

## Essential Oils and Their Constituents XXXI.

### Cyperenone—A New Sesquiterpene Ketone from Oil of *Cyperus scarosius*

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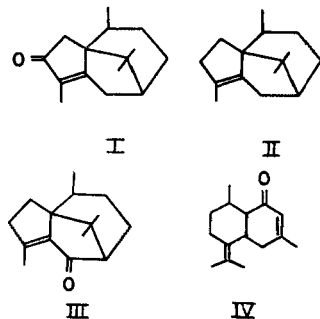
A new sesquiterpene ketone ( $C_{15}H_{22}O$ ; 2,4-dinitrophenylhydrazone, m.p. 227.5°) was isolated from the essential oil of *Cyperus scarosius* R.Br. On hydrogenation it gave a dihydro compound, and on deoxidation it yielded the tricyclic hydrocarbon cyperene. The ketone was synthesized from cyperene by chromic acid oxidation. It is assigned structure I and named cyperenone in view of its relationship to cyperene.

NAVES and Ardizio, in 1954, isolated from the essential oil of *Cyperus scarosius* R.Br. an  $\alpha,\beta$ -unsaturated sesquiterpene ketone, as the 2,4-dinitrophenylhydrazone (DNPH), m.p. 228–229° (1). The author also isolated an  $\alpha,\beta$ -unsaturated ketone from this oil, melting point of DNPH 227.5°. Infrared spectral data proved to be the same for both derivatives (2). Recently Couchman *et al.*, investigating the oil of *C. articulatus* L., reported the occurrence of a ketone (DNPH, m.p. 231–232°), articulone, to which they assigned structure IV. They found its DNPH identical to that prepared by Naves and Ardizio (3). Mixed melting point determination and infrared and X-ray diffraction analyses of these three dinitrophenylhydrazones have now proved them to be identical and therefore derived from the same ketone. This article presents the experimental results that establish the structure of this terpenoid as I. The name cyperenone is proposed for this compound in view of its relationship to cyperene (II) (4).

A pure sample of the substance was prepared by column and gas chromatography of the essential oil. The ketone possessed the molecular formula  $C_{15}H_{22}O$ . Ultraviolet analysis ( $\lambda$  max. 245.5  $\mu$ ,  $\log \epsilon$  3.988) showed the presence of  $\alpha,\beta$ -unsaturation and infrared analysis (strong bands at 1705 and 1665  $cm^{-1}$ ) confirmed this deduction.

Hydrogenation of cyperenone in acetic acid with platinum oxide afforded the dihydro-derivative (2,4-dinitrophenylhydrazone, m.p. 191–192°), indicating the presence of one double bond in the molecule and hence its tricyclic character. Lack of any characteristic infrared absorption in the 700–900  $cm^{-1}$  region suggested the tetrasubstituted nature of the double bond, and the absorption band at 1665  $cm^{-1}$  indicates its  $\alpha$ -position to the carbonyl group (5, 6). The NMR spectrum, which failed to exhibit any peak characteristic of an olefinic proton, further proved this assignment. (See Fig. 1.)

The ketone was converted to the corresponding deoxy compound by refluxing, with Raney nickel, its thioketal obtained by reaction with ethanedithiol and borontrifluoride etherate. Under the conditions



of reaction, the tetrasubstituted double bond remained unaffected and the resulting hydrocarbon was identified as cyperene (II). Cyperenone should, therefore, possess either structure I or III. The latter structure has recently been assigned to patchoulone, a new sesquiterpene ketone from oil of *C. rotundus* L. (5). Gas chromatographic, ultraviolet, and infrared spectral comparison proved that cyperenone and patchoulone were not identical.

Further evidence for structure I was obtained by preparing the ketone from cyperene (II) *via* oxidation of the hydrocarbon with chromium trioxide in glacial acetic acid. Identity of the natural and synthetic samples was established by comparing their infrared and ultraviolet spectra and X-ray diffraction patterns of their 2,4-dinitrophenylhydrazones. Further, dihydro-cyperenone derived from the synthetic cyperenone was identical with that obtained from the natural cyperenone (infrared analysis and mixed melting point of DNPH).

The NMR spectrum of cyperenone (in  $CCl_4$ ) was consistent with the proposed structure (Fig. 1). Bands at  $\tau = 9.43$  and  $9.33$  are due to the methyl group on tertiary carbon atom, and those at  $\tau = 9.24$  and  $8.89$  correspond to the geminal dimethyl group. The methyl group on the olefinic carbon atom exhibits long-range coupling and gives rise to a triplet at  $\tau = 8.35$ ,  $8.33$ , and  $8.31$ . The band at  $\tau = 8.03$  may be assigned to hydrogen atoms of the methylene group in  $\alpha$ -position to the carbonyl group. The NMR spectrum of cyperenone 2,4-dinitrophenylhydrazone, in  $CDCl_3$ , also exhibited the corresponding bands at  $\tau = 9.40$  and  $9.31$  ( $CH_3$  on tertiary C),  $\tau = 9.22$  and  $8.86$  (gem dimethyl),  $\tau = 8.10$  ( $CH_3$  on olefinic C), and  $\tau = 7.70$  and  $7.66$  ( $CH_2$  of ketomethylene).

On the basis of the experimental evidence assembled structure I is assigned to cyperenone.

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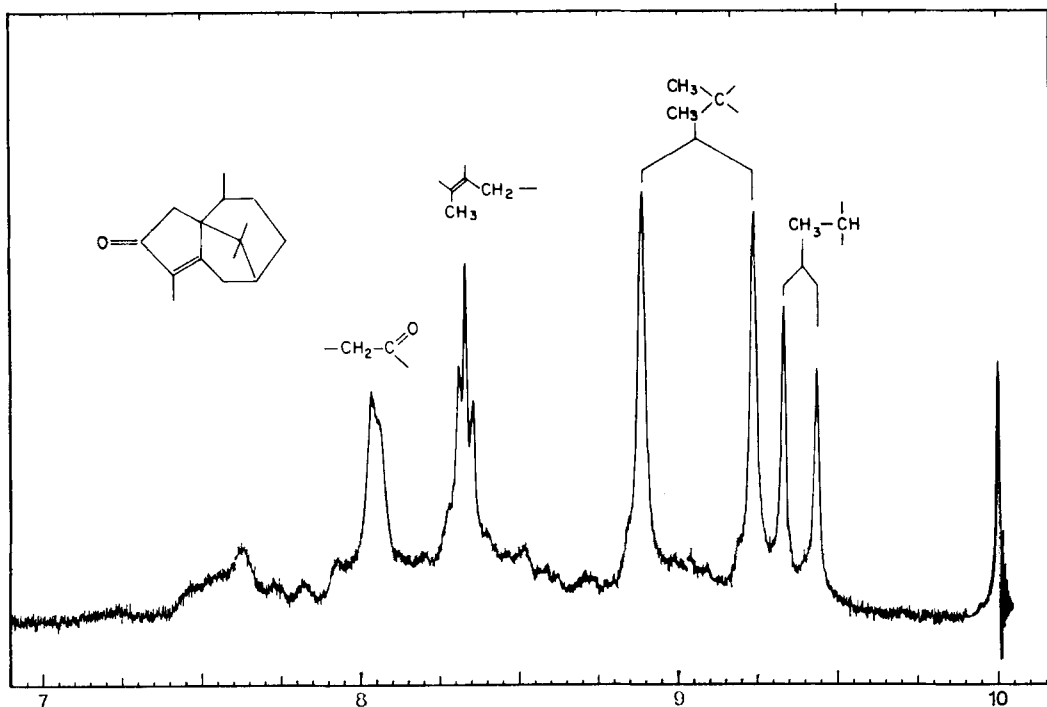


Fig. 1—NMR spectrum of cyperenone.

#### EXPERIMENTAL

Melting points are uncorrected. Gas chromatographic apparatus and procedures were described (7). The ultraviolet spectra were measured in ethanolic solution with a Beckman DU spectrophotometer. The infrared spectra were charted on a Perkin Elmer model 221 spectrophotometer. The NMR spectra were recorded with a Varian A-60 spectrometer. X-ray diffraction patterns were obtained employing Philips Debye-Scherrer powder cameras (diameter 114.83 mm.) and Cu K  $\alpha$  radiation. The essential oil of *C. scarosius* was obtained through the courtesy of Manaunlal Ramnarain, Kannauj, India.

**Isolation of Cyperenone.**—Oil of *C. scarosius* (3 Gm.) was chromatographed on alumina (Woelm grade I, 50 Gm.) and eluted successively with hexane (100 ml.), benzene (100 ml.), and ether (250 ml.). Gas chromatographic analysis (column, 20% Reoplex 400; temperature, 200°; helium, 75 ml./min.) showed that the fraction (342 mg.) recovered from the first 50 ml. of ether effluent contained about 70% cyperenone. The ketone was isolated by repeated injection of 20- $\mu$ l. samples from this fraction and collection of the effluent peak (retention time 26.4 min.) in carbon tetrachloride. Evaporation of the solvent and distillation of the product under reduced pressure afforded a pure sample of cyperenone (142 mg.) possessing the following characteristics: b.p. 136–138°/0.5 mm.;  $n_D^{20}$  1.513;  $\lambda_{max}$ . 245.5 m $\mu$ , log  $\epsilon$  3.988; I.R. absorption bands at 1705, 1665, 1460, 1442, 1424, 1385, 1332, 1309, 1282, 1245, 1195, 1184, 1147, 1110, 1085, 1058, 1042, 990, 970, 941, 897, and 887 cm.<sup>-1</sup> (phase CCl<sub>4</sub>); NMR bands at  $\tau$  = 9.43, 9.33, 9.24, 8.89, 8.35, 8.33, 8.31, 8.03 (in CCl<sub>4</sub>).

*Anal.*—Calcd. for C<sub>15</sub>H<sub>22</sub>O: C, 82.57; H, 10.09. Found: C, 82.03; H, 10.04.

**2,4-Dinitrophenylhydrazone of Cyperenone.**—The ketone (50 mg.) was dissolved in 2 ml. of ethanol and treated with the reagent solution prepared by dissolving 40 mg. of 2,4-dinitrophenylhydrazine in 0.2 ml. concentrated sulfuric acid and diluting first with 0.3 ml. of water and then with 1.0 ml. of ethanol. The derivative precipitated within a few minutes and was recrystallized from ethanol-ethylacetate mixture, m.p. 227.5°,  $\lambda_{max}$ . 390 m $\mu$ , log  $\epsilon$  4.335. Infrared absorption bands (in carbon tetrachloride): 1617, 1604, 1590, 1534, 1515, 1504, 1460, 1422, 1416, 1379, 1362, 1332, 1310, 1266, 1217, 1131, 1103, 1079, 1061, 1042, 988, 965, 920, and 829 cm.<sup>-1</sup>; NMR bands at  $\tau$  = 9.40, 9.31, 9.22, 8.86, 8.10, 7.70, and 7.66 (in CDCl<sub>3</sub>).

*Anal.*—Calcd. for C<sub>21</sub>H<sub>28</sub>N<sub>4</sub>O<sub>4</sub>: C, 63.32; H, 6.53; N, 14.07. Found: C, 62.97; H, 6.51; N, 13.89.

**Dihydrocyperenone.**—Cyperenone (31 mg.) was hydrogenated in acetic acid (2 ml.) in presence of 10 mg. of platinum oxide. Hydrogen uptake: 3.45 ml. (26°/750 mm.). The catalyst was filtered off and acetic acid removed by means of a vacuum evaporator. The residue was purified by chro-

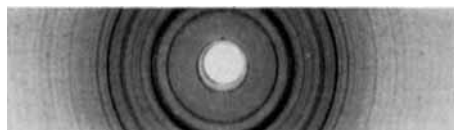


Fig. 2.—X-ray powder diffraction pattern of cyperenone 2,4-dinitrophenylhydrazone.

TABLE I.—X-RAY DIFFRACTION DATA FOR CYPERENONE-2,4-DINITROPHENYLHYDRAZONE<sup>a</sup>

<i>d</i> (Å.)	<i>I</i> / <i>I</i> <sub>1</sub>	<i>d</i> (Å.)	<i>I</i> / <i>I</i> <sub>1</sub>	<i>d</i> (Å.)	<i>I</i> / <i>I</i> <sub>1</sub>	<i>d</i> (Å.)	<i>I</i> / <i>I</i> <sub>1</sub>
15.20	45	4.72	20	3.40	80	2.27	10
7.65	10	4.28	15	3.28	15	2.18	7
7.03	70 <sup>b</sup>	3.93	30	3.11	30	2.16	7
5.90	15	3.83	35	2.97	15	2.09	8 <sup>b</sup>
5.71	60	3.70	10	2.78	8	1.97	8
5.48	100	3.54	10	2.56	15	1.91	8
5.24	15	3.49	7	2.36	7		

<sup>a</sup> Recrystallized from ethanol. <sup>b</sup> Unresolved doublet.

matography on 2 Gm. of alumina grade II (eluant: hexane).

*Anal.*—Calcd. for C<sub>15</sub>H<sub>24</sub>O: C, 81.76; H, 10.98. Found: C, 81.81; H, 10.90.

**2,4-Dinitrophenylhydrazone of Dihydrocyperenone.**—Dihydrocyperenone (22 mg.) was treated with 20 mg. of 2,4-dinitrophenylhydrazine as described for cyperenone. The derivative obtained was recrystallized from ethanol-ethylacetate mixture, m.p. 191–192°.

*Anal.*—Calcd. for C<sub>21</sub>H<sub>28</sub>N<sub>4</sub>O<sub>4</sub>: C, 62.98; H, 7.05 N, 13.99. Found: C, 62.73; H, 6.95; N, 13.72.

**Cyperene from Cyperenone.**—An ice-cooled mixture of cyperenone (45 mg.) and ethanedithiol (90 μl.) was treated with borontrifluoride etherate (100 μl.). Glacial acetic acid was added drop by drop until a homogeneous solution was obtained. After 4 hr., the reaction mixture was poured into an aqueous solution of potassium carbonate and extracted with ether. The ether extract was washed repeatedly with sodium chloride solution (10%), dried over anhydrous sodium sulfate, and evaporated. The residue was refluxed with a 5-ml. suspension of Raney nickel for 16 hr. The catalyst was filtered off, and the bulk of solvent was removed under reduced pressure. The concentrated solution was diluted with 5 ml. of water and extracted with petroleum ether. The extract was dried over anhydrous sodium sulfate and evaporated. The residue was analyzed by gas chromatography and found to exhibit a major peak at 8.5 min. (column, 20% Reoplex 400; temperature, 150°; helium, 75 ml./min.). The infrared spectrum of the sample obtained by collecting the effluent peak in carbon tetrachloride was identical to that of a pure reference sample of cyperene.

**Oxidation of Cyperene to Cyperenone.**—A solution of chromium trioxide (2.5 Gm.) in glacial acetic acid was slowly added, with stirring, to a solution of cyperene (3.0 Gm.) in glacial acetic acid. The reaction mixture was left overnight at room temperature, diluted with water, and extracted with ether. The extract was washed first with sodium bicarbonate solution (1%), then with water, and finally dried over anhydrous sodium sulfate. The crude product (2.7 Gm.) obtained following

evaporation of the solvent was chromatographed on 75 Gm. grade I alumina. The first fraction eluted with hexane (25 ml.) contained unreacted cyperene only. The following fraction obtained with benzene (450 ml.) was mainly composed of cyperenone, λ<sub>max</sub>. 245.5 mμ, log ε 4.014. The infrared spectrum was identical to that of natural cyperenone.

**Derivatives of Synthetic Cyperenone.**—The sample of synthetic cyperenone was converted to the following derivatives employing methods described for the natural product.

*A.*—2,4-Dinitrophenylhydrazone, m.p. 228°; λ<sub>max</sub>. 390 mμ, log ε 4.339; infrared and NMR spectra identical to those of the derivative of natural cyperenone.

*Anal.*—Calcd. for C<sub>21</sub>H<sub>28</sub>N<sub>4</sub>O<sub>4</sub>: C, 63.32; H, 6.53; N, 14.07. Found: C, 62.91; H, 6.42; N, 13.69.

*B.*—Dihydrocyperenone.

*Anal.*—Calcd. for C<sub>15</sub>H<sub>24</sub>O: C, 81.76; H, 10.98. Found: C, 81.7; H, 11.17.

*C.*—Dihydrocyperenone 2,4-dinitrophenylhydrazone, m.p. 190.5–191.5°.

*Anal.*—Calcd. for C<sub>21</sub>H<sub>28</sub>N<sub>4</sub>O<sub>4</sub>: C, 62.98; H, 7.05; N, 13.99. Found: C, 63.04; H, 7.14; N, 13.22.

**X-Ray Diffraction Data for 2,4-Dinitrophenylhydrazones of Cyperenone and Articulone.**—X-ray diffraction patterns for the 2,4-dinitrophenylhydrazones of natural and synthetic cyperenone samples were found to be identical to those obtained for the Naves-Ardizio sample and the articulone dinitrophenylhydrazone. The pattern is reproduced in Fig. 2, and the diffraction data for 27 most prominent lines are in Table I.

#### REFERENCES

- (1) Naves, Y. R., and Ardizio, P., *Bull. Soc. Chim. France*, **1954**, 332.
- (2) Nigam, I. C., Ph.D. Thesis, Agra University, Agra, India, 1960.
- (3) Couchman, F. M., Pinder, A. R., and Bromham, N. H., *Tetrahedron*, **20**, 2037(1964).
- (4) Trivedi, B., et al., *Tetrahedron Letters*, **19**, 1197(1964).
- (5) Motl, O., et al., *Chem. Ind. London*, **1963**, 1284; *Collection Czech. Chem. Commun.*, **29**, 1675(1964).
- (6) Horak, M., and Munk, P., *Collection Czech. Chem. Commun.*, **24**, 3023(1959).
- (7) Nigam, I. C., and Levi, L., *Can. J. Chem.*, **40**, 2083 (1962).