130. *Glycerol Ethers of Resacetophenone.*

By D. R. NADKARNI and T. S. WHEELER.

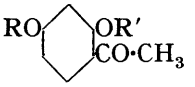
MOTWANI and WHEELER (J., 1935, 1098) studied the preparation of β-hydroxyethyl ethers of resacetophenone with a view to synthesising substances containing coumaran and γ-pyrone nuclei. We have examined the reactions between resacetophenone and glycerol α-monochlorohydrin and epichlorohydrin with a view to preparing glycerol ethers of resacetophenone, to be eventually employed in the synthesis of flavone derivatives of the type prepared by Motwani and Wheeler (*loc. cit.*). The interactions of glycerol, glycide, and glycerol α-monochlorohydrin with phenols have been studied previously by a number of workers; a summary of their results has been given by Marle (J., 1912, **101**, 305).

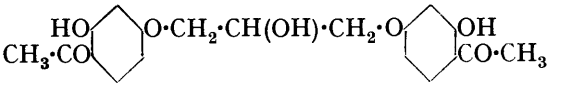
The condensation of glycerol α-monochlorohydrin with resacetophenone in the presence of dilute potassium hydroxide solution gave 2-*hydroxy*-4-(β*γ*-*dihydroxypropoxy*)*acetophenone* [I; R = $CH_2(OH)\cdot CH(OH)\cdot CH_2$, R′ = H] (70% yield) and *glycerol* α*γ*-*bis*-(3-*hydroxy*-4-*acetylphenyl*) *ether* (II) (20% yield); higher concentrations of the alkali gave larger yields of (II). The structure of (II) was confirmed by its preparation from epichlorohydrin,

resacetophenone, and sodium ethoxide by Boyd and Marle's method (J., 1908, **93**, 838) for glycerol αγ-diphenyl ether.

Epichlorohydrin, when condensed with resacetophenone in aqueous sodium hydroxide (Boyd and Marle, *loc. cit.*), gave 2-*hydroxy*-4-β*γ-epoxypropoxyacetophenone* (I; R = $O<\begin{matrix}CH_2\\ CH\cdot CH_2\end{matrix}$, R′ = H) and presumably 2 : 4-*bis*-(β*γ-epoxypropoxy*)*acetophenone*. The latter substance could not be purified.

2-*Hydroxy*-4-*γ-chloro*-β-*hydroxypropoxyacetophenone* [I; R = $CH_2Cl\cdot CH(OH)\cdot CH_2$, R′ = H] was obtained from epichlorohydrin and resacetophenone with 10% sodium hydroxide solution (1/80 mol.) as a catalyst (Boyd and Marle, J., 1910, **97**, 1789). With higher proportions of the alkali the monoglycide ether (I; R = $O<\begin{matrix}CH_2\\ CH\cdot CH_2\end{matrix}$, R′ = H) also separated.

(I.) 

 (II.)

Experimental.

2-*Hydroxy*-4-(β*γ-dihydroxypropoxy*)*acetophenone*.—A solution of potassium hydroxide (56 g.) in water (200 g.) was added to resacetophenone (76 g.) suspended in ice-cold water (75 c.c.), and the mixture heated with glycerol α-chlorohydrin (110·5 g.) at 100° for 3 hours. The oil (II, see below) which separated was removed, and the mother-liquor kept in the refrigerator for 48 hours. The resulting precipitate (yield, 70%) crystallised from aqueous alcohol in thin plates, m. p. 88°. It was soluble in water and gave a violet coloration with alcoholic ferric chloride (Found : C, 58·2; H, 6·2. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2%).

The *hydrazone*, obtained by warming an alcoholic solution with 50% hydrazine hydrate, crystallised from aqueous alcohol in pale yellow needles, m. p. 98° (Found : N, 11·5. $C_{11}H_{16}O_4N_2$ requires N, 11·7%). The *azine*, obtained by treatment of the ketone with hydrazine hydrate in glacial acetic acid, crystallised from alcohol in yellow needles, m. p. 292—294° (Found : N, 6·6. $C_{22}H_{28}O_8N_2$ requires N, 6·3%). The *phenylhydrazone*, crystallised from rectified spirit, had m. p. 119—120° (Found : N, 9·0. $C_{17}H_{20}O_4N_2$ requires N, 8·9%).

Glycerol αγ-Bis-(3-*hydroxy*-4-*acetylphenyl*) *Ether* (II).—The separated oil (II above; yield, 20%) solidified in the refrigerator and then crystallised from acetone in colourless needles, m. p. 161°. It was soluble in alkali and gave a violet coloration with alcoholic ferric chloride. It was also obtained when epichlorohydrin (45 g.) was heated with sodium (12 g.), alcohol (300 c.c.), and resacetophenone (152 g.) at 100° under reflux for 4 hours, and the mixture diluted with water (Found : C, 63·4; H, 5·6. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%).

The *hydrazone*, crystallised from alcohol, had m. p. 184° (Found : N, 14·2. $C_{19}H_{24}O_5N_4$ requires N, 14·4%). The *azine*, insoluble in all solvents, was purified by extraction with boiling acetic acid; m. p. above 300° (Found : N, 7·9. $C_{38}H_{40}O_{10}N_4$ requires N, 7·9%). The *phenylhydrazone* crystallised from alcohol in needles, m. p. 206° (Found : N, 10·2. $C_{31}H_{32}O_5N_4$ requires N, 10·4%).

2-*Hydroxy*-4-β*γ-epoxypropoxyacetophenone*.—An amorphous solid separated when a mixture of epichlorohydrin (23 g.), resacetophenone (38 g.), sodium hydroxide (12 g.), and water (250 c.c.) was kept at room temperature for a week. It was sparingly soluble in boiling glacial acetic acid, but did not separate except on dilution; it then formed a sticky mass. On addition of hydrazine hydrate to the boiling acetic acid solution an azine (?) insoluble in all solvents separated; for purification, it was extracted with boiling glacial acetic acid; m. p. above 300° [Found : C, 61·1; H, 6·4; N, 5·7. $C_{28}H_{32}O_8N_2$ (azine of I; R = R′ = $O<\begin{matrix}CH_2\\ CH\cdot CH_2\end{matrix}$) requires C, 64·1; H, 6·1; N, 5·3%]. A similar compound was also obtained by heating a mixture of epichlorohydrin (37 g.), resacetophenone (30·4 g.), potassium hydroxide (20 g.), and water (20 c.c.) at 120° for 3 hours (Found for the insoluble azine : C, 60·1; H, 6·2; N, 5·1%).

When the mother-liquor obtained after the removal of the presumed diglycide ether in the above condensation at room temperature was acidified with dilute hydrochloric acid, a sticky mass separated; repeatedly crystallised from acetic acid and finally from rectified spirit, it formed colourless needles, m. p. 78°. It was soluble in alkali and gave a violet coloration with alcoholic ferric chloride (Found : C, 63·4; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

The *acetyl* derivative (I; R = $O<\begin{matrix}CH_2\\ |\\ CH\cdot CH_2\end{matrix}$, R′ = $CO\cdot CH_3$), obtained by boiling the monoglycide ether with glacial acetic acid, crystallised from acetic acid as a reddish-brown powder, m. p. 198—200° (Found : C, 62·2; H, 5·8. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%).

The monoglycide ether did not give [I; R = $CH_2(OH)\cdot CH(OH)\cdot CH_2$, R′ = H] when heated with water in a sealed tube at 180° for 24 hours, though Lindemann (*Ber.*, 1891, **24**, 2149) and Marle (*loc. cit.*) have observed that phenyl glycide ethers react with water to produce glycerol aryl ethers under these conditions.

2-Hydroxy-4-γ-chloro-β-hydroxypropoxyacetophenone.—A mixture of epichlorohydrin (92·5 g.), resacetophenone (152 g.), sodium hydroxide (0·5 g.), and water (5 c.c.) was kept at room temperature for 6 weeks. It was then extracted with ether, and the excess of epichlorohydrin removed from the extract by distillation under reduced pressure. The oily residue solidified in the refrigerator after a week and then crystallised from rectified spirit in needles, m. p. 68° after softening at 58°. It was soluble in alkali and gave a violet coloration with alcoholic ferric chloride. The substance liquefied when kept over sulphuric acid and resolidified when exposed to air [Found : Cl, 13·6; loss after drying at 120°/2 mm. (a liquid resulted), 6·8. $C_{11}H_{13}O_4Cl,H_2O$ requires Cl, 13·5; H_2O, 6·9%. Found after drying : Cl, 14·9. $C_{11}H_{13}O_4Cl$ requires Cl, 14·5%].

When dissolved in aqueous sodium hydroxide and then acidified with acetic acid, this ether gave the monoglycide ether (I; R = $O<\begin{matrix}CH_2\\ |\\ CH\cdot CH_2\end{matrix}$, R′ = H), which on heating with concentrated hydrochloric acid at 100° for 2 hours reproduced the chlorohydrin ether.

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