

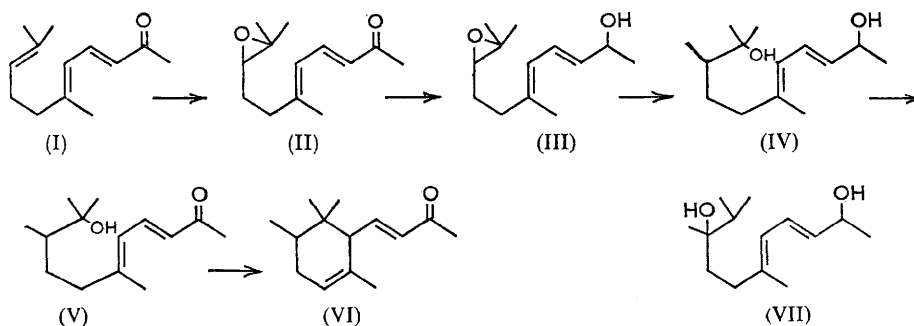
## 52. A Synthesis of Irone.

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$\psi$ -Ionone has been converted by a five-step procedure into racemic  $\alpha$ -irone. The additional methyl group was incorporated by the opening of a terminally placed epoxide group with methylmagnesium bromide.

SEVERAL syntheses of irone, the main perfume ingredient of violets, have been reported.<sup>1</sup> We now describe a new synthesis of  $\alpha$ -irone (VI) which has some merit of simplicity.

$\psi$ -Ionone (I) was smoothly converted into the epoxide (II) by the action of perphthalic acid. That the epoxidation occurred at the terminal ethylenic linkage of (I) was shown by the identical ultraviolet spectra of (I) and (II) as well as by the reactions outlined in the sequel. The epoxide (II) was reduced by methanolic sodium borohydride to the allylic alcohol (III), the structure of which was confirmed by the absence of a carbonyl band in the infrared spectrum as well as by the presence of the expected diene absorption in the ultraviolet spectrum. The alcohol oxide (III) reacted smoothly with methylmagnesium bromide



in tetrahydrofuran to give a compound formulated as the diol (IV) on the basis of its further reactions. The nucleophilic opening of the epoxide ring in the sense suggested would be expected from the recent steroid literature,<sup>2</sup> but a prior rearrangement of the epoxide to ketone followed by reaction to give a tertiary alcohol of structure (VII) instead of (IV) is not excluded by our evidence. Oxidation of the diol (IV) with active manganese dioxide<sup>3</sup> gave the dienone alcohol (V) with the expected spectral characteristics. The intensity of the ultraviolet absorption showed that about 15% of unoxidised diol (IV) was still present so the product was characterised as (V) by analysis of its 2,4-dinitrophenylhydrazone. Cyclisation of (V) with phosphoric acid according to Naves's method<sup>4</sup> gave racemic  $\alpha$ -irone (VI), identified as the phenylsemicarbazone and as the 2,4-dinitrophenylhydrazone as well as by its spectral characteristics.

Our synthesis of  $\alpha$ -irone has general implication for the preparation of 6-substituted ionones including no doubt the 6-hydroxy- and 6-keto-derivatives. We hope to report upon such compounds in due course.

## EXPERIMENTAL

M. p.s were taken on the Kofler block. All ultraviolet absorption spectra were determined in ethanol on the Unicam S.P. 500 spectrophotometer. Infrared spectra are for the pure compound unless specified to the contrary. Light petroleum refers to the fraction of b. p. 40–60°.

<sup>1</sup> Naves, Grampoloff, and Backmann, *Helv. Chim. Acta*, 1947, **30**, 599; Schinz, Ruzicka, Seidel, and Tavel, *ibid.*, p. 1810; Grütter, Helg, and Schinz, *ibid.*, 1952, **35**, 771; Kimmel, Surmatis, Weber, Chase, Sax, and Ofner, *J. Org. Chem.*, 1957, **22**, 1611; Eschinazi, *J. Amer. Chem. Soc.*, 1959, **81**, 2905.

<sup>2</sup> *Inter al.*, Turner, *J. Amer. Chem. Soc.*, 1952, **74**, 5363; Spero, Thompson, Magerlein, Hanze, Murray, Sebek, and Hogg, *ibid.*, 1956, **78**, 6213; Ringold, Batres, and Rosenkranz, *J. Org. Chem.*, 1957, **22**, 99; Ackroyd, Adams, Ellis, Petrow, and Stuart-Webb, *J.*, 1957, 4099.

<sup>3</sup> See Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.

<sup>4</sup> Naves, *Helv. Chim. Acta*, 1948, **31**, 911.

*ψ-Ionone Epoxide* (II).—*ψ*-Ionone (15 g.) in ether (50 ml.) was treated at 0° with stirring with monoperphthalic acid (15 g.) in the same solvent (300 ml.) and left for 24 hr. The solution was washed successively with aqueous sodium hydrogen carbonate, with 1N-aqueous sodium hydroxide, and with water. The dried (Na<sub>2</sub>SO<sub>4</sub>) solution gave on distillation *ψ*-ionone epoxide (13 g.), b. p. 118°/0.7 mm.,  $n_D^{25}$  1.5185,  $\lambda_{\max}$  291 m $\mu$  ( $\epsilon = 21,000$ ). This was characterised as the 2,4-dinitrophenylhydrazone. Prepared by the method of Braude and Timmons<sup>5</sup> this had m. p. (from ethanol) 159–160°,  $\lambda_{\max}$  392 m $\mu$  ( $\epsilon = 33,000$ ) (Found: C, 58.5; H, 6.05; N, 14.55. C<sub>19</sub>H<sub>24</sub>O<sub>3</sub>N<sub>4</sub> requires C, 58.75; H, 6.25; N, 14.45%).

*ψ-Ionol Epoxide* (III).—*ψ*-Ionone epoxide (13 g.) in methanol (200 ml.) at 0° was treated with sodium borohydride ( $\frac{1}{2}$  mol.) until the ketonic function had been reduced [ultraviolet control: disappearance of the band at 291 m $\mu$  and appearance of a new band ( $\epsilon = 20,000$  approx.) at 240 m $\mu$ ]. The excess of sodium borohydride was destroyed with acetic acid and then a slight excess of sodium hydrogen carbonate was added. The methanol was removed *in vacuo* and the residue extracted into ether, dried (Na<sub>2</sub>SO<sub>4</sub>), and then distilled to furnish *ψ-ionol epoxide* (12 g.), b. p. 105°/0.2 mm.,  $\lambda_{\max}$  240 m $\mu$  ( $\epsilon = 23,000$ ) (Found: C, 73.85; H, 10.55. C<sub>13</sub>H<sub>22</sub>O<sub>2</sub> requires C, 74.25; H, 10.55%).

*Reaction of ψ-Ionol Epoxide with Excess of Methylmagnesium Bromide*.—Magnesium (6 g.) was converted into the Grignard reagent, methyl bromide (20 ml.) in purified tetrahydrofuran (200 ml.) being used. To this solution was added slowly with stirring *ψ*-ionol epoxide (12 g.) in the same solvent (120 ml.), and the mixture left for 1 hr. The mixture was then refluxed for 4 hr., cooled, and treated with excess of saturated aqueous ammonium chloride at 0°. After ether extraction and drying over Na<sub>2</sub>SO<sub>4</sub> the ether and tetrahydrofuran were removed *in vacuo* at <40°. The residue could not be distilled owing to decomposition but it gave correct analytical data for the expected *glycol* (IV);  $\lambda_{\max}$  240 m $\mu$  ( $\epsilon = 25,000$ ) (Found: C, 74.3; H, 11.3. C<sub>14</sub>H<sub>26</sub>O<sub>2</sub> requires C, 74.3; H, 11.6%).

The glycol (10.3 g.) in dry ether (500 ml.) was shaken with active manganese dioxide (105 g.) at room temperature, and the progress of the oxidation followed by ultraviolet spectroscopy. After 48 hr. there was no further increase in the intensity of the band at 291 m $\mu$  ( $\epsilon = 18,000$ ). Removal of the manganese dioxide and of the ether in the usual way gave a residue (10 g.) which had  $\lambda_{\max}$  291 m $\mu$  ( $\epsilon = 18,000$ ) and showed an OH band in the infrared region (3625 cm.<sup>-1</sup>). It was characterised as the ketol (V) by the preparation of the 2,4-dinitrophenylhydrazone, m. p. 173° (from benzene–light petroleum)  $\lambda_{\max}$  392 m $\mu$  ( $\epsilon = 32,000$ ) (Found: C, 58.9; H, 7.15; N, 14.1. C<sub>20</sub>H<sub>28</sub>O<sub>5</sub>N<sub>4</sub> requires C, 59.4; H, 7.0; N, 13.85%).

*Synthesis of α-Irone*.—The ketol (V) (see above) (10 g.) was added dropwise with good stirring to phosphoric acid (90%; 30 ml.)<sup>4</sup> at 30°, and the mixture stirred for 15 min. Excess of ice–water was added, and the cyclised product extracted into ether. The ether was removed, and the residue steam-distilled to give an oil, b. p. 73°/0.3 mm.,  $n_D^{25}$  1.5000,  $\lambda_{\max}$  228 m $\mu$  ( $\epsilon = 11,200$ ) and *ca.* 290 m $\mu$  ( $\epsilon = 2000$ ), the latter band indicating the presence of some β-ironone. The oil gave a phenylsemicarbazone, m. p. (initially) 165° raised to 172° on recrystallisation from ethanol (Found: C, 74.55; H, 8.6; N, 12.5, 12.65. Calc. for C<sub>21</sub>H<sub>29</sub>ON<sub>3</sub>: C, 74.3; H, 8.6; N, 12.4%). Authentic synthetic α-ironone gave a derivative of the same m. p., undepressed on admixture. The infrared spectra (in chloroform) were identical. Conversion into the 2,4-dinitrophenylhydrazone and crystallisation from methanol gave a derivative, m. p. 103–104° undepressed on admixture with an authentic specimen<sup>4</sup> of the same m. p. prepared from authentic synthetic α-ironone through the phenylsemicarbazone, m. p. 172°.

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<sup>5</sup> Braude and Timmons, *J.*, 1953, 3136.