A characteristic of some of these salts, especially the iodide, is their tendency to develop electrostatic charges, interfering with accurate weighing or transferring of small samples. All preparations were by simple metathesis without oxidation–reduction or change of structure.

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## Isolation of Tazettine and Lycorine from Certain *Hymenocallis* Species

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As part of a systematic survey of the alkaloids of the *Amaryllidaceae* we wish to report the isolation of tazettine and lycorine from several *Hymenocallis* species. The alkaloid tazettine has been isolated from *Lycoris radiata*,[1,2] *Narcissus tazetta*,[3] *Ungernia sewerzowii*[4,5] and *Galanthus nivalis*.[6] Although Greathouse and Rigler[7] have demonstrated the presence of unspecified alkaloids in *H. galvestonensis*, the only chemical study of *Hymenocallis spp.* was conducted by Gorter[8] who isolated lycorine from *H. littoralis* in 0.0015% yield. Lycorine appears to be the most wide-spread alkaloid of the *Amaryllidaceae*.

The isolation of a crude alkaloid fraction from the bulbs was achieved by a conventional procedure. Nearly 90% of this crude fraction was soluble in benzene and concentration of the benzene solution gave most of the tazettine that could be isolated. A minute quantity of lycorine was detected in the benzene-insoluble residues.

TABLE I

ISOLATION OF TAZETTINE AND LYCORINE FROM *Hymenocallis spp.*

| Species | Yield of crude alkaloids, % | Yield of tazettine, % | Yield of crude lycorine, % |
|---|---|---|---|
| *H. caymanensis* Herb.[a] | | | |
| 3.59 kg. bulbs only | 0.09[c] | 0.062 | 0.004 |
| 20.4 kg. bulbs only | .07[c] | .045 | .001 |
| 3.24 kg. leaves only | .15[d] | .009[d] | ... |
| *H. occidentalis* (leConte) Kunth[b] | | | |
| 3.93 kg. bulbs only | .14 | .046 | .004 |
| *H. littoralis* Salisb.[e,f] | | | |
| 240 g. bulbs only | .09 | .03 | ... |

[a] Obtained from the Los Angeles State and County Arboretum, Arcadia, California. [b] Obtained from W. H. Duncan, University of Georgia, Athens, Georgia. [c] All yields are based on wet weight of bulb unless otherwise designated. [d] Based on dry weight of leaves; loss of weight on drying at 71°, 91%. [e] Obtained from C. G. Van Tubergen, Ltd., Haarlem, The Netherlands. [f] Isolation performed by Dr. H. A. Lloyd of this Laboratory.

Tazettine and lycorine were identified by analytical data and rotation and by the preparation of known derivatives. The infrared absorption spectrum of the lycorine isolated was identical with that of an authentic sample.[9] While the structure of lycorine has been largely elucidated, only portions of the tazettine molecule are known with certainty.[10]

### Experimental[11]

**Isolation of the Crude Alkaloid Fraction.**—The bulbs of *H. caymanensis*, 20.4 kg., were ground in a Ball and Jewell grinder. The ground material was mixed with 20 l. of ethanol containing 160 g. of *d*-tartaric acid and allowed to stand overnight. The mixture was stirred for 2 hours at 55°. The solution (4 l.) was siphoned from the solid material and the solid was stirred with 8 l. of 1% ethanolic tartaric acid for 2 hours at 55°. The mixture was allowed to stand two days at 20° and then approximately 10 l. of solution was removed through a siphon. The residue was stirred with 11 l. of 1% ethanolic tartaric acid at 55° for 2 hours. The solution was siphoned from the solid and the liquid remaining with the solid was removed by vacuum filtration. The combined solutions were filtered in an International Chemical Centrifuge and concentrated to 5 l. The concentrate was diluted with 2.5 l. of water, treated with 2 l. of 2 *N* hydrochloric acid and extracted 16 times with 200-ml. portions of chloroform. The chloroform solution was discarded after a test for alkaloids proved negative. The aqueous solution was made basic with solid potassium carbonate and extracted 45 times with 200-ml. portions of chloroform. The chloroform solution was extracted 38 times with 200-ml. portions of 2 *N* hydrochloric acid and the aqueous solution was made basic with solid potassium carbonate. The alkaloid was removed from the aqueous solution by 30 extractions with 200-ml. portions of chloroform. The chloroform solution was concentrated, dried and further concentrated to constant weight, 14.99 g. (0.0734%).

**Isolation of Tazettine and Lycorine.**—A portion of the crude alkaloid mixture from *H. caymanensis* weighing 1.84 g. was extracted with 25 ml. of thiophene-free benzene and the hot solvent was decanted from the gummy residue. This residue, 0.22 g., was treated in a similar manner with 10 ml. of hot ethyl acetate. The material that was insoluble in ethyl acetate, 0.14 g., was dissolved in 5 ml. of hot ethanol. The ethanolic solution crystallized upon standing to give 12 mg. of crude lycorine, m.p. 250–255° dec. Concentration of the benzene solution gave crude tazettine which was recrystallized twice from ethanol, 0.70 g., m.p. 208–210° dec. Concentration of the ethyl acetate extract and trituration with ethanol gave an additional 0.02 g. of tazettine, m.p. 202–208° dec. The mother liquors from the crystallization of tazettine were dissolved in 20 ml. of benzene and chromatographed on 31.0 g. of alumina. Elution with ethyl acetate followed by chloroform gave an additional 0.35 g. of crude tazettine which was recrystallized from ethanol, 0.23 g., m.p. 207–209° dec. An additional 50 mg. of crude lycorine, m.p. 223–232° dec., was obtained from the chloroform–ethanol eluates of this column. The total yield of crude lycorine was 62 mg. (0.004% based on the wet weight of the bulb). The total yield of tazettine based on the wet weight of the bulb was 0.062%. An analytical sample of tazettine was crystallized

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[1] H. Kondo, K. Tomimura and S. Ishiwatari, *J. Pharm. Soc. Japan*, **52**, 51 (1932).

[2] E. Späth, H. Kondo and F. Kuffner, *Ber.*, **69**, 1086 (1936).

[3] E. Späth and L. Kahovec, *ibid.*, **67**, 1501 (1934).

[4] S. Norkina and A. Orechoff, *ibid.*, **69**, 500 (1936).

[5] E. Späth, A. Orechoff and F. Kuffner, *ibid.*, **69**, 2446 (1936).

[6] G. R. Clemo and D. G. I. Felton, *Chemistry and Industry*, 807 (1952).

[7] G. A. Greathouse and N. E. Rigler, *Am. J. Botany*, **28**, 702 (1941).

[8] K. Gorter, *Bull. Jard. Bot. Buitenzorg*, [3] **1**, 352 (1920).

[9] Kindly furnished by Prof. K. Wiesner.

[10] The chemistry of tazettine, lycorine and other alkaloids of the *Amaryllidaceae* has been reviewed recently by J. W. Cook and J. D. Loudon in R. H. F. Manske, "The Alkaloids," Vol. II, Academic Press, Inc., New York, N. Y., 1952, p. 331. For more recent developments in the chemistry of the two alkaloids, see E. J. Forbes, J. H. Mason and R. Robinson, *Chemistry and Industry*, 946 (1953); K. Wiesner, W. I. Taylor and S. Uyeo, *ibid.*, 46 (1954); T. R. Govindachari and B. S. Thyagarajan, *ibid.*, 374 (1954); R. Robinson, *ibid.*, 1317 (1953); E. Wenkert, *ibid.*, 1088 (1953); R. B. Kelly, W. I. Taylor and K. Wiesner, *J. Chem. Soc.*, 2094 (1953); H. Kondo and coworkers, *Annual Rept. ITSUU Lab. (Tokyo)*, **1**, 21 (1950); *ibid.*, **2**, 18 (1951), *ibid.*, **3**, 65 (1952), [*C. A.*, **47**, 7516 (1953)], *ibid.*, **4**, 30 (1953).

[11] All melting points were observed on a Kofler microscope hotstage and are corrected. Analyses were performed by Dr. W. C. Alford and his staff. Infrared and ultraviolet absorption spectra were determined by Mrs. Iris J. Siewers.

from ethanol, m.p. 208–210° dec. (reported 212–213° (vac.),[2] 210–211°,[3,4] 208–209°,[1] 207–208°[6]); $[\alpha]^{24}_{\mathrm{D}}$ +160.4° (*c* 1.92, chloroform) (reported $[\alpha]^{22}_{\mathrm{D}}$ +162.3°,[5] $[\alpha]^{25}_{\mathrm{D}}$ 150.3°,[3] $[\alpha]^{18}_{\mathrm{D}}$ +165.8°[2]).

*Anal.* Calcd. for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.20, H, 6.52; N, 4.20.

The ultraviolet absorption spectrum in ethanol shows $\lambda_{max}$ 242 mμ (log ε 3.69), $\lambda_{max}$ 295 mμ (log ε 3.65), $\lambda_{min}$ 262 mμ (log ε 2.62).

**Tazettine Picrate.**—Prepared in aqueous ethanol and recrystallized from ethanol, the picrate formed yellow prisms, m.p. 211–213° dec. (reported 192°[1,12] 205–208°,[4] 213°[6]).

*Anal.* Calcd. for $C_{24}H_{24}N_4O_{12}$: C, 51.43; H, 4.32; N, 10.00. Found: C, 51.35; H, 4.47; N, 9.95.

**Tazettine Methiodide.**—Prepared in ethanol and recrystallized three times from ethanol, the methiodide formed colorless prisms, m.p. 223–224° dec. (reported 238°,[1] 220° dec.,[3] 220–223°,[4] 211–213° dec.[6])

*Anal.* Calcd. for $C_{19}H_{24}NO_5I\cdot{}^1/_2H_2O$: C, 47.31; H, 5.22; N, 2.90. Found: C, 47.44; H, 5.20; N, 2.78.

**Tazettine Methopicrate.**—A solution of 0.114 g. of tazettine methiodide in 5 ml. of water was treated with aqueous picric acid until no further precipitation occurred. The precipitate was recrystallized from aqueous ethanol, 0.105 g., m.p. 237–239° dec. (reported[6] 234° dec.).

*Anal.* Calcd. for $C_{25}H_{26}N_4O_{12}$: C, 52.26; H, 4.56; N, 9.75. Found: C, 52.23; H, 4.70; N, 9.90.

**Tazettine Acetate.**—A solution of 0.659 g. of tazettine, 3 ml. of pyridine and 1 ml. of acetic anhydride was refluxed for one hour. The solution was concentrated, dissolved in chloroform and washed once with 5% sodium carbonate solution and once with water, dried and concentrated to a viscous oil that would not crystallize. The oil was chromatographed on 30.0 g. of alumina. Elution with benzene gave 252 mg. of oil that crystallized on trituration with ethyl acetate, m.p. 119–122°. The solid was recrystallized twice from aqueous methanol, 185 mg., m.p. 124–126° (reported 125–126.5°,[3] 124–125°[1]).

*Anal.* Calcd. for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.45; H, 6.32; N, 3.51.

**Purification of Lycorine.**—An aqueous suspension of 300 mg. of crude lycorine was acidified with dilute hydrochloric acid. The precipitated lycorine hydrochloride was dissolved by heat and the brown solution was decolorized with Darco. Upon cooling, 295 mg. of **lycorine hydrochloride monohydrate** crystallized as colorless elongated prisms, m.p. 213–215° (reported 206°,[15] 216°,[7] 228–234° dec.,[13] 258° dec.[14]); $[\alpha]^{27}_{\mathrm{D}}$ +45.7° (*c* 0.34, water) (reported $[\alpha]^{18}_{\mathrm{D}}$ +40.5°,[13] $[\alpha]^{9}_{\mathrm{D}}$ +96.8°,[14] $[\alpha]_{\mathrm{D}}$ +43°[15]).

*Anal.* Calcd. for $C_{16}H_{20}NO_5Cl$: C, 56.22; H, 5.90; N, 4.10. Found: C, 55.96; H, 5.66; N, 4.33.

When a solution of 295 mg. of this hydrochloride was made basic, 214 mg. of lycorine, m.p. 247–252° dec., was precipitated. Two recrystallizations from pyridine gave colorless prisms, m.p. 250–255° dec.[16] (reported 266–267° dec.,[17] 270° dec.,[13] 275° dec.,[18] 277°[7]); $[\alpha]^{27}_{\mathrm{D}}$ −75.1° (*c* 0.16, abs. ethanol) (reported $[\alpha]^{21}_{\mathrm{D}}$ −76°,[13] $[\alpha]^{10}_{\mathrm{D}}$ −95.8°,[17] $[\alpha]^{13}_{\mathrm{D}}$ −123.7°,[18] $[\alpha]^{2}_{\mathrm{D}}$ −120°[15]).

*Anal.* Calcd. for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.57; H, 6.16; N, 4.77.

**Dihydrolycorine.**—To a suspension of platinum, prepared by the atmospheric hydrogenation of 100 mg. of platinum oxide in 5 ml. of glacial acetic acid, was added a solution of 1.33 mmoles of lycorine in 10 ml. of glacial acetic acid. The reduction stopped when 107% of the theoretical amount of hydrogen had been absorbed. The catalyst was separated by filtration and the acetic acid was removed under an air jet. The residue was dissolved in water and made basic with 10% sodium carbonate solution. The precipitated dihydro base, 351 mg., m.p. 230–237° dec., was recrystallized from pyridine–ethanol (1:4) to give 237 mg. of pure base, m.p. 236–237° dec. (reported[15] 247°).

*Anal.* Calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.56; H, 6.47; N, 5.02.

**Lycorine Diacetate.**—By the procedure of Reichstein,[13] 100 mg. of lycorine gave 71 mg. of lycorine diacetate, m.p. 217–218.5° dec. (reported 215–216°,[14] 219–221°[13]); $[\alpha]^{26}_{\mathrm{D}}$ +26.8° (*c* 1.22, chloroform) (reported $[\alpha]^{18}_{\mathrm{D}}$ +26.6°,[13] $[\alpha]^{9}_{\mathrm{D}}$ +31.5°[14]).

*Anal.* Calcd. for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.51; H, 5.58; N, 3.72.

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[12] The respective melting points of the hydrochloride and picrate of tazettine are reported to be 192 and 214° in *C. A.*, **26**, 4818 (1932) and 214 and 192° in *Chem. Zentr.*, **103**, II, 877 (1932). Recourse to an original copy of reference 1 indicates that the values reported by *C. A.* are in error.

[13] A. Hunger and T. Reichstein, *Helv. Chim. Acta*, **36**, 824 (1953).

[14] H. Kondo and K. Tomimura, *J. Pharm. Soc. Japan*, **48**, 36 (1928).

[15] K. Gorter, *Bull. Jard. Bot. Buitenzorg*, [3] **2**, 1 (1920).

[16] The melting point of this sample of lycorine, when observed in an evacuated capillary, was 282–282.5° dec. This variation in melting point under different conditions has not been reported previously; indeed, reference 13 records the melting point of lycorine on a Kofler block.

[17] A. J. Ewins, *J. Chem. Soc.*, **97**, 2406 (1910).

[18] Y. Asahina and Y. Sugii, *Arch. Pharm.*, **251**, 357 (1913).

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## Observations on the Forms of Allose and Its Phenylosazone

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In another investigation,[4] a crystalline product was identified as a mixture of DL-allose and D-allose. To attain this objective, it was necessary to establish the nature of the crystalline phases exhibited by this rare hexose and its phenylosazone. β-D-Allose[5]

TABLE I

X-RAY POWDER DIFFRACTION PATTERNS OF THE DIMORPHOUS AND RACEMIC FORMS OF ALLOSE AND ITS PHENYLOSAZONE

| β-D- (or β-L)- Allose, m.p. 128° | β-D- (or β-L)- Allose, m.p. 141° | DL- Allose, m.p. 180° | D-(or L)- *ribo*-Hexose phenyl- osazone[a] | DL-*ribo*- Hexose phenyl- osazone[a] |
|---|---|---|---|---|
| 4.02[b] (1)[c] | 4.26[b] (1)[c] | 4.31[b] (1)[c] | 4.89[b] (1)[c] | 4.66[b] (1)[c] |
| 4.60 (2) | 2.90 (2) | 5.94 (2) | 3.22 (2) | 5.72 (2) |
| 4.21 (3) | 5.96 (3) | 2.87 (3) | 7.68 (3) | 4.23 (3) |
| 3.61 (4) | 2.69 (4) | 3.75 (4) | 4.42 (4) | 3.16 (4) |
| 2.40 (5) | 2.36 (5) | 2.32 (5) | 3.88 (5) | 3.76 (5) |
| 3.14 (6) | 2.46 (5) | 2.51 (6) | 10.26 (6) | 4.42 (5) |
| 5.43 (6) | 3.67 (6) | 5.88 (6) | 4.04 (7) | 8.82 (6) |
| 7.18 (6) | 6.39 (6) | 3.94 (7) | 2.44 (8) | 3.27 (7) |
| 2.89 (7) | 1.92 (7) | 6.35 (7) | 2.84 (8) | 10.13 (7) |
| 2.00 (8) | 2.01 (7) | 1.92 (8) | 5.22 (8) | 2.00 (8) |
| 2.72 (8) | 3.11 (7) | 2.10 (8) | 3.58 (9) | 2.45 (8) |
| 14.09 (8) | 3.22 (7) | 2.22 (8) | 6.51 (10) | 2.84 (8) |
| | | | 6.91 (10) | 3.63 (9) |
| | | | 8.72 (11) | 7.76 (10) |

[a] The osazones were freshly recrystallized; the racemic form melted at 177–180° dec. and the optically active forms at 162–163° dec. [b] Main interplanar spacings, CuK$_\alpha$ radiation. [c] Relative intensity, estimated visually; 1, strongest band.

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[1] The Ohio State University.

[2] National Bureau of Standards, Washington, D. C.

[3] Veterans Administration Hospital, Omaha, Nebraska.

[4] M. L. Wolfrom and J. N. Schumacher, *Science*, **119**, 587 (1954).

[5] F. P. Phelps and F. Bates, THIS JOURNAL, **56**, 1250 (1934).