alcohol-bath. The temperature was adjusted to the desired temperature by means of liquid nitrogen introduced into a coil of copper tubing immersed in the bath liquid. The solution in the bulb was stirred by a helix of wire whose up and down motion was magnetically controlled. The pressure in the system was measured with a mercury manometer. The volume of the system was known in order to apply a correction for uncondensed gases. The temperature when crystals first appeared in the solution upon cooling was measured with a single junction copper–constantan thermocouple and a Rubicon, type B, precision potentiometer.

TABLE I

FREEZING POINTS OF BROMOCHLOROMETHANE–CARBON DIOXIDE SYSTEM

Mole % CO_2	F.p., °C.	Eutectic	Press., cm.
0	−87.9		0.2
4.6	−89.9		14.8
6.0	−90.5		19.8
8.4	−91.3		21.9
10.6	−92.1	−92.1	23.6
12.1	−90.4	−92.1	31.1
15.0	−85.5	−92.1	48.0
21.6	−80.0		79.3
29.2	−73.8		122.6
38.8	−69.7	−92.1	160.7
60[a]	−64.2		242
80[a]	−60.3		316
100[b]	−56.6		388.5

[a] Estimated from smooth curve. [b] "International Critical Tables," Vol. III, McGraw-Hill Book Co., Inc., New York, N. Y., 1928, p. 235.

TABLE II

FREEZING POINTS OF DIBROMODIFLUOROMETHANE–CARBON DIOXIDE SYSTEM

Mole % CO_2	F.p., °C.	Eutectic	Press., cm.
0	−141.6		0.5
0.7	−141.4	−142.5	.4
2.3	−127.7	−142.7	.4
5.0	−114.8	−142.7	2.8
9.7	−104.0		11.4
16.2	− 93.2		27.7
20.1	− 88.2		38.1
28.2	− 80.7		78.9
41.7	− 74.6	−142.6	111.00
47.2	− 71.7		145.0
60[a]	− 67.3		193
80[a]	− 61.4		289
100[b]	− 56.6		388.3

[a] See footnote *a* in Table I. [b] See footnote *b* in Table I.

TABLE III

FREEZING POINTS OF BROMOTRIFLUOROMETHANE–CARBON DIOXIDE SYSTEM

Mole % CO_2	F.p., °C.	Press., cm.	°C. for 76 cm.
0	−168	5	−64.7
0.8	−154.2	4.5	
1.1	−150.9		
2.0	−137.0		
4.9	−121.8	8.4	
10.0	−107.6	21.0	−74.7
22.2	− 92.7	49.2	−81.7
33.8	− 83.7	79.0	−84.1
46.7	− 76.9	121.7	
60[a]	− 71.0	187	−84.0
80[a]	− 62.9	285	−81.7
100[b]	− 56.6	388.5	−78.5

[a] See footnote *a* in Table I. [b] See footnote *b* in Table I.

Materials.—The bromochloromethane was purified by distillation in a multiple plate fractionating column; b.p. 68.0° at 76 cm.; f.p. −87.9°. The dibromodifluoromethane after several distillations had a freezing point of −141.6°. The bromotrifluoromethane as procured contained about 10% carbon dioxide as impurity. After purification a solidification temperature of −168 ± 2° was obtained.

Results.—The data are presented in Tables I–III. For the system CH_2BrCl–CO_2, the eutectic temperature is −92.1° at 10.6 mole per cent. CO_2; for the system CBr_2F_2–CO_2, −142.6° at 0.5 mole per cent. CO_2; and for the system $CBrF_3$–CO_2, at −170° at a concentration less than 0.5 mole per cent. CO_2.

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Terpenoids. I. The Triterpenes of the Cactus *Lemaireocereus Thurberi*

BY CARL DJERASSI, L. E. GELLER AND A. J. LEMIN[1]

RECEIVED DECEMBER 22, 1952

In connection with a study now under way in this Laboratory[2] on the alkaloids of certain cacti, it appeared of interest also to investigate the non-basic constituents of certain members of the *Cactaceae* family. The present note is concerned with such an examination of the cactus *Lemaireocereus Thurberi*, the only species of the genus *Lemaireocereus*, the natural habitat of which extends as far north as Arizona.[3] This cactus, reaching up to 21 feet in height, is particularly abundant in northern Mexico in the states of Sonora, Nayarit, Sinaloa and Baja California where it is known as "pitahaya dulce"[4] and it is often used by the natives for natural fences. The specimens employed in the present study were obtained through the cooperation of Dr. R. R. Humphrey, University of Arizona, who collected them near Hermosillo, Sonora.

A chemical study of the alcoholic extract of the dried and pulverized plant indicated the total absence of alkaloids, in marked contrast to the abundance of alkaloids in some related genera.[2] Similarly, the neutral portion yielded only negligible amounts of crystalline material, but there was an appreciable, water-soluble, glycosidic fraction. Acid hydrolysis of this material yielded a neutral and an acidic component. The former appears to be an unknown triterpene ($C_{30}H_{46}O_3$), the infrared spectrum (Fig. 1) of which showed bands at 2.80 and 5.65 μ characteristic of a free hydroxyl group and a five-membered lactone ring. The substance formed a monoacetate with infrared carbonyl

(1) Syntex Post-doctorate Fellow, 1952–1953.

(2) C. Djerassi, *et al.*, to be published.

(3) N. L. Britton and J. N. Rose, "The Cactaceae," Vol. II, p. 98, Carnegie Institution of Washington, Washington, D. C., 1920.

(4) H. Bravo, "Las Cactaceas de Mexico," Mexico, D. F., 1937, p. 269.

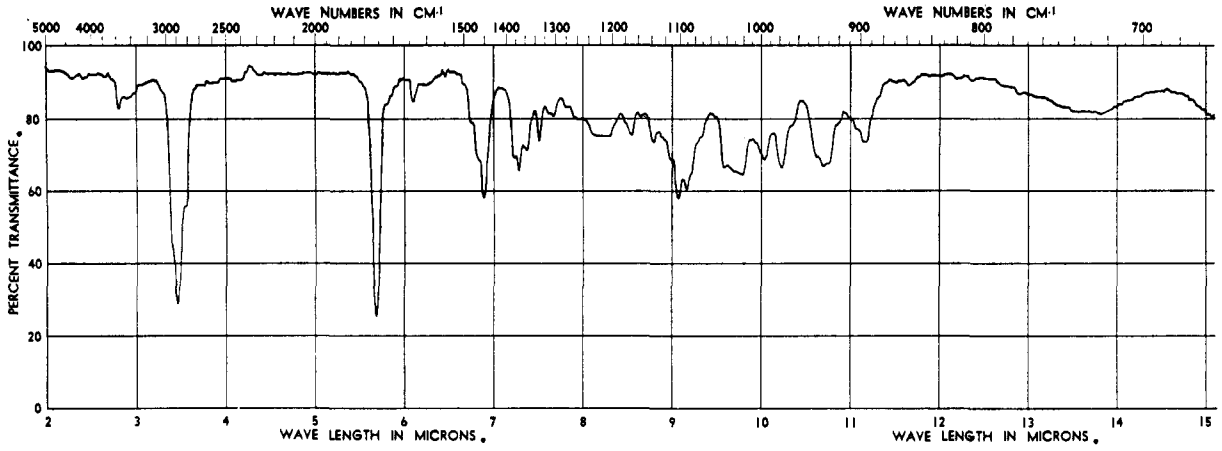

Fig. 1.—Infrared spectrum of thurberogenin in chloroform solution (0.1 mm. sodium chloride cell).

bands at 5.66 and 5.80 μ and was unsaturated to tetranitromethane, but showed no selective absorption in the ultraviolet. Further work on the structure of this compound, which we have named provisionally "thurberogenin," is contemplated when additional supplies of plant become available.

The acidic sapogenin was readily identified as the known oleanolic acid and was further characterized as the methyl ester, acetate and methyl ester acetate. Oleanolic acid has been isolated from over twenty different plant sources in the free state and as the glycoside[5] but it has never been encountered in a cactus. In fact, this appears to be the first report of the isolation of triterpenes from the *Cactaceae* family and it has prompted us to undertake a chemical investigation of representatives of the sub-tribe *Cereanae* to which belong all of the giant cacti indigenous to this continent. Preliminary results indicate that the occurrence of triterpenes is the rule rather than exception in these plants and that a number of new triterpenes will be found; these will form the subjects of future communications.

Experimental[6]

Isolation of Thurberogenin.—Two kilos of the cactus *Lemaireocereus thurberi* (collected in August, 1952, by Dr. R. R. Humphrey 10 miles north of Hermosillo on the road to Nogales) was cut into small pieces, dried for 2 days at 80–90°, passed through a meat grinder and the dry material (303 g.) was extracted continuously in a soxhlet extractor with 2 l. of ethanol until the extract was colorless (2 days). The dark green solution was evaporated to dryness under reduced pressure and the residue (65 g.) was extracted repeatedly with ether. The ether extract gave no precipitate with Mayer reagent and yielded only traces of oily material when processed in the usual manner for alkaloids. The ether-insoluble, semi-crystalline glycosidic portion (36 g.) was refluxed for 3.5 hours with 125 cc. of methanol and 31 cc. of concd. hydrochloric acid. After addition of excess 10% sodium hydroxide solution, the mixture was extracted thoroughly with ether. Evaporation of the dried ether extract followed by crystallization from methanol–chloroform afforded 1.4 g. (0.46%) of colorless needles of *thurberogenin*[7] with m.p. 283–285° (293–295° Kofler), $[\alpha]^{22}D$ +11°, $\lambda_{max}^{CHCl_3}$ 2.80 and 5.65 μ (*cf.* Fig. 1), no selective ultraviolet absorption above 215 mμ, light yellow color with tetranitromethane.

Anal. Calcd. for $C_{30}H_{48}O_3$: C, 79.24; H, 10.20. Found: C, 79.21; H, 10.23.

Infrared evidence was adduced for the presence of the hydroxyl function as a secondary hydroxyl group attached to a a six-membered (or larger) ring. Thus, oxidation of a small sample of thurberogenin with chromium trioxide–sulfuric acid in acetone solution followed by crystallization from methanol–chloroform afforded crystals with m.p. 233–236°, the infrared spectrum of which showed no more hydroxyl band, but in addition to the 5.65 μ lactone band there was present a second carbonyl band of equal intensity at 5.90 μ, indicative of a six-membered (or higher) ketone. No selective absorption was found in the ultraviolet region.

Thurberogenin acetate, prepared by the acetic anhydride–pyridine method (room temperature), crystallized from methanol–chloroform as needles with m.p. 249–252°, $[\alpha]^{22}D$ +45°, $\lambda_{max}^{CHCl_3}$ 5.66, 5.80 and 8.00 μ, yellow color with tetranitromethane.

Anal. Calcd. for $C_{32}H_{48}O_4$: C, 77.37; H, 9.74. Found: C, 77.14; H, 9.50.

Isolation of Oleanolic Acid.—The alkaline solution from the above described hydrolysis deposited a crystalline sodium salt, which was filtered, dissolved in ethanol and acidified with dilute hydrochloric acid. The solution was extracted with ether, washed, dried and evaporated and the residue was crystallized from methanol–chloroform to yield 5.5 g. (1.8%) of **oleanolic acid** with m.p. 308–310°,[8] λ_{max}^{Nujol} 2.88 and 5.88 μ. A sample was sublimed in high vacuum before analysis.

Anal. Calcd. for $C_{30}H_{48}O_3$: C, 78.89; H, 10.59. Found: C, 78.51; H, 10.43.

Oleanolic acid acetate was obtained as needles after crystallization from methanol–chloroform; m.p. 264–267°,[9] undepressed upon admixture with an authentic specimen

(5) In addition to the plant sources enumerated by E. Hardegger and F. G. Robinet (*Helv. Chim. Acta*, **33**, 1871 (1950)), oleanolic acid has also been encountered in *Clematis* root (K. Ishiwatari, K. Nakano and F. Shinkawa, *J. Pharm. Soc., Japan*, **64**, 34 (1944)), in *Thymus vulgaris* (E. J. Rowe, J. E. Orr, A. H. Uhl and L. M. Parks, *J. Am. Pharm. Assoc.*, **38**, 122 (1949)), in *Prunus mume* (Y. Takizima, *J. Agr. Chem. Soc., Japan*, **23**, 8 (1949)), in *Crataegus oxyacanthal* (T. Bersin and A. Müller, *Helv. Chim. Acta*, **35**, 1891 (1952)), in *Randia* (J. Gedeon, *Arch. Pharm.*, **285**, 127 (1952)), and in a number of Western Australian plants (D. E. White, *et al.*, *J. Chem. Soc.*, 4065 (1952)). The most convenient source still appears to be spent cloves (L. Ruzicka and K. Hofmann, *Helv. Chim. Acta*, **19**, 114 (1936)).

(6) Melting points are uncorrected and were obtained on the Fisher–Johns block. The infrared spectra were measured on a Baird Associates double beam recording spectrometer. All rotations were determined in chloroform solution.

(7) The physical constants of thurberogenin (though not of its acetate) are quite similar to those reported for authentic oleanolic acid lactone which has been synthesized recently by D. H. R. Barton and N. J. Holness (*J. Chem. Soc.*, 78 (1952)). However, a mixture melting point with a sample kindly supplied by Dr. Barton showed a marked depression.

(8) *Inter al.*: A. W. van der Haar, *Rec. trav. chim.*, **46**, 775 (1927), m.p. 307–308°.

(9) E. Wedekind and W. Schicke, *Z. physiol. Chem.*, **195**, 132 (1931), report m.p. 268°, $[\alpha]D$ +74.5° (chloroform).

obtained from spent cloves,[5,10] $[\alpha]^{22}D$ +70°, $\lambda_{max}^{CHCl_3}$ 5.80, 5.90 and 7.98 μ. The infrared spectra of the two specimens were identical.

Oleanolic acid methyl ester, prepared by diazomethane treatment in ether–methanol solution, crystallized from methanol–chloroform as colorless crystals with m.p. 198–199°, $[\alpha]^{22}D$ +69°,[11]

Oleanolic acid acetate methyl ester, obtained by diazomethane treatment of the acetate, exhibited m.p. 217–219°, $[\alpha]^{22}D$ +65°,[12] after crystallization from chloroform–methanol.

Acknowledgment.—The presently used plant specimens were obtained during a collection trip for related cacti under a grant from the American Heart Association.

(10) We are indebted to Dr. T. G. Halsall of the University of Manchester, England, for this sample.

(11) W. A. Jacobs and E. E. Fleck, *J. Biol. Chem.*, **96**, 341 (1932), report m.p. 197–198°, $[\alpha]D$ +75° (chloroform).

(12) A. Winterstein and G. Stein, *Z. physiol. Chem.*, **199**, 64 (1931), give m.p. 218–220°, $[\alpha]D$ +66.7°, +70.4°.

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Heterocyclic Compounds from Ethylanilines

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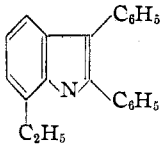
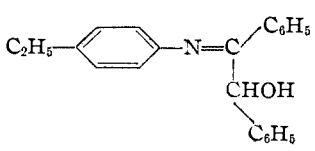
With the ready availability of *o*- and *p*-ethylnitrobenzene, it seemed desirable to hydrogenate them to the corresponding anilines and utilize these in organic syntheses. *o*-Ethylaniline reacted with benzoin in the presence of fused zinc chloride at 130° to give 49% of 2,3-diphenyl-7-ethylindole (I), a method used previously for the preparation of 2,3-diphenylindole itself.[1] Under the same conditions *p*-ethylaniline yielded only the Schiff base N-(1,2-diphenyl-2-hydroxyethylidene)-*p*-ethylaniline (II) in 20% yield.



I



II

o-Ethylaniline and *p*-ethylaniline gave 8- and 6-ethylquinolines, respectively, in 74 and 45% yields under the conditions of the Skraup reaction. Both quinolines were characterized as their methiodides. 6-Ethylquinoline was oxidized to the corresponding amine oxide by a standard procedure.[2] While the acetate resisted all attempts at purification, the picrate crystallized readily.

Experimental

***o*-Ethylaniline** was prepared by the hydrogenation of *o*-ethylnitrobenzene in the presence of Raney nickel. The yield was 78%, b.p. 99–105° (18 mm.) (210–211°),[3] $n^{25}D$ 1.5562.

2,3-Diphenyl-7-ethylindole.—A mixture of 60.5 g. of *o*-ethylaniline, 106 g. of benzoin, 75 g. of freshly dehydrated zinc chloride and 150 cc. of benzene was heated at 130° in a rocking autoclave for 3 hours. The resulting clear resin was dissolved in ethanol and diluted with water. The product which precipitated at this point was separated by filtration, washed with water and crystallized first from hexane and then from ethanol to yield 73 g. (49%) of 2,3-diphenyl-7-ethylindole. m.p. 112–114°. An analytical sample was recrystallized from ethanol, m.p. 113–114°.

Anal.[4] Calcd. for $C_{22}H_{19}N$: C, 88.9; H, 6.43; N, 4.72. Found: C, 89.1; H, 6.57; N, 4.94.

8-Ethylquinoline was prepared by a modification of the previously described Skraup reaction[5] in 36% conversion and 74% yield, b.p. 132–135° (20 mm.) (256°),[5] $n^{25}D$ 1.5993 ($n^{25}D$ 1.6020).[5]

8-Ethylquinoline methiodide was prepared by heating 9 g. of the quinoline with 28 g. of methyl iodide in a bomb at 100° for 18 hours. The 8 g. (47%) of crude product was crystallized twice from ethyl acetate–methanol, m.p. 138–139°.

Anal. Calcd. for $C_{12}H_{14}NI$: C, 48.2; H, 4.69. Found: C, 47.5; H, 4.67.

***p*-Ethylaniline** was prepared in the same way as the ortho isomer in 93% yield, b.p. 98° (14 mm.)–108° (19 mm.) (95–96° (10 mm.))[6], $n^{25}D$ 1.5520 ($n^{22}D$ 1.5529)[7].

N-(1,2-Diphenyl-2-hydroxyethylidene)-*p*-ethylaniline was prepared by heating 60.5 g. of *p*-ethylaniline, 106 g. of benzoin, 75 g. of freshly dehydrated zinc chloride and 150 cc. of benzene in a bomb for 3 hours at 130°. After the reaction mixture had been diluted with ethanol, the crude product was separated by filtration, washed with water and dried. On boiling with hexane 2.0 g. of the zinc chloride salt of *p*-ethylaniline remained insoluble. It was separated by filtration and crystallized twice from ethanol, dec. pt. 244–247°. It was soluble in hot water and gave a flocculent precipitate with aqueous silver nitrate.

Anal. Calcd. for $C_8H_{11}N \cdot {}^1/_2ZnCl_2$: C, 50.8; H, 5.82; N, 7.41. Found: C, 51.4; H, 5.89; N, 7.75.

Cooling of the hexane solution yielded 30 g. (20%) of crude N-(1,2-diphenyl-2-hydroxyethylidene)-*p*-ethylaniline, m.p. 102–103°. This product was recrystallized twice for analysis, m.p. 103–104°.

Anal. Calcd. for $C_{22}H_{21}NO$: C, 83.8; H, 6.67; N, 4.40. Found: C, 83.3; H, 6.71; N, 4.43.

6-Ethylquinoline was prepared in the same way as the 8-isomer in 23% conversion and 45% yield, b.p. 132–140° (17 mm.), $n^{25}D$ 1.6017. Redistillation yielded pure 6-ethylquinoline, b.p. 135–136° (14 mm.), $n^{25}D$ 1.6009, d^{25}_{25} 1.043, $M^{25}D$ calcd. 51.73, $M^{25}D$ found 51.55.

Anal. Calcd. for $C_{11}H_{11}N$: C, 84.1; H, 7.01; N, 8.92. Found: C, 83.9; H, 6.92; N, 9.08.

6-Ethylquinoline picrate melted at 205.0–205.5°.

Anal. Calcd. for $C_{17}H_{14}O_7N_4$: C, 52.9; H, 3.63; N, 14.5. Found: C, 53.0; H, 3.59; N, 14.1.

6-Ethylquinoline methiodide was prepared by warming 8 g. of 6-ethylquinoline with 25 g. of methyl iodide. The crude product (15 g., 99%) was separated by filtration and crystallized twice from methanol, m.p. 194.0–194.5°.

Anal. Calcd. for $C_{12}H_{14}NI$: C, 48.2; H, 4.69. Found: C, 48.5; H, 4.83

6-Ethylquinoline-N-oxide Acetate.—A mixture of 73 g. of 6-ethylquinoline, 175 cc. of glacial acetic acid and 175 cc. of 30% hydrogen peroxide was held at 50° for 24 hours. Distillation at 25 mm. to a pot temperature of 110° left as a residue 87 g. (78%) of crude oxide. This material was crystallized three times from benzene with previous treatment of the solution with Norite, but the product always separated as an oil before crystallizing, m.p. 66–67°.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 66.9; H, 6.44. Found: C, 64.3; H, 6.54.

6-Ethylquinoline-N-oxide picrate melted at 156–157°.

Anal. Calcd. for $C_{17}H_{14}O_8N_4$: C, 50.7; H, 3.48; N, 13.9. Found: C, 51.1; H, 3.55; N, 13.8.

(1) F. R. Japp and T. S. Murray, *J. Chem. Soc.*, **65**, 889 (1894).

(2) H. J. Den Hertog and W. P. Combe, *Rec. trav. chim.*, **70**, 581 (1951).

(3) F. Beilstein and A. Kuhlberg, *Ann.*, **156**, 206 (1870).

(4) All of the analyses are microanalyses performed by Mr. Donald Stoltz, Miss Winifred Harden and Mrs. Helen LeMay of these laboratories.

(5) R. A. Glenn and J. R. Bailey, THIS JOURNAL, **63**, 639 (1941).

(6) G. Vavon and V. M. Mitchovitch, *Bull. soc. chim.*, [4] **45**, 961 (1929).

(7) E. Schreiner, *J. prakt. Chem.*, [2] **81**, 599 (1910).