangeable on shaking with deuterium oxide, due to the enolic OH. The spectrum is unaltered by the addition of trifluoroacetic acid. Adams, *et al.*,[5] reduced **2** catalytically in the presence of rhodium and then further with lithium aluminium hydride to obtain a 2-hydroxy-1-hydroxymethylpyrrolizidine of undefined stereochemistry, differing from macronecine. Assuming addition of hydrogen to the unhindered side of the enol double bond, the initial reduction product should be (±)-1β-carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine (**5**) and the final product should be (±)-2β-hydroxy-1β-hydroxymethyl-8α-pyrrolizidine (**9**). This stereochemistry is supported by an analysis of the nmr spectrum of the diol[3] and has now been confirmed by conversion of the substance into (±)-heliotridane by reaction with thionyl chloride followed by removal of the chlorine atoms by hydrogenolysis. The β configuration of the 2-hydroxyl group was confirmed when the 2α-hydroxy-1β-hydroxymethyl diastereomer (**10**), prepared by catalytic reduction of 1β-hydroxymethyl-1α,2α-epoxy-8α-pyrrolizidine (**6**),[6] proved to be different from **9**.

The hydrogenation of **2** in the presence of platinum and ruthenium catalysts also led to **5**, but in the presence of Raney nickel at elevated temperature and pressure this product was accompanied by approximately 15% of another isomer. Although the mixed product was difficult to resolve, nmr spectra revealed signals additional to those of **5** and later found to correspond with those of the 1α-carbethoxy-2α-hydroxy isomer (**3**). Evidently, some *cis* addition of hydrogen had occurred to the more hindered side of the double bond. On treat-

(1) A. Danilova, L. Utkin, and P. S. Massagetov, *Zh. Obshch. Khim.*, **25**, 831 (1955).

(2) A. V. Danilova and L. M. Utkin, *ibid.*, **30**, 345 (1960).

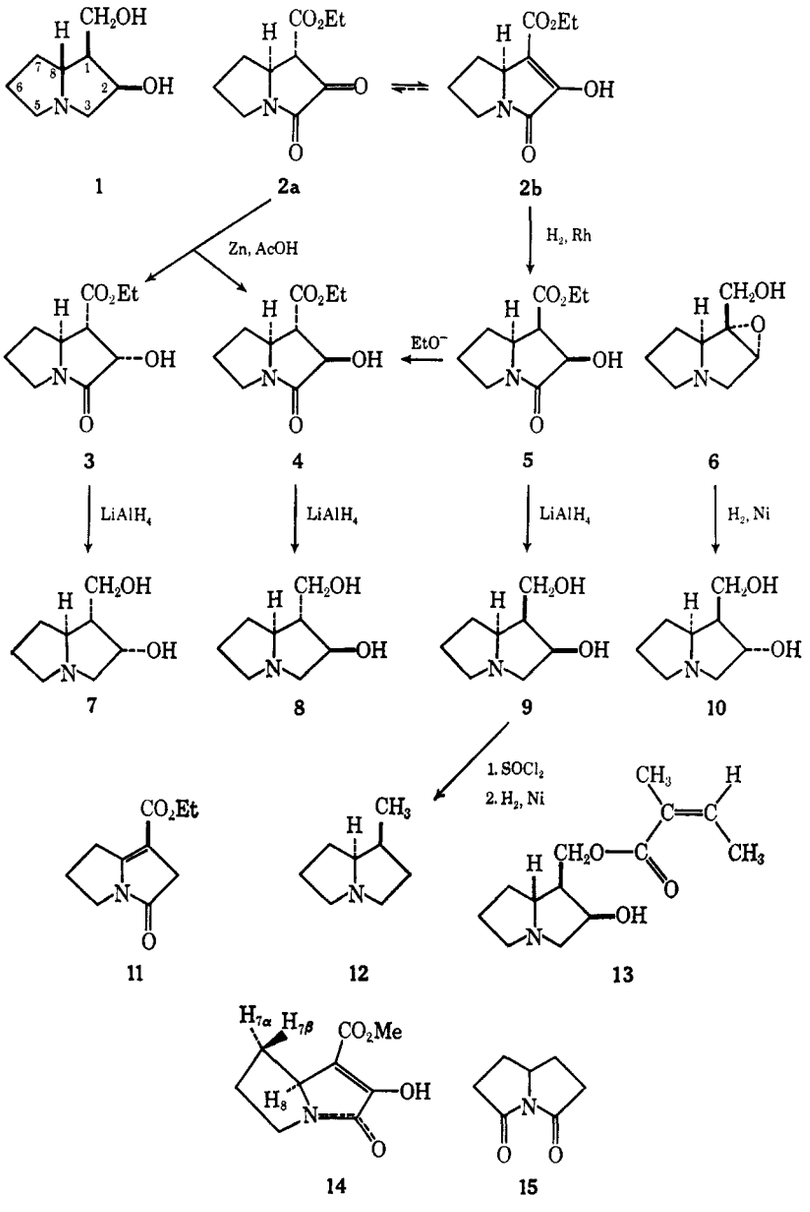
(3) A. J. Aasen, C. C. J. Culvenor, and L. W. Smith, *J. Org. Chem.*, **34**, 4137 (1969).

(4) A preliminary announcement has been made: A. J. Aasen and C. C. J. Culvenor, *Chem. Commun.*, 34 (1969).

(5) R. Adams, S. Miyano, and M. D. Nair, *J. Amer. Chem. Soc.*, **83**, 3323 (1961).

(6) We thank Mr. R. S. Sawhney for the initial preparation of **10** in this way.

CHART I



ment with sodium ethoxide, **5** readily underwent epimerization at C-1 to give the thermodynamically more stable 1α-carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine (**4**). Reduction of **2** with sodium borohydride led to **4** as the major product together with a small amount of **5**. The further reduction of **4** with lithium aluminum hydride gave 1α-hydroxymethyl-2β-hydroxy-8α-pyrrolizidine (**8**).

The desired reduction of **2** to a derivative with a 2α-hydroxyl group was finally accomplished with zinc and acetic acid. The product was largely the 1α-carbethoxy-2α-hydroxy compound (**3**) with a small proportion of the 1α-carbethoxy-2β-hydroxy isomer (**4**), suggesting that reduction occurred through the keto form (**2a**). Lithium aluminum hydride reduction of **3** gave 2α-hydroxy-1α-hydroxymethyl-8α-pyrrolizidine (**7**), identified as (±)-macronecine by comparison of infrared and nmr spectra with those of authentic (+)-macronecine (**1**). The stereochemistry of **3** and **7** follows from the fact that **7** differs from the other three possible diastereoisomers, **8**–**10**.

Resolution of (±)-macronecine was accomplished by fractional crystallization of the bromocamphorsulfonate salts, both the (+) and the (−) forms being obtained apparently optically pure, their constants comparing satisfactorily with values quoted for natural (+)-macronecine (Table I). The structure of macrophylline is now fully defined as **13**.

TABLE I

COMPARISON OF SYNTHETIC AND NATURAL MACRONECINE

Compd	Natural[a]	Synthetic (+)	Synthetic (−)
Free base mp, °C	126–128	129	128–128.5
[α]D (ethanol), deg	+49.29	+42.6	−42.1
Registry no.		21824-61-3	21823-66-5
Hydrochloride mp, °C	152–153	152–152.5	151.5–153.5
[α]D (ethanol), deg	+49.37	+40.5	−41.3
Registry no.		21823-67-6	21823-68-7
Bromocamphorsulfonate mp, °C		198–200	193–195
[α]D (ethanol), deg		+84.5	+50.1
Registry no.		21823-69-8	21823-70-1

[a] Reference 1.

An unsuccessful attempt was made to obtain a 2α-hydroxyl group by effecting inversion at C-2 in the 1-carbethoxy derivatives **4** and **5** by means of a displacement reaction of their tosylates with potassium acetate. The only reaction observed was elimination with rearrangement, giving the 1,8 olefin (**11**), previously prepared from the tosylate of **5** and potassium *t*-butoxide.[7]

The identification of the diastereomeric 2,9-diols is most readily accomplished by means of their nmr spectra, which are reproduced in Figure 1 for reference purposes. The vicinal coupling constants, $J_{1,2}$ and $J_{1,8}$, which might provide an independent check on the stereochemistry of the diols, cannot readily be obtained from these spectra. They are available, however, from the spectra of the 1-carbethoxy intermediates and are consistent with the conclusions reached, the observed values being 6.2 cps for *cis* protons and 8.5–10 cps for *trans* protons. The 3-oxopyrrolizidine derivatives exhibit an interesting upfield shift of the 7β hydrogen atom. The spectra of the 1-carbethoxy-3-oxo compounds, **3**, **4**, and **5**, contained low-intensity peaks in the δ 1.0–1.3 region partly obscured by the triplet due to the methyl group. Initially suspect as impurity peaks, their source was clarified by the preparation of 1-carbomethoxy-2,3-dioxopyrrolizidine. With no other signals in the vicinity, the spectrum of this compound clearly exhibited a broad one-proton multiplet centered near δ 1.15 due to one of the H-7 protons. The rest of the spectrum consists of a three-proton envelope, centered near δ 2.3, due to the other H-7 proton and the two H-6 protons, a two-proton multiplet, centered near δ 3.4, due to the H-5 protons, a four-line multiplet, δ 4.22, due to H-8, and the methyl singlet, δ 3.8. The H-8 multiplet is collapsed to a doublet, δ 10.8 cps, by irradiation at δ 2.3 and to a broad, unresolved singlet by irradiation at δ 1.15. Thus the proton, δ 1.15, is coupled to H-8 to the extent of 10.8 cps. The other H-7–H-8 coupling is 4.4 cps. We conclude that the highly shielded proton is H-7β, *trans* to H-8α. The other 3-oxo compounds, **3**, **4**, and **5**, exhibit a similar if slightly less intense shielding, H-7β having δ 1.38 (*ca.* 1.3 and *ca.* 1.5, respectively, in these substances. We attribute the shielding to the unsubstituted ring being buckled in such a way that H-7β comes forward over the C-8–N bond and into the shielding zone of the lactam grouping as in diagram **14**. The CO_2Et group could possibly contribute to the shielding only in the 1β-carbethoxy compound (**5**), in which H-7β is actually less affected than in **3** and **4**. The effect is also present in 3,5-dioxopyrrolizidine (**15**), for which we find $\delta_{1\beta} = \delta_{7\beta} = 1.7$ ppm and $\delta_{1\alpha} = \delta_{7\alpha} = 2.4$ ppm, even though the shielded protons are now present in a fairly rigid ring with reduced scope for buckling.

Experimental Section

Analyses were made by the Australian Microanalytical Service, Melbourne. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU 6D instrument, using a 70-eV ionization potential and direct entry of samples into the ion chamber.

(±)-1-Carbethoxy-2,3-dioxo-8α-pyrrolizidine (2), (±)-1β-carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine (5), and (±)-2β-hydroxy-1β-hydroxymethyl-8α-pyrrolizidine (9) were prepared as described by Adams, *et al.*,[5] with one modification. In the catalytic reduction of ethyl pyrrole-2-acetate over rhodium catalyst, the use of acetic acid as solvent was found to give a substantial proportion of the product as the N-acetyl derivative. The desired pyrrolidine was the sole product when ethanol was used as solvent together with 1 mol of acetic acid. Compound **5** had nmr ($CDCl_3$) δ_1 3.6, δ_2 4.80, and δ_8 *ca.* 3.9 ($J_{1,2} = 6.2$ Hz, $J_{1,8} = 6.2$ Hz).

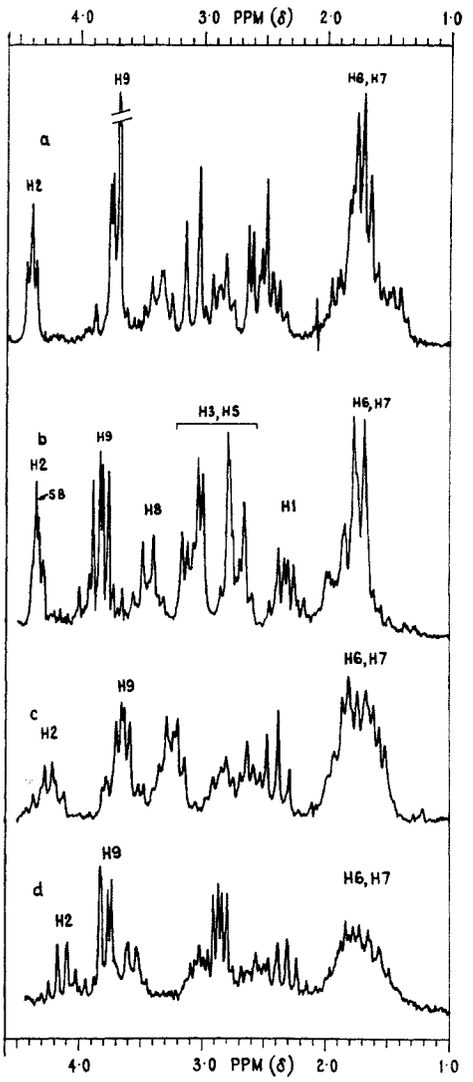


Figure 1.—Nuclear magnetic resonance spectra of 2-hydroxy-1-hydroxymethylpyrrolizidine derivatives, measured at 100 Mcps: (a) 2α-hydroxy-1α-hydroxymethyl-8α-pyrrolizidine [(±)-macronecine, **1** and **7**] in $CDCl_3$; (b) 2β-hydroxy-1β-hydroxymethyl-8α-pyrrolizidine (**9**) in D_2O; (c) 2β-hydroxy-1α-hydroxymethyl-8α-pyrrolizidine (**8**) in $CDCl_3$; (d) 2α-hydroxy-1β-hydroxymethyl-8α-pyrrolizidine (**10**) in D_2O.

(±)-1α-Carbethoxy-2α- (and 2β-) hydroxy-3-oxo-8α-pyrrolizidine (3 and 4).—A mixture of 2 (10 g), activated zinc powder (20 g), and glacial acetic acid (100 ml) was stirred under nitrogen at room temperature for 6 hr. The filtered solution was diluted with water (500 ml) and extracted with chloroform. The solvent and some acetic acid were removed under reduced pressure. The white crystalline residue was recrystallized from acetone to give 1α-carbethoxy-2α-hydroxy-3-oxo-8α-pyrrolizidine (**3**) as needles: yield 6.19 g (61%); mp 158–160°; nmr ($CDCl_3$) δ_1 2.83, δ_2 4.55, and δ_8 *ca.* 4.38 ($J_{1,2} = 6.2$ Hz, $J_{1,8} = 8.6$ Hz).

Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.3; H, 7.1; N, 6.6; O, 30.0. Found: C, 56.6; H, 7.2; N, 6.4; O, 29.9.

The mother liquor, dissolved in a few milliliters of acetone and seeded with a crystal of the 2β-hydroxy isomer (**4**), obtained by epimerization of **5** (below), gave **4** as long prisms: yield 0.98 g

(7) B. M. Goldschmidt, *J. Org. Chem.*, **27**, 4057 (1962).

(8) N. J. Leonard, L. R. Hruda, and F. W. Long, *J. Amer. Chem. Soc.*, **69**, 690 (1947).

(10%); mp and mmp 106°; nmr ($CDCl_3$) δ_1 2.85, δ_2 4.86, and δ_8 *ca.* 3.8 ($J_{1,2}$ = 9.7 Hz, $J_{1,8}$ = 8.3 Hz); ir indistinguishable from that of **4** derived from **5**.

(±)-Macronecine (7).—A solution of **3** (3.18 g) in dry tetrahydrofuran (100 ml) was added dropwise to a cooled (0°) suspension of lithium aluminium hydride (3.46 g) in tetrahydrofuran (80 ml). The mixture was refluxed for 2 hr and cooled, and excess hydride was decomposed with wet tetrahydrofuran. The solution was filtered and the precipitate was extracted with dilute hydrochloric acid. The acid extract was strongly basified with sodium hydroxide and extracted with chloroform. The chloroform extract was combined with the tetrahydrofuran solution, and the solvents were removed to leave an oil (1.58 g) which spontaneously crystallized. Recrystallization from acetone gave (±)-macronecine as optically inactive needles (1.22 g, 52%), mp 109–110°. The mass spectrum was virtually identical with that of authentic (+)-macronecine. The nmr spectrum (100 Mcps, $CDCl_3$) is shown in Figure 1; a spectrum measured at 60 Mcps in $CDCl_3$ was identical with a spectrum of natural (+)-macronecine measured under the same conditions.[3]

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.1; H, 9.6; N, 8.9; O, 20.3. Found: C, 61.2; H, 9.5; N, 8.6; O, 20.3.

Resolution of (±)-Macronecine.—The racemate (**7**, 600 mg) and ammonium α-bromo-D-camphor-π-sulfonate (1260 mg) were dissolved in ethanol (10 ml). Solvent and ammonia were distilled off under reduced pressure. Fresh ethanol (10 ml) was added and again removed. The salts were redissolved in ethanol (10 ml) and acetone was added until cloudiness appeared. After removal of an amorphous precipitate by centrifugation, the solution was kept overnight at 0° to give the salt of (+)-macronecine as needles: yield 819 mg, mp 198–200°; $[\alpha]^{18}D$ +84.5° (*c* 1.3, ethanol). Two recrystallizations from ethanol–acetone did not change the melting point and specific rotation. A solution of the salt in dilute hydrochloric acid was washed with chloroform, basified strongly with sodium hydroxide, and thoroughly extracted with chloroform. The residue obtained after removal of the solvent was recrystallized from acetone to give (+)-macronecine as long needles: mp 129°; $[\alpha]^{18}D$ +42.6° (*c* 1.1, ethanol) (lit.[1] mp 126–128°, $[\alpha]D$ +49.29°). A mixture melting point could not be carried out because the sample of macronecine used for spectral studies[3] had decomposed. The hydrochloride, prepared in ethanol, crystallized as long needles from ethanol-ether: mp 152–152.5°; $[\alpha]^{18}D$ +40.5° (*c* 1.4, ethanol) (lit.[1] mp 152–153°, $[\alpha]D$ +49.37°).

Anal. Calcd for $C_8H_{16}NO_2Cl$: C, 49.6; H, 8.3; N, 7.2; O, 16.5; Cl, 18.3. Found: C, 50.0; H, 8.4; N, 7.1; O, 16.4; Cl, 18.2.

The mother liquor, left at room temperature for 3 days, gave the salt of (−)-macronecine as solid prisms: yield 428 mg, mp 193–195°; $[\alpha]^{18}D$ +50.1° (*c* 1.1, ethanol); unaltered after two recrystallizations from ethanol–acetone. A mixture with the corresponding salt of (+)-macronecine melted at 155–165°. Recovery of the free base as described above gave (−)-macronecine as fine needles from acetone: mp 128–128.5°; $[\alpha]^{18}D$ −42.1° (*c* 1.0, ethanol). The hydrochloride of (−)-macronecine, also prepared as above, had mp 151.5–153.5°, $[\alpha]^{18}D$ −41.3° (*c* 0.8, ethanol). Two other resolution experiments were performed, with the same results.

(±)-1α-Carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine (4).—The 1β-carbethoxy-2β-hydroxy compound (**5**, 4.02 g) was dissolved in dry ethanol (50 ml) and added to a cooled (ice bath) solution of sodium (560 mg) in ethanol (150 ml). The temperature was allowed to rise slowly. After *ca.* 10 min, the solution started to become brown. The mixture was immediately poured into 1 *N* HCl and the solution was extracted with chloroform. If the reaction time was too long or the temperature was too high, complete conversion into a black tar resulted, while incomplete epimerization occurred when the reaction was stopped before color appeared. The solvent was removed and the residue was crystallized to give **4** as long needles (fast) or solid prisms (slowly): yield 3.19 g (79%) from acetone–petroleum ether (bp 40–60°); mp 106°, depressed 15–20° when mixed with **5** (mp 135–137°). The mass spectrum showed a molecular ion, *m/e* 213.

Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.3; N, 7.1; N, 6.6; O, 30.0. Found: C, 56.2; H, 7.0; N, 6.6; O, 30.2.

(±)-1α-Hydroxymethyl-2β-hydroxy-8α-pyrrolizidine (8).—A solution of **4** (666 mg) in dry tetrahydrofuran (30 ml) was added slowly to a cooled (0°) slurry of lithium aluminium hydride (500 mg) in tetrahydrofuran (30 ml). The mixture was refluxed for 3 hr, cooled, and filtered after excess hydride had been destroyed with wet tetrahydrofuran. The hydroxides were washed with dilute hydrochloric acid and the washings were strongly basified with sodium hydroxide and extracted repeatedly with chloroform. The tetrahydrofuran and chloroform solutions were combined and the solvents were removed, leaving (±)-2β-hydroxy-1α-hydroxymethyl-8α-pyrrolizidine (**8**) as a gum, yield 167 mg (34%), which crystallized slowly (3 days, room temperature) from acetone as short needles: yield 113 mg; mp 99–101°; mass spectrum virtually identical with that of macronecine; nmr ($CDCl_3$) reproduced in Figure 1. The hydrochloride was prepared in ethanol and crystallized as needles from ethanol–ether; mp 127–128°.

Anal. Calcd for $C_8H_{16}NO_2Cl$: C, 49.6; H, 8.3; N, 7.2; O, 16.5; Cl, 18.3. Found: C, 49.7; H, 7.9; N, 7.3; O, 16.8; Cl, 18.0.

1β-Hydroxymethyl-2α,3α-epoxy-8α-pyrrolizidine (6).—This epoxide was prepared in improved yield by a modification of the procedure of Culvenor, *et al.*[9] Pertrifluoroacetic acid, prepared by slow addition of a solution of hydrogen peroxide (87%, 2.2 ml) to trifluoroacetic anhydride (12.7 ml) in methylene chloride (20 ml), was added to a suspension of supinidine (1.55 g) and disodium hydrogen phosphate (39 g) in methylene chloride (*cf.* Emmons and Pagano[10]). The mixture was refluxed for 2 hr, water was added, and the mixture was made alkaline with sodium hydroxide and extracted repeatedly with chloroform. The extract yielded a gum (1.22 g) which was crystallized from acetone to give the α epoxide **6**: yield 469 mg (27%); mp 145°, undepressed on admixture with an authentic sample.

1β-Hydroxymethyl-2α-hydroxy-8α-pyrrolizidine (10).—A solution of **6** (166 mg) in absolute ethanol (15 ml) was shaken with hydrogen at atmospheric pressure and room temperature in the presence of Raney nickel (W-2). The theoretical amount of hydrogen was absorbed in 4 hr. The filtrate was distilled under reduced pressure, leaving a colorless oil (157 mg). The oil was dissolved in *ca.* 20 ml of water, basified with ammonia, and extracted repeatedly with chloroform. The nmr spectrum of the extracted material (43 mg) indicated the presence of isoretronecanol as the major component. The aqueous phase was concentrated under reduced pressure. The colorless residue, yield 110 mg (65%), crystallized slowly (2–3 days) as large prisms from acetone. The crystals were very hygroscopic: mp (evacuated tube) 91–93°; mass spectrum virtually identical with that of macronecine; nmr (H_2O) reproduced in Figure 1; $[\alpha]^{20}D$ −114° (*c* 0.9, ethanol). A crystalline hydrochloride could not be obtained. The picrolonate was prepared in ethanol and crystallized as long yellow needles, mp 198–199°.

Anal. Calcd for $C_8H_{15}NO_2 \cdot C_{10}H_8N_4O_5$: C, 51.3; H, 5.5; N, 16.6; O, 26.6. Found: C, 51.6; H, 5.6; N, 16.5; O, 26.7.

(±)-1-Carbomethoxy-2,3-dioxo-8α-pyrrolizidine.—The ethyl ester **2** (400 mg) was added to a solution of sodium (131 mg) in methanol (250 ml) and the mixture was refluxed. Aliquots (25 ml) withdrawn to follow the transesterification were concentrated to dryness, a little dilute hydrochloric acid was added, and the mixed esters were extracted with chloroform and their nmr spectra were taken. After 5 days of refluxing the solutions, the spectra revealed the presence of about 30% unchanged **2**. Additional sodium (339 mg) in methanol (70 ml) was added and the refluxing was continued for another 3 days. The mixture was worked up as described for the aliquots. Traces of **2** in the crude product were removed by crystallization: yield 214 mg; mp 158–160°. The mass spectrum showed a molecular ion, *m/e* 197.

Anal. Calcd for $C_9H_{11}NO_4$: C, 54.8; H, 5.6; N, 7.1. Found: C, 55.2; H, 5.6; N, 6.9.

(±)-1α-Carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine Tosylate.—A solution of **4** (300 mg) and *p*-toluenesulfonyl chloride (600 mg) in dry pyridine (10 ml) was kept at 0° for 16 hr. The mixture was poured into ice–water and extracted with chloroform. The solvent was removed, leaving a crystalline residue which was washed with water to remove traces of **4**. Crystallization from acetone (a few drops)–ether–petroleum ether gave the tosylate as solid prisms: yield 230 mg; mp 101°. The nmr and ir spectra were consistent with the structure.

Reaction of Potassium Acetate with the Tosylates of 5 and 4.—A solution of the tosylate of **5** (138 mg) and potassium acetate

(9) C. C. J. Culvenor, G. M. O'Donovan, and L. W. Smith, *Aust. J. Chem.*, **20**, 757 (1967).

(10) W. D. Emmons and A. S. Pagano, *J. Amer. Chem. Soc.*, **77**, 89 (1955).

(150 mg) in dry ethanol (15 ml) was refluxed for 3.5 hr. Water (25 ml) was added and the mixture was extracted with chloroform. The solvent was removed and the residue was crystallized from acetone–petroleum ether to give 1-carbethoxy-3-oxo-1,8-dehydropyrrolizidine (11): yield 69 mg (94%); mp 89–90° (lit.[7] mp 88.9–90°). Ir, nmr, and mass spectra confirmed the structure of the product. Decoupling studies revealed a long-range coupling of 1.2 cps between the protons in 2 and 7 positions. When the tosylate of **5** (25 mg) and potassium acetate (29 mg) were kept in 2 ml of ethanol at room temperature for 26 hr and worked up as described, thin layer chromatography of the product showed the presence of starting material and some of the 1,8 olefin 11 (*ca.* 30%). No reaction occurred if acetic acid was added to the mixture under conditions of room temperature for 4 days or 100° for 8 hr. The tosylate of **4** was treated with potassium acetate in ethanol similarly and gave the olefin 11 in good yields.

Conversion of 9 into (±)-Heliotridane.—The diol **9** (425 mg) was added to freshly distilled thionyl chloride (10 ml) at 0° and the solution was refluxed for 90 min. After removal of excess thionyl chloride under reduced pressure, the residue was taken up in water and the solution was washed with chloroform, made alkaline with potassium carbonate, and extracted with chloroform to give a colorless oil (244 mg). The oil was dissolved in ethanol (8 ml) and reduced with hydrogen and Raney nickel. The catalyst was removed and the filtrate was diluted with 0.5 *N* sulfuric acid, washed with chloroform, basified with ammonia, and extracted with light petroleum ether (bp 30–40°). The product was distilled in a bulb tube, giving a liquid (80 mg) which formed a picrolonate, needles from ethanol; mp 146–147°, undepressed on admixture with (+)-heliotridane picrolonate; mp 155°, prepared from (+)-isoretronecanol by a similar procedure. The ir spectrum of the free base was identical with that of (−)-heliotridane[11] and its nmr spectrum (100 Mcps, $CDCl_3$) was identical with that of (+)-heliotridane and different from that of (+)-pseudoheliotridane prepared from (+)-trachelanthamidine by the above procedure.

Reduction of 2 with Sodium Borohydride.—A solution of **2** (434 mg) in dimethoxyethane (5 ml) was added dropwise to sodium borohydride (93 mg) in dimethoxyethane (5 ml). After 5 min, excess hydride was destroyed with a few drops of acetic acid and the mixture was poured into water (60 ml) and extracted with chloroform. Removal of solvent left a gum (368 mg) which crystallized from acetone–light petroleum ether, giving **4**; yield 179 mg, mp 103°, undepressed on admixture with an authentic sample. The mother liquor was submitted to preparative tlc (silica gel, 5% methanol in chloroform), giving additional **4**, yield 59 mg, R_f 0.67, together with **5**, yield 38 mg, R_f 0.60, mp 128°, undepressed on admixture with an authentic sample and with the same ir spectrum.

Registry No.—**3**, 21850-63-5; **4**, 21823-71-2; **6**, 15211-07-1; **7**, 21823-73-4; **8**, 21850-64-6; **9**, 21823-78-9; **10**, 21823-74-5; **10** (picrolonate), 21823-75-6; (±)-1-carbomethoxy-2,3-dioxo-8α-pyrrolizidine, 21823-76-7; (±)-1α-carbethoxy-2β-hydroxy-3-oxo-8α-pyrrolizidine tosylate, 21823-77-8.

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N,N'-Dinitrosopiperazine

JOSEPH B. LAMBERT,[1a] JACK L. GOSNELL, JR.,[1b] DAVID S. BAILEY, AND BRUCE M. HENKIN[1c]

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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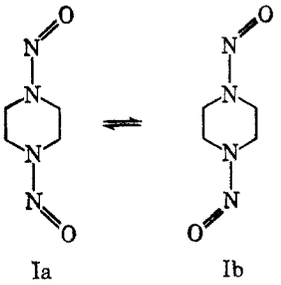
The conformational properties of N,N'-dinitrosopiperazine have been investigated in detail. In solution, both *syn* and *anti* forms are present, with a predominance of the latter. Only the *anti* form appears to be present in the solid. The *R* value obtained from the nmr spectrum of the *anti* form indicates that the molecule is either a boat form or a flattened chair in solution. The ir and Raman spectra (4000–50 cm^{-1}) have been examined in the solid to obtain information concerning molecular symmetry.

An sp^2 atom in an otherwise saturated six-membered ring generally flattens the surrounding portion of the molecule, as has been demonstrated for a number of simple cyclohexanones.[2] A pair of adjacent sp^2 atoms, as in cyclohexene, force a six-membered ring into the half-chair conformation. Trigonal atoms at opposite (1, 4) corners of the ring produce either a severely flattened chair or, if the methylene–methylene torsional strain is too great, a twist boat. The latter circumstance has been found to be the case for 1,4-cyclohexanedione[3] for some of its derivatives, and possibly for 1,4-dimethylenecyclohexanes.[4] Additional trigonal centers, *e.g.*, in cyclohexadienes, serve to flatten the ring even more.[5,6]

The factors that contribute to these conformational alterations are not fully understood. We have chosen to investigate the conformational properties of N,N'-dinitrosopiperazine (I) because of its formal resem-



Ia Ib

blance to the dione and because it possesses several modes of conformational flexibility. The amine nitrogen in a nitrosamine such as I is probably very close to being trigonally hybridized, because of delocalization of the lone pair into the nitroso group. Chow and Colón[7] have calculated that the polar form is present to

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