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THE CHEMISTRY OF LUNARIA ALKALOIDS. I.

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WE wish to report some findings concerning the chemistry of lunarine, which support and augment the conclusions reached recently by Potier and Le Men.[1]

Extraction of the seeds of Lunaria biennis Moench gave lunarine hydrate as needles, m.p. 230-235° (followed by partial solidification and remelting at 270-275° dec.), $[\alpha]_D +304°$ (c,0.467 in chloroform) (Found: C, 66.16; H, 7.27; N, 9.61; OMe, 0.0; NMe, 0.0; Equiv., 455.6. Calc. for $C_{25}H_{31}O_4N_3.H_2O$: C, 65.91; H, 7.30; N, 9.23%; Equiv., 455.5). These properties are in good agreement with those reported by Steinegger and Reichstein,[2] Hansen,[3] Boit,[4] and Janot and Le Men.[5]

Janot and Le Men[5] recorded the ultra-violet spectrum of lunarine, and in a recent paper, Potier et al.[6] stated that the spectrum was not changed

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[1] P. Potier and J. Le Men, Bull. Soc. Chim. 456 (1959).

[2] E. Steinegger and T. Reichstein, Pharm. Acta Helv. 22, 258 (1957).

[3] O. R. Hansen, Acta Chem. Scand. 1, 656 (1947).

[4] H. G. Boit, Chem. Ber. 87, 1082 (1954).

[5] M. M. Janot and J. Le Men, Bull. Soc. Chim. 1841 (1956).

[6] P. Potier, J. Le Men and M. M. Janot, Bull. Soc. Chim. 201 (1959).

on making the solution alkaline. We have found that the spectrum of lunarine in alkaline solution is quite different from that in neutral solution. The chief difference is the replacement of the two peaks near 300 mμ by a single maximum at 354 mμ (See Table 1). A surprisingly similar shift to longer wavelengths occurs on changing to a strongly acid solvent. Both these changes are reversible, and are associated with a weak acid and weak basic functions of pK_a' 11.94 and -1.81 respectively. In contrast, protonation of the basic function of lunarine responsible for salt formation (pK_a' 8.02) results in only slight changes in the spectrum.

Lunarine contains a strong band in the carbonyl region of the infrared spectrum, 1704 cm^{-1}, ascribed by Potier and Le Men[1] to a ketone group. We have made similar findings. Reduction of lunarine with lithium borohydride in methanol gives a mixture of two compounds separable by chromatography. The major product is lunarinol I, m.p. 250-253°, $[\alpha]_D$ +194° (c, 0.443 in methanol). (Found: C, 68.42; H, 7.96; N, 9.55. Calc. for $C_{25}H_{33}O_4N_3$: C, 68.31; H, 7.57; N, 9.56%). Lunarinol I is probably identical with the lunarinol reported by Potier and Le Men.[1] The other product is the isomer, lunarinol II, m.p. 260-270° dec., $[\alpha]_D$ + 166.5° (c, 0.52 in methanol) (Found: C, 68.48; H, 7.33; N, 9.56. $C_{25}H_{33}O_4N_3$ requires C, 68.31; H, 7.57; N, 9.56%).

Neither of this compounds has a peak near 1700 cm^{-1} in the infra-red spectrum, and it is considered that they are stereoisomeric alcohols formed by reduction of a ketone group present in lunarine. In neutral solution their ultra-violet spectra are similar to that of lunarine, but no shift to longer wavelengths occurs on making the solutions alkaline. It may be inferred that the presence of the ketone group is necessary for this shift to occur, and therefore that in lunarine the ketone group is separated from the main chromophore by an enolizable -CH-group.

TABLE 1. Ultra-violet spectra of lunarine derivatives

		λ_{max} mμ (ε)	
	Ethanol	0.1 M NaOH	10 M HCl
Lunarine	208 (29,200) 224 (26,000) 296 (22,100) 315 (17,300)	224 (28,800) 355 (27,500)	236 (24,200) 354 (24,400)
Lunarinol I	210 (25,700) 296 (19,000) 319 (17,400)	215 (59,000) 296 (21,600) 319 (21,300)	234 (21,600) 354 (21,100)
Lunarinol II	216 (34,100) 296 (20,300) 316 (18,300)	218 (55,400) 296 (21,200) 314 (20,400)	238 (24,800) 353 (24,400)
Tosyl-lunarine	205 (35,700) 228 (30,300) 295 (19,500) 320 (16,500)	235 (33,700) 360 (23,200)	212 (29,000) 234 (37,700) 354 (26,600)

Lunarine, on prolonged treatment with toluene-p-sulphonyl chloride in pyridine, gives a monotosyl derivative, m.p. 230-233°, $[\alpha]_D$ + 285° (c, 0.43 in chloroform) (Found: C, 63,03; H, 6.55; N, 6.71; S, 5.42. $C_{32}H_{37}O_6N_3S.H_2O$ requires C, 63.03; H, 6.45; N, 6.89; S, 5.26%) which is recovered unchanged after refluxing with methanolic potassium hydroxide. It is insoluble in dilute acids, which fact shows that the basic nitrogen atom of lunarine is present as a acylable -NH- of -NH_2 group. Since only a monotosyl derivative is formed other acylable hydroxyl or -NH- groups are absent. The ultra-violet spectra show that the weak acidic and weak basic functions of lunarine are still present in this derivative.

We have confirmed the remarkable observations of Steinegger and Reichstein[2] concerning the reaction between lunarine and methyl iodide. The product, m.p. above 330°, $[\alpha]_D + 224°$ (c, 0.3 in water), has an infrared spectrum differing in only minor respects from that of lunarine hydriodide (Found: C, 51.89; H, 5.79; N, 7.19; OMe, 0.0; NMe, 0.0. Calc. for $C_{25}H_{31}O_4N_3.HI.H_2O$: C, 51.45; H, 5.87; N, 7.20. Calc. for $C_{25}H_{31}O_4N_3.CH_3I.H_2O$: C, 52.25; H, 6.07; N, 7.03; NMe (1), 4.72%). It is reconverted into lunarine by dilute ammonia and there seems little doubt that it is the hydriodide (cf. Boit[4]). This last observation probably indicates that the basic nitrogen atom is sterically hindered.

Pyrolysis of lunarine yields a complex mixture of products, in which we have identified ammonia (as ammonium picrate). This accords well with the recorded formation of ammonia in oxidation,[2] and thermal alkaline[1] degradation reactions, and it is indicative of the presence of an $-NH_2$ group in the molecule.

Hydrolysis of lunarine with hydrochloric acid affords a quantitative yield of the dihydrochloride of an aliphatic diamine $C_5H_{14}N_2$, m.p. 250-253°, $[\alpha]_D - 0.05°$ (c, 0.99 in water). (Found: C, 34.09; H, 8.90; N, 15.49; Cl, 40.75; N-alkyl, 0.0. $C_5H_{14}N_2.2HCl$ requires C, 34.30; H, 9.20; N, 16.00; Cl, 40.50%). This is probably identical with the compound mentioned by Potier and Le Men[1] as being formed by alkaline degradation of lunarine. The corresponding picrate formed needles, m.p. 211-212°.

Comparison of the dihydrochloride of the diamine with authentic samples showed that it was not identical with either pentamethylenediamine dihydrochloride or diaminoneopentane dihydrochloride,[7] and we tentatively suggest that the diamine has structure (I) for the following reasons. When a solution of

$$(CH_3)_2C(NH_2).CH_2.CH_2.NH_2$$

I

the diamine dihydrochloride is titrated with alkali, the shape of the pH-titration curve shows that there is slight interaction between the amino groups. Comparison with curves obtained with ethylenediamine dihydrochloride, where strong interaction is evident, and with tetramethylenediamine dihydrochloride, where no interaction is revealed, suggests that the two amino groups are separated by three carbon atoms. The fact that the diamine dihydrochloride, which is virtually devoid of optical activity, is formed from the optically active lunarine under conditions in which the possibility of racemization can be discounted, is taken to exclude all asymmetrical structures. Of those structures not excluded by this reasoning, (I), (II), and the meso form of (III), (I) is considered to be the most likely one, since it accounts best for the observation,[5] which we have verified, that lunarine gives negative results in C-methyl determinations. Furthermore, structure (I) is the most

$CH_3.CH_2.CH(CH_2.NH_2)_2$ $\qquad$ $CH_3.CH(NH_2).CH_2.CH(NH_2).CH_3$

II $\qquad$ III

attractive on biogenetical considerations.

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[7] A. Lambert and A. Lowe, J. Chem. Soc. 1517 (1947).

There is abundant evidence in the infra-red spectrum of lunarine for the presence of amide links. It is a reasonable assumption, based on the ease of formation of the diamine by acid hydrolysis, that the C_5-diamine moiety is connected to the remainder of the molecule by one (or possibly two) such links. If we postulate that only one amide link is present here, and that the more hindered $-NH_2$ group of the diamine is free, then an explanation is available for the ready formation of ammonia from lunarine.

Details of this work and of further studies which are in progress will be published later.

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