and melted at 196–197°. Recrystallization from ethanol did not change its melting point. The n.m.r. spectrum in methanol-d_4 consisted of a symmetrical, complex multiplet between 7.75 and 7.00 p.p.m. due to the aromatic protons, a broad concentration-dependent resonance at 3.90 p.p.m. due to the NH proton; and a sharp singlet at 2.58 p.p.m., with Se^{77}–H satellites, due to the methyl protons.

Anal. Calcd. for $C_8H_8N_2Se$: C, 45.5; H, 3.8; N, 13.3; Se, 37.4. Found: C, 45.7; H 3.8; H, 13.2; Se, 37.3.

Se-Methyl-1,3-diphenylpseudoselenourea.—The similar treatment of 0.83 g. (0.003 mole) of 1,3-diphenylselenourea with methyl iodide yielded 0.66 g. (73%) which melted at 92–93°. Recrystallization from ethanol raised the melting point to 94–95°.

Anal. Calcd. for $C_{14}H_{14}N_2Se$: C, 58.1; H, 4.8; N, 9.7; Se, 27.4. Found: C, 58.7; H, 4.8; N, 9.6; Se, 26.9.

The n.m.r. spectrum in $CDCl_3$ consisted of a complex multiplet centered near 7.25 p.p.m. due to the aromatic protons, a very broad, concentration-dependent resonance near 5.6 p.p.m. due to the NH proton, and a sharp singlet at 2.12 p.p.m., with Se^{77}–H satellites, due to the methyl protons.

N-Methylseleno-2-benzimidazolinone.—A solution of 3.4 g. (1.28 ml., 0.02 mole) of carbon diselenide in 150 ml. of carbon tetrachloride was added dropwise over a 2-hr. period with stirring to a refluxing solution of 3.0 g. (0.025 mole) of N-methyl-*o*-phenylenediamine[8] in 150 ml. of carbon tetrachloride. Refluxing was continued for 16 hr. A slow stream of nitrogen was passed through the reaction mixture during the entire period. The mixture was then cooled and filtered to yield 2.1 g. (50%) of product, m.p. 173–174° dec. Recrystallization from ethanol under nitrogen gave fine colorless needles, m.p. 184–185° dec. When mixed with the product from the direct methylation of seleno-2-benzimidazolinone, the melting point was depressed to 166–177° dec.

Anal. Calcd. for $C_8H_8N_2Se$: C, 45.5; H, 3.8; N, 13.3; Se, 37.4. Found: C, 45.6; H, 4.2; N, 13.4; Se, 37.3.

1-Methyl-1,3-diphenylselenourea.—A solution of 1.7 g. (0.64 ml., 0.01 mole) of carbon diselenide in 100 ml. of carbon tetrachloride was added dropwise over a 2-hr. period with stirring to a refluxing solution of 1.1 g. (0.012 mole) of aniline and 44 ml. (0.40 mole) of N-methylaniline in 200 ml. of carbon tetrachloride. Refluxing was continued for an additional 3 hr. A slow stream of nitrogen was passed through the mixture during the entire period. The resulting solution was concentrated at reduced pressure at 50°, treated with 250 ml. of ice-cold 2 *N* hydrochloric acid, and extracted with ether. The ether extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated to a syrup. The syrup was dissolved in 25 ml. of hot carbon tetrachloride and treated with hexane until a slight cloudiness appeared. Cooling to 0° overnight yielded 1.7 g. (59%) of dense pale yellow crystals, m.p. 98–99°. When mixed with the product from the direct methylation of 1,3-diphenylselenourea, the melting point was depressed to 68–78°.

Anal. Calcd. for $C_{14}H_{14}N_2Se$: C, 58.1, H, 4.8; N, 9.7; Se, 27.4. Found: C, 58.1; H, 4.9; N, 9.7; Se, 27.9.

(8) N-Methyl-*o*-phenylenediamine, b.p. 87–87.5° (0.3 mm.), $n^{27}D$ 1.6111, was prepared by the method of H. Irving and O. Weber [*J. Chem. Soc.*, 2296 (1959)]. Its identity was confirmed by n.m.r. analysis.

Synthesis and Absolute Configuration of the Enantiomeric 3-Benzylphthalides

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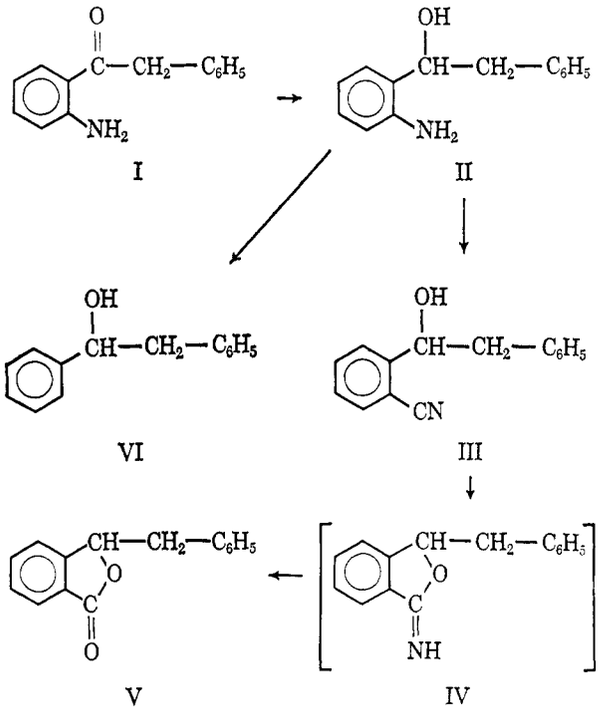
In connection with an investigation of the preparation of optically active bromo lactones by asymmetric bromination of unsaturated acids in the presence of Cinchona alkaloids,[2] we were interested in determining the absolute configuration of 3-benzylphthalide (V). Usual methods of resolution could not be used on V, which lacks basic or acidic groups, nor on the corresponding hydroxy acid, which is stable only as a salt in strongly basic solutions. Optically active V was therefore prepared by the following route. The known ketone I[3] was reduced to the amino alcohol II, which was easily resolved through its salts with (−)-dibenzoyltartaric acid. Diazotization of (−) II, followed by reaction with cyanocuprate (I), gave a crude product with strong —OH and C≡N bands in the infrared, evidently III. Chromatography of crude III over alumina yielded (+)-3-benzylphthalide (V). The ease of cyclization of III to V is not exceptional, as several γ- or δ-hydroxynitriles are known to be transformed into lactones under very mild conditions: thus, for instance, *o*-hydroxy-α-phenylcinnamonitrile gives 3-phenylcoumarin simply on refluxing with water.[4] Such an easy transformation of the nitrile group in III can only be explained with an intramolecular attack by the hydroxyl on the nitrile group to give V, through the imine IV. It is almost certain that the optically active lactone is formed with retention of configuration, as no logical mechanism involving inversion can be hypothesized for such a reaction.



The absolute configuration of (+) II was deduced by transforming it into (+)-1,2-diphenylethanol (VI), through diazotization, followed by reduction with hypophosphorous acid. A large excess of the reducing agent was required, as, otherwise, phenanthrene was formed as the main product by dehydration and Pschorr cyclization. On the basis of the specific rotation of VI, II with $[\alpha]^{20}D$ +30° should have an optical purity of more than 95%. As (+) VI is known to have the (*S*) configuration,[5] the same holds for (+)

(1) Taken in part from the Ph.D. Thesis of N. Macchioni.

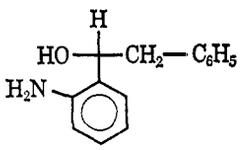
(2) G. Berti and A. Marsili, *Angew. Chem.*, **75**, 1026 (1963); *Chim. Ind.* (Milan), **46**, 312 (1964).

(3) D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 3440 (1953).

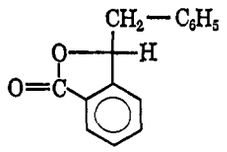
(4) W. Borsche and F. Streitberger, *Ber.*, **37**, 3163 (1904).

(5) G. Berti, F. Bottari, and B. Macchia, *Chim. Ind.* (Milan), **45**, 1527 (1963).

II, which, therefore, corresponds to the Fischer projection VII. Furthermore, if the hypothesis of configurational retention in the transformation of II into V is right, (+) V has the (*R*) configuration (VIII).



VII



VIII

Experimental Section

Melting points were determined on the Kofler apparatus. Specific rotations were determined on a Perkin-Elmer photoelectric polarimeter, Model 141.

1-(*o*-Aminophenyl)-2-phenylethanol (II).—A solution of 5.28 g. (25 mmole) of 2′-amino-2-phenylacetophenone (I)[3] in 100 ml. of methanol was treated slowly, under stirring, with 1.73 g. (32 mmoles) of potassium borohydride in 18 ml. of 0.001 *N* sodium hydroxide. Water was added after 15 hr. and the precipitate was crystallized from hexane, to give 4.90 g. of II, white plates, m.p. 129–130°.

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 79.05; H, 7.04.

Resolution of II.—A solution of 2.13 g. (10 mmoles) of (±) II and 3.76 g. (10 mmoles) of (−)-dibenzoyltartaric acid monohydrate in 25 ml. of ethyl acetate was diluted with 20 ml. of benzene and set aside at 0° for 15 hr. The precipitated salt (2.6 g.) was crystallized from ethyl acetate–benzene to give 1.3 g. of a product, m.p. 108–109° (A), $[\alpha]^{20}D$ −48.5° (*c* 1.1, ethyl acetate).

Anal. Calcd. for $C_{14}H_{15}NO \cdot C_{18}H_{14}O_8$: N, 2.45. Found: N, 2.65.

The combined mother liquors were evaporated almost to dryness *in vacuo* and diluted with benzene, to give 1.6 g. of a salt, m.p. 110–115° (B), $[\alpha]^{20}D$ −85.5° (*c* 0.9, ethyl acetate). A more extensive purification of the diastereoisomeric salts was not convenient, because of their tendency to decompose.

The free bases were obtained from the salts by heating them 15 min. on a steam bath with 2 *N* sodium carbonate. The precipitates were crystallized from chloroform, in which the enantiomeric bases are much less soluble than the racemate, a fact which facilitates the achievement of a high optical purity. The salt A gave 0.3 g. of (*S*) II, m.p. 150–151°, $[\alpha]^{20}D$ +29°. The salt B yielded 0.3 g. of (*R*) II, m.p. 149–150°, $[\alpha]^{20}D$ −28.6°; a second crystallization from chloroform gave a product with m.p. 150–151°, $[\alpha]^{20}D$ −30°, $[\alpha]^{20}_{546}$ −36°, $[\alpha]^{20}_{436}$ −90°, $[\alpha]^{20}_{365}$ −242° (*c* 0.52, chloroform).

Deamination of II.—A solution of 250 mg. (1.17 mmoles) of II, $[\alpha]^{20}D$ +29°, in 1.5 ml. of 2 *N* hydrochloric acid was cooled at 0° and treated dropwise with 82 mg. (1.18 mmoles) of sodium nitrite in 0.5 ml. of water. After 20 min. at 0°, 1.6 ml. of 50% hypophosphorous acid was added, the solution was left 15 min. at 0° and 4 hr. at room temperature and then extracted with ether, and the ether layer was washed with 2 *N* sodium hydroxide, dried over magnesium sulfate, and evaporated. The residue was taken up in petroleum ether (b.p. 30–50°) and chromatographed over neutral alumina (activity II). Petroleum ether eluted 25 mg. of phenanthrene, m.p. 98–99°; ethyl ether eluted 75 mg. of 1,2-diphenylethanol (VI), m.p. 64–65°, $[\alpha]^{20}D$ + 53.0° (*c* 0.9, ethanol), optical purity about 95%, whose infrared spectrum was identical with that of an authentic sample.[5] When the reduction of the diazo compound was carried out with 1 g. of sodium hypophosphite in 8 ml. of concentrated hydrochloric acid, phenanthrene was the main product, while only a very small amount of VI was isolated.

(+)-(*R*)-3-Benzylphthalide (VIII).—A solution of 300 mg. (1.4 mmoles) of II, $[\alpha]^{20}D$ −28.6°, in 1.4 ml. of 2 *N* hydrochloric acid was diazotized with 98 mg. (1.4 mmoles) of sodium nitrite at 0°, then brought to pH 6.5 with sodium bicarbonate, poured into a solution prepared from 250 mg. of potassium cyanide and 170 mg. of cuprous cyanide in 4 ml. of water, heated 1 hr. at 50°, and then extracted with ether. The ether layer was washed with 2 *N* sodium hydroxide, dried over magnesium sulfate, and evaporated. The viscous red residue could not be purified; it showed strong infrared bands at 2.95 (OH) and 4.50 μ (CN), but no carbonyl bands. It was taken up in benzene and passed through a column of neutral alumina (activity II). Elution with benzene gave 100 mg. of a colorless solid, which was crystallized from hexane to give 3-benzylphthalide, m.p. 93–95°, $[\alpha]^{20}D$ +53°, $[\alpha]^{20}_{546}$ +58°, $[\alpha]^{20}_{436}$ +93°. The infrared spectrum showed slight differences from that of racemic V in Nujol mull, but not in chloroform solution.

Acknowledgment.—This work was supported by a grant from the Consiglio Nazionale delle Ricerche.

Buxus Alkaloids. X.[1] The Isolation and Constitution of Cyclovirobuxeine-B[2]

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The elucidation of the structure[3] and configuration[4] of cyclobuxine-D (I), an alkaloid isolated from *Buxus sempervirens* L.,[5] was first reported in 1962. Cyclobuxine-D was shown to be the prototype of a new class of steroidal alkaloids which contain a cyclopropane ring and which have a substitution pattern at C-4 and C-14 which is intermediate in the biogenetic scheme, between lanosterol- and cholesterol-type steroids. Subsequent studies have characterized the following structurally related alkaloids: cyclomicrophylline-A (II, $R^1 = R^2 = CH_3$)[6]; cyclomicrophylline-B (II, $R^1 = CH_3$; $R^2 = H$)[6,7]; cyclomicrophylline-C (II, $R^1 = H$; $R^2 = CH_3$)[6]; cyclobuxamine-H (III, $R^1 = R^2 = R^3 = R^4 = H$)[8]; cyclovirobuxine-D (III, $R^1 = R^4 = CH_3$; $R^2 = R^3 = H$)[9]; cycloprotobuxine-C (IV, $R^1 = H$; $R^2 = CH_3$)[10,11]; cycloprotobuxine-D (IV, $R^1 = R^2 = H$)[12]; cycloprotobuxine-A (IV, $R^1 = R^2 = CH_3$)[7]; baleabuxine[7]; and cyclobuxoxine.[1] In addition, several new alkaloids containing a novel 9(10→19)abeo steroidal diene system[13,14] and irehine (20α-dimethylamino-Δ⁵-pregnen-3β-ol)[15] have recently been isolated from *Buxus sempervirens* L. The isolation from *Buxus sempervirens* L. and elucidation of the structure of an additional new alkaloid, cyclovirobuxeine-B (V), is described in the present report.

Cyclovirobuxeine-B was isolated from the "moderate bases" obtained by the fractionation procedure de-

(1) Part IX: S. M. Kupchan and E. Abushanab, *J. Org. Chem.*, **30**, 3931 (1965).

(2) This investigation was supported in part by research grants from the National Institutes of Health (HE-02952 and HE-02275).

(3) (a) K. S. Brown, Jr., and S. M. Kupchan, *J. Am. Chem. Soc.*, **84**, 4590 (1962); (b) *ibid.*, **86**, 4414 (1964).

(4) K. S. Brown, Jr., and S. M. Kupchan, *ibid.*, **84**, 4592 (1962); **86**, 4424 (1964).

(5) K. Heusler and E. Schlittler, *Helv. Chim. Acta*, **32**, 2226 (1949).

(6) T. Nakano and S. Terao, *Tetrahedron Letters*, 1035, 1045 (1964).

(7) D. Herlem-Gaulier, F. Khuong-Huu-Lainé, E. Stanislas, and R. Goutarel, *Bull. soc. chim. France*, 657 (1965).

(8) K. S. Brown, Jr., and S. M. Kupchan, *J. Am. Chem. Soc.*, **86**, 4430 (1964).

(9) K. S. Brown, Jr., and S. M. Kupchan, *Tetrahedron Letters*, 2895 (1964). The convention on use of letter suffixes to designate substitution pattern at C-3 and C-20 nitrogen functions is described in this reference.

(10) J. P. Calame and D. Arigoni, *Chimia* (Aarau), **18**, 185 (1964).

(11) T. Nakano and M. Hasegawa, *Tetrahedron Letters*, 3679 (1964).

(12) S. M. Kupchan and E. Kurosawa, *J. Org. Chem.*, **30**, 2046 (1965).

(13) S. M. Kupchan and W. L. Asbun, *Tetrahedron Letters*, 3145 (1964).

(14) D. Stauffacher, *Helv. Chim. Acta*, **47**, 968 (1964).

(15) Z. Voticky and J. Tomko, *Collection Czech. Chem. Comm.*, **30**, 348 (1965).