# A New Synthesis of Rosoxides. *cis*- and *trans*-2-(2-Methyl-1-propen-1-yl)-4-methyltetrahydropyran

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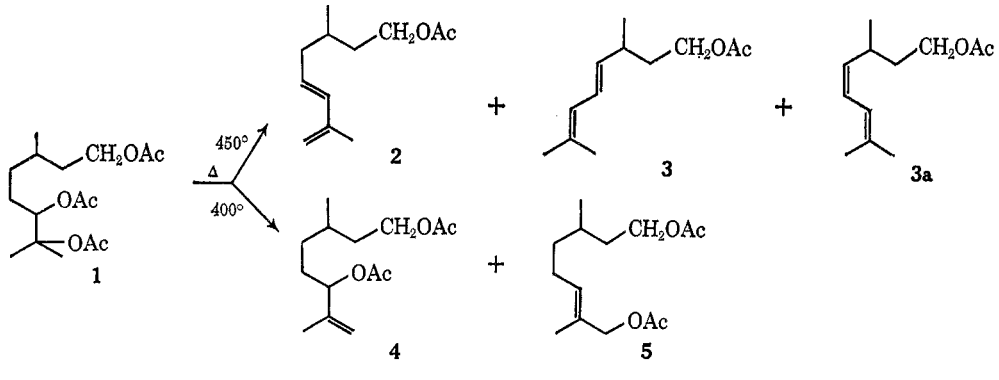
Pyrolysis of 2,6-dimethyl-2,3,8-triacetoxyoctane (**1**) at *ca.* 450° affords mainly *trans*-2,6-dimethyl-1,3-octadien-8-yl acetate (**2**), minor amounts of *trans* and *cis* isomers **3** and **3a**, respectively, an intermediate 2,6-dimethyl-3,8-diacetoxy-1-octene (**4**), and its allylomer **5**. In the presence of acids and acid salts, the pyrolysis favors the formation of **3** and **3a** over **2**. Rosoxide, *cis*- and *trans*-2-(2-methyl-1-propen-1-yl)-4-methyltetrahydropyran (**6** and **6a**), is obtained, in almost quantitative yield, through the facile acid cyclization of *trans*-2,6-dimethyl-1,3-octadien-8-ol (**8**) derived from **2**. On the other hand, the acid cyclization of *trans*- and *cis*-isomeric alcohols **9** and **9a**, derived from **3** and **3a**, is more difficult and affords, in addition to rosoxides **6** and **6a**, substantial amounts of their terminal methylene isomers **7** and **7a** as well as hydroxyrosoxides **10** and **10a**.

Rosoxide, *cis*- and *trans*-2-(2-methyl-1-propen-1-yl)-4-methyltetrahydropyran (**6** and **6a**), a minor but important olfactive ingredient of rose otto and geranium oil,[2] has been synthesized by various methods[3] difficult to scale up.

We would like to report a practical and economic synthesis of a key intermediate in the synthesis of rosoxides **6** and **6a**, namely, *trans*-2,6-dimethyl-1,3-octadien-8-yl acetate (**2**), which was reported earlier in impure state through a difficult synthetic route.[2]

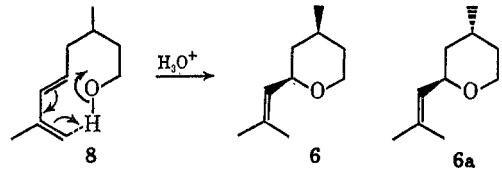
When 2,6-dimethyl-2,3,8-triacetoxyoctane (**1**) is pyrolyzed at *ca.* 450–475°, a mixture is obtained consisting of *ca.* 70–75% *trans*-2,6-dimethyl-1,3-octadien-8-yl acetate (**2**), 8–10% *trans*- and *cis*-2,6-dimethyl-2,4-octadien-8-yl acetate (**3** and **3a**), and 15–20% a mixture of 2,6-dimethyl-3,8-diacetoxy-1-octane (**4**) and its allylomer 2,6-dimethyl-1,8-diacetoxy-2-octene (**5**). Both **4** and **5** are eventually converted into **2** upon recycling. The overall yield of **2** from either **1** or **4** is *ca.* 75%.




It is noteworthy that the pyrolysis of **1** and **4** affords mainly *trans*-2,6-dimethyl-1,3-octadien-8-yl acetate (**2**) as the main component (the presence of the *cis* isomer **2a** could not be ascertained by vpc on a CW 20M column) and only minor amounts of *trans*- and *cis*-2,6-dimethyl-2,4-octadien-8-yl acetate (**3** and **3a**). However, in the presence of $KHSO_4$ or *p*-toluenesulfonic acid, **3** and **3a** are the major products of the pyrolysis. Oxalic acid, on the other hand, affords mainly **2**. The intermediate, 2,6-dimethyl-3,8-diacetoxy-1-octene (**4**), which becomes the major reaction product of the pyrolysis of **1** at *ca.* 400°, pyrolyzes further at higher temperatures (450–475°) to yield a pyrolysate identical with that of **1**.

Table I gives the data of the pyrolysis of both **1** (with or without catalysts) and **4**.

In the presence of strong mineral acids at room tem, perature, *trans*-2,6-dimethyl-1,3-octadien-8-ol (**8**), obtained from the corresponding acetate **2**, readily cyclizes-in almost quantitative yield, into a 9:1 mixture of isomeric rosoxides **6** and **6a**.




However, the cyclization of *trans*-2,6-dimethyl-2,4-octadien-8-ol (**9**), derived from **3**, requires more drastic conditions and affords substantial amounts of the terminal methylene rosoxide isomers, *cis*- and *trans*-2-(2-methyl-2-propen-1-yl)-4-methyltetrahydropyran (**7** and **7a**, respectively),[4] together with some *cis*- and *trans*-2-(2-methyl-2-hydroxyprop-1-yl)-4-methyltetra-

(1) Presented at the 153rd National Meeting of the American Chemical Society, Miami, Fla., April 1967, Division of Cellulose, Wood, and Fiber Chemistry, Lecture 28.

(2) (a) C. F. Seidel, *et al.*, *Helv. Chim. Acta*, **42**, 1830 (1959); (b) U. S. Patent 3,161, 657 (1964); (c) Y. R. Naves, *et al.*, *Bull Soc. Chim. Fr.*, 645 (1961).

(3) U. S. Patent 3,161,657 (1964); G. Ohloff, *et al.*, *Angew. Chem.*, 578 (1961); German Patent 1,137,730 (1962); British Patent 1,010,056 (1956); French Patent 1,319,202 (1963); *Helv. Chim. Acta*, **48**, 182 (1965); A. Malera and Y. R. Naves, *Comp. Rend.*, **252**, 1937 (1961); Y. R. Naves and P. Ochsner, *Helv. Chim. Acta*, **45**, 397 (1962); U. S. Patent 3,166,575 (1965); French Patent 1,312,034 (1962); U. S. Patent 3,163,658 (1964); U. S. Patent 3,166,576 (1965); M. Julia and B. Jacquet, *Bull. Soc. Chim. Fr.*, 1983 (1963); French Patent 1,539,094 (1967). The list of patents is only partial and keeps on growing.

(4) See Naves and Ochsner.[3]

TABLE I

| Starting material | Catalyst | Temp of pyrolysis, °C | Time, min | Rate of pyrolysis, ml/min | Yield[a] of 3a + 2 + 3, % | Isomeric distribution[b] 3a | 2 | 3 | Recovered intermediate, % 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1% $KHSO_4$ | 260–280 | 10 | Batchwise | 50 | 16 | 27 | 57 | 35 | 4 |
| 1 | 1% *p*-toluenesulfonic acid | 170–200 | 30 | Batchwise | 50 | 18 | 11 | 64 | 7 | 10 |
| 1 | 1% oxalic acid | 280–330 | 70 | Batchwise | 50 | 5 | 75 | 20 | 14 | 25 |
| 1 | None[c] | 475 | ... | 10 | 75 | 5 | 88 | 7 | 17 | 18 |
| 4 | None[c] | 475 | ... | 15 | 77 | 6 | 86 | 8 | 4 | 12 |

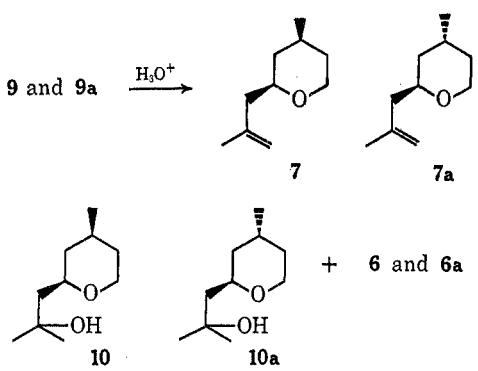
[a] Yield based on amount of consumed starting material (1 or 4) minus recovered intermediates 4 and 5. [b] Determined by vpc on a CW 20M 0.25-in. column at 200°. [c] Pyrolysis in a stainless steel, 15 ft × 0.25 in. tube coiled in 80 spirals, 22-mm o.d., capacity 52 ml, packed into a 4-ft upright furnace.

TABLE II

ACID CYCLIZATION OF 8, 9, AND 9a TO ROSOXIDE AND DERIVATIVES

| Starting material (1 part) | Catalyst (2 parts) | Solvent | Temp, °C | Time, min | Reaction product, % 7, 7a | 6, 6a | 10, 10a | Unreacted material, % 8 | 9 | 9a |
|---|---|---|---|---|---|---|---|---|---|---|
| 8 | 2.5% $H_2SO_4$ | $H_2O$ | 100 | 90 | 4 | 87 | 9 | >10 | | |
| 8 | 10% $H_2SO_4$ | $H_2O$ | 100 | 120 | 14 | 73 | 13 | >10 | | |
| 8 | 20% $H_2SO_4$ | $H_2O$ | 25 | 600 | ... | 99 | 1 | >10 | | |
| 8 | 30% $H_2SO_4$ | $H_2O$ | 25 | 60 | ... | 100 | ... | >5 | | |
| 8 | 50% $H_2SO_4$ | $H_2O$ | 25 | 150 | 4 | 70 | 26 | >10 | | |
| 8 | 50% $H_2SO_4$ | $H_2O$ | 25 | 250 | 5 | 11 | 84 | >10 | | |
| 8 | 62% $H_2SO_4$ | $H_2O$ | 25 | 1 | 1 | 2 | 97 | >50 | | |
| 8 | 42% $H_3PO_4$ | $H_2O$ | 25 | 360 | ... | 99 | 1 | ... | | |
| 9 | 30% $H_2SO_4$ | $H_2O$ | 25 | 1680 | 4 | 96 | ... | ... | 76 | |
| 9 | 35% $H_2SO_4$ | $H_2O$ | 25 | 240 | 30 | 59 | 11 | 10 | 12 | |
| 9 | 35% $H_2SO_4$ | $H_2O$ | 25 | 480 | 2 | 8 | 90 | ... | ... | |
| 9 | 45% $H_2SO_4$ | $H_2O$ | 25 | 120 | 22 | 78 | ... | ... | 54 | |
| 9 | 45% $H_2SO_4$ | $H_2O$ | 25 | 960 | 25 | 75 | ... | ... | 40 | |
| 9 | 45% $H_2SO_4$ | $H_2O$ | 100 | 10 | 4 | 15 | 81 | ... | ... | |
| 9 | 62% $H_2SO_4$ | $H_2O$ | 25 | 5 | ... | ... | 100 | ... | >5 | |
| 9 | 1.5% *p*-Tos | Benzene | 82 | 840 | 27 | ... | 73 | ... | 15 | |
| 9a | 30% $H_2SO_4$ | $H_2O$ | 25 | 1320 | 2 | 98 | ... | ... | 54 | |

hydropyran (**10** and **10a**) and only minor amounts of rosoxides **6** and **6a**.




Both the hydration with strong mineral acids of **7** and **7a** to **10** and **10a** and, in particular, their hydrogenation, with Pd–C, to dihydrorosoxides [*cis*- and *trans*-2-(2-methyl-prop-1-yl)-4-methyltetrahydropyran] proceed at a faster rate than with their isomeric rosoxides **6** and **6a**.

Table II shows the progress of acid cyclization of **8**, **9**, and **9a** under various conditions to yield isomeric rosoxides **6** and **6a** and **7** and **7a**, and hydroxyrosoxides **10** and **10a**. In most of the cases the *cis*- and *trans*-isomeric ratio was about 9:1 (vpc on CW 20M column).

## Experimental Section

**2,6-Dimethyl-3,8-diacetoxy-1-octene (4) and 2,6-Dimethyl-2,3,8-triacetoxyoctane (1).**—Citronellyl acetate (60 g) in 40% formic acid (21 g) was hydroxylated by adding at 75–80°, within 0.5 hr, 30% $H_2O_2$ (37 g); the reaction was complete after 3–4 hr (vpc, SE-30, 225°). The reaction mixture was mixed with water (50 ml) and extracted with benzene (30 ml), and, after evaporation of the solvent, the residue (63 g) of 95% pure 2,6-dimethyl-2,3-dihydroxyoctan-8-yl acetate was acetylated with acetic anhydride (110 g) under reflux for 3–4 hr (140–142°).

Upon fractionation through a 1-ft Goodloe column, the following cuts were obtained: (1) (70 g), bp 80° (2 mm); (2) 2,6-dimethyl-3,8-diacetoxy-1-octene (**4**, 6 g, 96% pure), bp 110–115° (2 mm), $n^{20}D$ 1.4460, sapon equiv 413 (theory 432); (3) 2,6-dimethyl-2,3,8-triacetoxyoctane (**1**, 70 g, 95% pure), bp 140–145° (2 mm), $n^{20}D$ 1.4440, sapon equiv 509 (theory 530).

**Pyrolysis of 1.**—Triacetate **1** (275 g) was pyrolyzed at 10 ml/min at 475° in the apparatus described in Table I. After washing with water, neutralization, and distillation as described in the previous example, the following cuts (Table III) were obtained (vpc, 20M, 0.25-in. column, 200°).

TABLE III

| Cut | Bp, °C (mm) | Yield, g | $n^{20}D$ | Components, % X[a] | 3a | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 80 (2) | 2 | 1.4690 | 80 | 20[b] | | | | |
| 2 | 100 (2) | 90 | 1.4665 | 5 | 88 | 7 | | | |
| 3 | 120 (2) | 92 | 1.4520 | | | | 10[b] | 35 | 45 |

[a] Mostly hydrocarbons. [b] Includes **2**, **3**, and **3a**.

**Pyrolysis of 4.**—Diacetate **4** (100 g) was pyrolyzed at a rate of 15 ml/min at 475° in the apparatus described in Table I. The pyrolysate was treated as in **1**, giving the cuts below (Table IV).

***trans*-2,6-Dimethyl-1,3-octadien-8-yl Acetate (2) and *trans*-2,6-Dimethyl-1,3-octadien-8-ol (8).**[3]—Cut 2 (100 g) obtained in the two previous examples from the pyrolysis of **1** and **4** afforded, upon distillation through a 2-ft Goodloe column, 80 g of a main cut of *trans*-2,6-dimethyl-1,3-octadien-8-yl acetate (**2**): 98% pure (vpc, SE-30, 220°); bp 80–83° (3 mm); $n^{20}D$ 1.4680; sapon equiv 284 (theory 285.7); uv $\lambda_{max}$ 230 mμ (ε 33,800) and

TABLE IV

| Cut | Bp, °C (mm) | Yield, g | $n^{20}D$ | Components, % X[a] | 3a | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 80 (2) | 30 | 1.4570 | 80 | | 20[b] | | | |
| 2 | 100 (2) | 500 | 1.4650 | | 6 | 86 | 8 | | |
| 3 | 120 (2) | 205 | 1.4525 | | | 15[b] | | 30 | 55 |

[a] Mostly hydrocarbons. [b] Includes **2**, **3**, and **3a**.

237 (23,100) [lit.[2a] $\lambda_{max}$ 231.5 mμ (10,700) and 235 (8500)]; ir 6.2 and 11.35 (terminal $=CH_2$) and 10.34 μ (*trans* band).

The nmr spectrum follows: H at $C_3$, d, δ 6.25, $J_{3,4}$ = 15 Hz (*trans*); H at $C_4$, d of t, δ 5.65; 2 H of $CH_2=$, s, δ 4.9; 2 H of $OCH_2$, t, δ 4.16, $J$ = 7 Hz; 3 H of OAc, s, δ 2.02; 3 H of $CH_3C=$, s, δ 1.84; 3 H of $CH_3CH<$, d, δ 0.9, $J$ = 5 Hz.

The compound had a pleasant, fruity, pearlike odor. Upon hydrogenation of a sample in the presence of 5% Pd-C catalyst, it was converted into 2,6-dimethyl-8-octanyl acetate and was identified with an authentic sample by ir. Saponification of **2** with a 10% KOH alcoholic solution afforded *trans*-2,6-dimethyl-1,3-octadien-8-ol (**8**) in 95% yield. Distillation gave a main cut: bp 100° (4 mm); $n^{20}D$ 1.4860; purity 98% (vpc, SE-30, 0.25 in. × 6-ft column at 200°), uv $\lambda_{max}$ 230 mμ (ε 25,810), 237, (9700); ir 6.2 and 11.4 ($=CH_2$) and 10.4 μ (*trans* band).

The nmr spectrum follows: H at $C_3$, d, δ 6.25, $J_{3,4}$ = 15 Hz (*trans*); H at $C_4$ m, δ 5.68; 2 H of $CH_2=$, s, δ 4.86; 2 H of $OCH_2$, t, δ 3.7, $J$ = 6 Hz; 3 H of $CH_3C=$, s, δ 1.83; 3 H of $CH_3CH<$, d, δ 0.91, $J$ = 5 Hz.

The ε values reported by Seidel, *et al.*[2a] were substantially lower, indicating a product of lesser purity.

*Anal.* Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.63; H, 11.59.

**2,6-Dimethyl-1,8-diacetoxy-2-octene (5) and 2,6-Dimethyl-1,8-dihydroxy-2-octene.**—Cut 3 (100 g) from the previous distillations of the pyrolyzates of **1** and **4** was redistilled through a 1-ft Goodloe column and gave, after removal of **4**, bp 110–115° (2 mm), $n^{20}D$ 1.4462, a main cut (50 g), bp 125–130° (2 mm), $n^{20}D$ 1.4530, of a 12:88 *cis* and *trans* isomer mixture (vpc, SE-30, 200°) of 2,6-dimethyl-1,8-diacetoxy-2-octene (**5**), sapon equiv 430 (theory 440 for $C_{14}H_{24}O_4$, mol wt 256). The mass spectrum showed a weak peak at *m/e* 256 and a strong one at *m/e* 214 representing a loss of ketene to yield 2,6-dimethyl-1-hydroxy-8-acetoxyoctane.

The nmr spectrum follows: H at $C_3$, t, δ 5.27, $J$ = 7 Hz; 2 H of $CH_2O$, s (minor, 15%); δ 4.51, s (major, 85%); δ 4.38 (*cis* and *trans* isomers of OAc at $C_1$); 6 H of 2OAc, 2 s, δ 1.99 and 2.02; 3 H of $CH_3C=$, s, δ 1.63; 3 H of $CH_3CH$, d, δ 0.93, $J$ = 4 Hz.

Upon saponification with 50% methanolic KOH, the compound yielded the corresponding glycol, bp 110–115° (2–3 mm), $n^{20}D$ 1.4780, as a mixture of *cis* and *trans* isomers of 2,6-dimethyl-1,8-dihydroxy-2-octene ($C_{10}H_{20}O_2$), mol wt 172.

The nmr spectrum follows: H at $C_3$, t, δ 5.32, $J$ = 7 Hz (major isomer, 85%); t, δ 5.17, $J$ = 7 Hz (minor isomer, 15%) (*cis* and *trans* isomer of OH at $C_1$); 2 H of $CH_2OH$, s, δ 3.88, with minor impurity, d, δ 4.02, $J$ = 5 Hz; 2 H of $CH_2OH$, t, δ 3.56, $J$ = 6 Hz; 2 H of OH, s, δ 3.07; 2 H of $CH_2CH_2OH$, m, δ 2.01; 3 H of $CH_3C=$, s, δ 1.51; 3 H of $CH_3CH<$, d, δ 0.87, $J$ = 6 Hz.

**Pyrolysis with $KHSO_4$. Preparation of 3, 3a, 9, and 9a.**—Triacetate **1** (46 g) and $KHSO_4$ (0.5 g) were heated in a modified Claisen–Vigreux flask at 250–270° and kept at this temperature for 5–8 min while 7 g of acetic acid distilled at 100–130°. The pot temperature was then raised to 310° and the distillate was collected at 250–260°. The crude distillate (35 g) was washed with water (2 volumes) and neutralized with 10% soda ash. It afforded upon redistillation the following cuts (Table V) (vpc, CW 20M, 200°).

TABLE V

| Cut | Bp, °C (mm) | Yield, g | $n^{20}D$ | Components, % 3a | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|
| 1 | 100 (2) | 16.5 | 1.4600 | 18 | 11 | 64 | | |
| 2 | 140 (2) | 12.0 | 1.4500 | | | | 90 | 10 |
| 3 | 160 (2) | 2.0 | 1.4600 | | | | 50 | 50 |

Both *cis*-2,6-dimethyl-2,4-octadien-8-yl acetate (**3a**) and *trans*-2,6-dimethyl-2,4-octadien-8-yl acetate (**3**) were obtained by redistillation of cut 1 through a 2-ft Goodloe column. The pure products had the constants given below.

***trans*-2,6-Dimethyl-2,4-octadien-8-yl acetate (3)** gave the following data: bp 94° (3 mm); $n^{20}D$ 1.4755; sapon equiv 282 (theory 285.7); ir 10.45 μ (*trans* band); uv $\lambda_{max}$ 237 mμ (ε 29,400) and 230 (27,050). Hydrogenation over Pd–C afforded 2,6-dimethyloctan-8-yl acetate.

The nmr spectrum follows: 3 H for H at $C_3$, H at $C_4$, and H at $C_5$, m, H at $C_4$, δ 6.27; H at $C_3$, δ 5.75; H at $C_5$, δ 5.4, $J_3$ = 1.2 Hz, $[(CH_3)_2C<]$, $J_{4,5}$ = 15 Hz (*trans*), $J_{3,4}$ = 10 Hz, $J_{5,6}$ = 8 Hz; 2 H of $OCH_2$, t, δ 4.1, $J$ = 6 Hz; 3 H of OAc, s, δ 2.21; 6 H of $(CH_3)_2CH$, d, δ 1.75, $J$ = 7 Hz; 3 H of $CH_3CH$, d, $J$ = 7 Hz.

***trans*-2,6-Dimethyl-2,4-octadien-8-ol (9)** was obtained by saponification of **3**: bp 100° (3 mm); $n^{20}D$ 1.4960; lemon, rosy odor; ir 10.45 μ (*trans* band); uv $\lambda_{max}$ 237 mμ (ε 29,000) and 230 (27,335).

The nmr spectrum follows: 3 H for H at $C_3$, H at $C_4$, and H at $C_5$, m, H at $C_4$, δ 6.26, H at $C_3$, δ 5.75, H at $C_5$, δ 5.42, $J_{4,5}$ = 15 Hz (*trans*), $J_{5,6}$ = 8 Hz, $J_{3,4}$ = 10 Hz; 2 H for $CH_2O$, t, δ 3.62, $J$ = 6 Hz, H at $C_6$, δ 2.34, m, covered by OH proton; 6 H of $(CH_3)_2C<$, s, δ 1.75; 3 H of $CH_3CH$, d, δ 1.02, $J$ = 7 Hz.

*Anal.* Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.89; H, 11.85.

***cis*-2,6-Dimethyl-2,4-octadien-8-yl acetate (3a)** gave the following data: bp 84° (3 mm); $n^{20}D$ 1.4755 (90% pure); ir 13.25 μ (*cis* band); uv $\lambda_{max}$ 237 mμ (ε 27,400). Hydrogenation over Pd–C yielded 2,6-dimethyloctan-8-yl acetate, identified with an authentic sample by infrared analysis.

The nmr spectrum follows: 2 H for H at $C_3$ and H at $C_4$, d, δ 6.15, $J_{3,4} \cong 8$ Hz; H at $C_4$, t, δ 5.12, $J \cong 9$ Hz, $J_{3,5} + J_{4,5} \cong 8$ Hz, $J_{4,5}$ = 5.5–11.5 Hz (*cis*), H at $C_3$ and H at $C_4$ are almost magnetically equivalent; 2 H of $CH_2O$, t, δ 4.05, $J$ = 6 Hz; 3 H of OAc, s, δ 2.04; 6 H of $(CH_3)_2C<$, 2 s, δ 1.75 and 1.81; 3 H of $CH_3CH$, d, δ 1, $J$ = 7 Hz.

***cis*-2,6-Dimethyl-2,4-octadien-8-ol (9a)** was obtained from saponification of **3a**: bp 90–95° (3 mm); $n^{20}D$ 1.4940; green, rosy odor; ir 13.95 μ (*cis* band); uv $\lambda_{max}$ 237 mu (ε 26,650).

The nmr spectrum follows: 2 H for H at $C_3$ and H at $C_4$, d, δ 5.95, $J \cong 8$ Hz; H at $C_5$, m, δ 5, 2 H for $CH_2O$, t, δ 3.5, $J$ = 6 Hz; 1 H for OH, s, δ 3.25; 6 H for $(CH_3)_2C<$, 2, s, δ 1.73 and 1.77; 3 H for $CH_3CH$, d, δ 1, $J$ = 7 Hz.

Hydrogenation over Pd–C afforded 2,6-dimethyloctan-8-ol, with which it was identified by ir with an authentic sample.

*Anal.* Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.75; H, 11.65.

**Pyrolysis with Oxalic Acid.**—Triacetate **1** (35 g) and oxalic acid (0.35 g) were heated in a modified Claisen–Vigreux flask at 280–300° for 30 min while acetic acid was collected (*ca.* 12 g). The residue was then distilled under vacuum, yielding the following cuts (Table VI) (vpc, 20M, 200°).

TABLE VI

| Cut | Bp,° C (mm) | Yield, g | $n^{20}D$ | Components, % 3a | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|
| 1 | 110(3) | 10 | 1.4570 | 5 | 75 | 20 | | |
| 2 | 130(3) | 13.5 | 1.4520 | | | | 40 | 60 |

**Pyrolysis with *p*-Toluenesulfonic Acid.**—Triacetate **1** (50 g) and *p*-toluenesulfonic acid (0.5 g) were heated in a modified Claisen–Vigreux flask at 165–190° (20 mm). The distillate, which collected at 100–150° within 0.5 hr, was washed with 2 volumes of water and neutralized with 10% soda ash. It amounted to 29 g, $n^{20}D$ 1.4670, which, upon distillation, yielded the following cuts (Table VII), (vpc, 20M, 200°).

TABLE VII

| Cut | Bp, °C (mm) | Yield, g | $n^{20}D$ | Components, % X[a] | 3a | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 86 (2) | 1 | 1.4857 | 80 | | 20[b] | | | |
| 2 | 100 (2) | 1.8 | 1.4720 | | 18 | 11 | 64 | | |
| 3 | 110 (2) | 2 | 1.4620 | | | 20[b] | | 35 | 45 |
| 4 | 135 (2) | 6 | 1.4480 | | | | | 40 | 60 |

[a] Mostly hydrocarbons. [b] Includes **2**, **3**, and **3a**.

**Cyclization of 8.**—*trans*-2,6-Dimethyl-1,3-octadien-8-ol (**8**, 100 g) and 30% $H_2SO_4$ (100 ml) were agitated under a $N_2$ atmosphere for 1.5 hr at room temperature (20–30°) until a sample of the reaction mixture showed the disappearance of the starting ma-

terial (vpc, SE-30, 200°). Upon distillation, a main cut, 94 g, bp 77° (15 mm), $n^{20}$D 1.4545, of a 91:9 isomeric mixture of **6** and **6a** (vpc, 20M, 90°) was obtained.

**Cyclization of 9.**—*trans*-2,6-Dimethyl-2,4-octadien-8-ol (**9**, 16 g), benzene (32 ml), and *p*-toluenesulfonic acid (0.5 g) were refluxed for 14 hr; upon neutralization and evaporation of the solvent, 13 g were obtained, $n^{20}$D 1.4620, showing the following composition: 23% **7** and **7a**; 53% **6**; 9% **6a**; and 15% unreacted **9**.

**Cyclization of 9a.**—*cis*-2,6-Dimethyl-2,4-octadien-8-ol (**9a**, 15 g) and 30% $H_2SO_4$ (15 ml) were vigorously agitated at room temperature (20–30°) for 22 hr. The reaction mixture, after neutralization, afforded 14 g, which showed the following composition (vpc, 20M, 90°): 1% **7** and **7a**; 39% **6**; 6% **6a**; and 54% unreacted **9a**.

***cis* and *trans*-2-(2-Methyl-2-hydroxyprop-1-yl)-4-methyltetrahydropyran (10 and 10a).**—*trans*-2,6-Dimethyl-2,4-octadien-8-ol (**9**, 100 g) was fed within 5 min, under cooling at 0–10°, into 62.5% $H_2SO_4$ (100 ml); the temperature was left to reach 20–25° within 5 min. The reaction product was then poured onto 30% NaOH (200 ml) under cooling (30–40°), and the top layer separated; it afforded, upon distillation, 75 g of a main cut, bp 75–80° (2 mm), $n^{20}$D 1.4480, of a 95:5 *cis–trans* mixture of hydroxyrosoxide (**10** and **10a**) (vpc, SE-30, 190°).

**Conversion of 10 into a Mixture of Rosoxides 6 and 6a.**—Hydroxyrosoxide **10** (100 g), benzene (400 ml), and concentrated $H_2SO_4$ (4 g) were heated under reflux for 1 hr (80–82°) while water was azeotroped off in a Dean–Stark trap. The mixture, after neutralization and distillation, afforded 70 g, $n^{20}$D 1.4550, consisting of 30% **7**, 2% **7a**, 64% **6**, and 4% **6a** (vpc, CW 20M, 90°); *cf.* ref 4.

***cis*-Rosoxide** [*cis*-2-(2-methyl-1-propen-1-yl)-4-methyltetrahydropyran, **6**], separated by distillation through a Nester–Faust Teflon spinning-band column, gave the following data: bp 86° (20 mm); $n^{20}$D 1.4535.

The nmr spectrum follows: H at $C_1$, d, fine splitting, $\delta$ 5.09, $J$ = 8.5 Hz; H at $C_2$ and H at $C_6$, m, $\delta$ 3.9; H at $C_6$, six-peak m, composed of 3 d, with axial fixed conformation, $\delta$ 3.38, $J_{gem}$ = 12 Hz, $J'$ = 12 Hz, $J''$ = 2.5 Hz; 6 H of $(CH_3)_2C=$, 2 d, $\delta$ 1.68, and 1.65, $J$ = 1 Hz; 3 H of $CH_3CH$, d, $\delta$ 0.90, $J$ = 5 Hz.

***trans*-Rosoxide** [*trans*-2-(2-methyl-1-propen-1-yl)-4-methyltetrahydropyran, **6a**, separated by distillation through a Nester–Faust Teflon spinning-band column, gave the following data: bp 88–89° (20 mm); $n^{20}$D 1.4580.

The nmr spectrum follows: H at $C_1$, d, fine splitting, $\delta$ 5.22, $J$ = 8 Hz; H at $C_2$, six-peak m, composed of 3 d, $\delta$ 4.29, $J$ = 8 Hz, $J'$ = 8 Hz, $J''$ = 4 Hz, 2 H at $C_6$, m, nearly equivalent protons owing to flipping of conformation of *trans* configuration, $\delta$ 3.5–3.8; 6 H of $(CH_3)_2C=$, d, $\delta$ 1.66 and 1.69, $J$ = 1 Hz; 3 H of $CH_3CH$, d, $\delta$ 1.04, $J$ = 6 Hz.

**Registry No.**—**1**, 23062-48-8; **2**, 23102-71-8; **3**, 23042-11-7; **3a**, 23061-96-3; **4**, 23062-49-9; *trans*-**5**, 23061-97-4; **6**, 876-17-5; **6a**, 876-18-6; **8**, 23062-00-2; **9**, 23062-01-3; **9a**, 23062-02-4; **10**, 23062-03-5; **10a**, 23062-04-6; *cis*-2,6-dimethyl-1,8-dihydroxy-2-octene, 23062-05-7; *trans*-2,6-dimethyl-1,8-dihydroxy-2-octene, 23062-07-9; *cis*-**5**, 23062-08-0.

# Cherylline, a 4-Phenyl-1,2,3,4-tetrahydroisoquinoline Alkaloid

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A 4-phenyl-1,2,3,4-tetrahydroisoquinoline alkaloid, cherylline, has been isolated from *Crinum powellii*. The alkaloid has been assigned the structure **12** from spectral, degradative, and synthetic evidence. A facile synthesis of (±)-O,O-dimethyl-N-demethylcherylline (**5**) provided an intermediate capable of resolution. N-Methylation of the *S* enantiomer (**10a**) provided a product, the hydrochloride of which was identical with O,O-dimethylcherylline hydrochloride.

Isolation and separation procedures reported during the past 20 years have provided relatively few phenolic *Amaryllidaceae* alkaloids.[2] We wish to report the isolation and structure of cherylline, a new representative of this rare type of phenolic alkaloid. Cherylline,[3] which is optically active, has been isolated in *ca.* 0.004% yield from the alkali-soluble crude alkaloids of several species of *Crinum*. The nmr spectrum of cherylline in DMSO-$d_6$ exhibits an $A_2B_2$ pattern ($\delta$ 6.91 and 6.64) characteristic of a 1,4-disubstituted aromatic ring, two one-proton singlets ($\delta$ 6.49 and 6.23) indicative of two *para*-oriented protons on a second aromatic ring, and two three-proton singlets at $\delta$ 3.51 ($OCH_3$) and 2.24 ($NCH_3$) in addition to a few less well-defined signals. The ultraviolet spectrum of the compound has maxima at 285 and 280 mμ which undergo a bathochromic shift to 299 mμ upon the addition of base. The mass spectrum and elemental analysis of the alkaloid indicate a molecular weight of 285 and the empirical formula $C_{17}H_{19}NO_3$. These results are consistent with a compound containing two aromatic rings (both phenolic), N-methyl and methoxyl groups, and a $C_3H_5$ fragment. Structure **1** is in agreement with the spectroscopic data. Proof that the alkaloid does contain this skeleton was obtained by converting cherylline into O,O-dimethylcherylline (**1**, $CH_3O$ instead of OH) with diazomethane. This fully methylated derivative exhibited $R_f$ values on silica gel with several different solvent systems that were identical with those found for synthetic (±)-6,7-dimethoxy-4-(4′-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**6**). The ir spectra (KBr) of the hydrochlorides of both compounds were superimposable, thus confirming their chemical identity.[4]

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(2) For a recent review, see W. C. Wildman in "The Alkaloids," Vol. XI, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1968, Chapter 10.

(3) A comparison of cherylline and the phenolic alkaloid (crinin) isolated by H.-G. Boit, *Chem. Ber.*, **87**, 1704 (1954), has been performed by W. Döpke, Humboldt University, Berlin, who found the alkaloids to be identical. It is proposed that "crinin" should be referred to as cherylline to avoid confusion in the literature with crinine, a nonphenolic alkaloid.

(4) It was necessary to run the ir spectra in KBr pellets because of solubility problems. While the ir spectrum of an enantiomer frequently differs from that of the racemate when measured in the solid state, in this case the spectra are fortuitously superimposable and can be used as proof of chemical identity.