by these authors, it was found desirable to wash the benzene solution of the crude amide with several times the amount of 5% hydrochloric acid called for by them.

The crude amides were dissolved in hot ethyl or *n*-propyl alcohol, diluted in several instances with water. The solutions were filtered hot after the addition of activated carbon together with kieselguhr, and the filtrates chilled to obtain the recrystallized products. A substantial quantity of a second crop of satisfactory purity was obtained by concentration of the mother liquors from the recrystallization of the derivatives of *p*-bromoaniline and 3-bromo-4-aminotoluene. The melting points reported are the best values obtained after recrystallization from a variety of solvents.

The derivatives and their properties are listed in Table I. All melting points are corrected.

De Paul University
Chicago, Illinois
Malcolm F. Dull[2]
William J. Byer[3]

Received December 8, 1947

---

[2] Present address: Department of Chemistry, University of Pittsburgh, Pittsburgh, Pa.

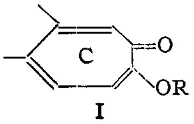
[3] Present address: 1537 Juneway Terrace, Chicago 26, Ill.

COMMUNICATIONS TO THE EDITOR

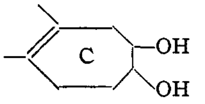
THE STRUCTURE OF RING C OF COLCHICINE[1]

Sir:

It has been suggested,[2] without experimental support, that ring C of colchicine is seven-membered (I, R = CH_3). We have obtained evidence which favors the Dewar and definitely excludes the Windaus[3] formulation.



I

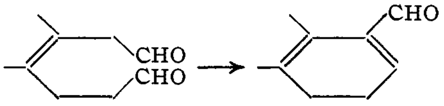


II

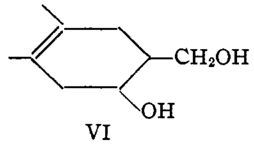
Colchiceine (I, R = H) (m. p. 175.5–176°; calcd. for $C_{21}H_{23}O_6N$: C, 65.45; H, 5.97; N, 3.66. Found: C, 65.65; H, 6.06; N, 3.45; benzoate, m. p. 207–209°, calcd. for $C_{28}H_{27}O_7N$: C, 68.70; H, 5.90; N, 2.86. Found: C, 68.87; H, 5.90; N, 2.78), prepared from purified colchicine,[4] was reduced with Raney nickel in methanol at room temperature and atmospheric pressure for one day, taking up three moles of hydrogen. The product was first crystallized from methanol, yielding about 26% of crude hexahydrocolchiceine[5] (II), m. p. 195.5–197°. Repeated crystallization from methanol–ether afforded the pure compound, m. p. 205.5–206° (calcd. for $C_{21}H_{29}O_6N$: C, 64.39; H, 7.47; N, 3.58. Found: C, 63.68; H, 7.39; N, 3.65; diacetate, m. p. 167°; calcd. for $C_{25}H_{33}O_8N$: C, 63.14; H, 6.99; N, 2.95. Found: C, 63.01; H, 6.83; N, 3.37).

Hexahydrocolchiceine was oxidized with periodic acid in 50% aqueous methanol at *p*H 4. At a lower *p*H side reactions appeared to take place. In a typical experiment hexahydrocolchiceine, m. p. 201–202°, $[\alpha]^{21.5}\text{D} -205 \pm 1°$ (c = 1.544, methanol), $[\alpha]^{19}\text{D} -162 \pm 1°$ (c = 1.436, 50% aqueous methanol) gave an uptake of 0.86 mole periodate after ten minutes, 0.92 mole after ninety minutes, unchanged after eighteen hours. At the end of the reaction, the rotation of the reaction mixture (50% aqueous methanol) had fallen to $[\alpha]^{19}\text{D} -109 \pm 1°$ (c = 1.401). These results indicate the presence of one 1,2-glycol group in hexahydrocolchiceine.

A chloroform extract of the reaction mixture yielded a yellow mobile sirup (III), strong Schiff and Tollens reactions, and reduced Fehling solution. On standing, it slowly lost its aldehydic properties. Efforts to obtain a semicarbazone or dimedone derivative have been unsuccessful, but an alcoholic solution of III with 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid gave amorphous mono-2,4-dinitrophenylhydrazone, m. p. 103–107° (dec.) (after chromatography on alumina) (calcd. for $C_{27}H_{29}O_8N_5$: C, 58.77; H, 5.30; N, 12.7. Found: C, 59.65; H, 5.39; N, 12.84). The oxidation of II presumably gives the dialdehyde (IV) which cyclises spontaneously to the monoaldehyde (V), or the dehydrogenation product from V.



IV V



VI

On the Windaus structure, hexahydrocolchiceine would be a 1,3-glycol (VI) and no oxidation should occur with periodate; the above results are in agreement with (I).

Work is continuing on this and other reduction products of colchicine and its derivatives.

Department of Chemistry
University of Rochester
Rochester, New York
H. R. V. Arnstein
D. S. Tarbell
H. T. Huang
G. P. Scott

Received March 25, 1948

---

[1] Aided by a grant from the National Institute of Health.

[2] Dewar, *Nature*, **155**, 141 (1945).

[3] Windaus, *Ann.*, **439**, 59 (1924).

[4] Ashley and Harris, *J. Chem. Soc.*, 677 (1944).

[5] Bursian, *Ber.*, **71**, 245 (1938).