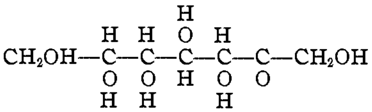
The author wishes to thank the Medical Fellowship Board of the National Research Council for the award of a fellowship which made possible the carrying out of this research. He also expresses his deep indebtedness to Dr. C. S. Hudson for many valuable suggestions.

## Summary

A new crystalline ketose, *d*-glucoheptulose, of configuration



$$\begin{array}{ccccccccccc} & & & & & \mathrm{H} & & & & & \\ & \mathrm{H} & & \mathrm{H} & & \mathrm{O} & & \mathrm{H} & & & \\ \mathrm{CH_2OH}— & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & —\mathrm{CH_2OH} \\ & \mathrm{O} & & \mathrm{O} & & \mathrm{H} & & \mathrm{O} & & \mathrm{O} & \\ & \mathrm{H} & & \mathrm{H} & & & & \mathrm{H} & & & \end{array}$$

has been synthesized from *d*-$\alpha$-glucoheptose by use of the procedure which Montgomery and Hudson have recently developed for the synthesis of ketoses from aldoses through the Lobry de Bruyn rearrangement. It proves to be the optical enantiomorph of the ketose which Bertrand and Nitzberg recently made through the action of the sorbose bacterium upon a solution of $\alpha$-glucoheptitol and their ketose is accordingly *l*-glucoheptulose. The rotation of *d*-glucoheptulose, which does not exhibit mutarotation, is near the value that was predicted by the rotatory relations developed by Hudson. The existence of this ketose, of the calculated rotation, is strong evidence that Hudson's calculation of $+67$ for the $[\alpha]_D$ value of an unknown $\alpha$-*d*-glucose, of the 1,A = 1,4-ring type, is substantially correct.

WASHINGTON, D. C.

---

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WEST VIRGINIA UNIVERSITY]

# ESTERS OF CYCLOHEXYLRESORCINOL AND PARA-CYCLOHEXYLPHENOL[1]

BY VIRGIL GREENE LILLY AND C. E. GARLAND

RECEIVED FEBRUARY 6, 1930 PUBLISHED MAY 8, 1930

In view of the excellent germicidal properties of some of the alkyl and aryl substituted hydroxy derivatives of benzene[2] and their general low toxicity, some esters, of the salol type, have been prepared using cyclohexylresorcinol[2,3] and *p*-cyclohexylphenol, with a hope that they may prove of therapeutic value.[4]

In general, esters of cyclohexylresorcinol are rather difficult to prepare, while those of *p*-cyclohexylphenol are less so. Cyclohexylresorcinol does

---

[1] This communication is an abstract of part of a thesis submitted by Virgil Greene Lilly in partial fulfilment of the requirements for the degree Master of Arts in Chemistry at West Virginia University.

[2] For a list of important contributions see Bartlett and Garland, THIS JOURNAL, **49**, 2098 (1927).

[3] Philips, U. S. Patent 1,650,036.

[4] Kursanoff, *Ann.*, **318**, 309 (1901); Wuyts, *Bull. soc. chim. Belg.*, **26**, 304 (1912); Schrauth and Görig, *Ber.*, **56**, 1900 (1923); v. Braun, *Ann.*, **472**, 61 (1929).

not form a crystalline salt when treated with sodium hydroxide, or when cyclohexylresorcinol is dissolved in an indifferent solvent and treated with metallic sodium, but gives a red mass of horn-like consistency. In many of the esterification reactions attempted it appeared to undergo a kind of polymerization to give tar-like products which we were unable to purify. The sodium salt of *p*-cyclohexylphenol crystallizes easily from aqueous solution in thin plates. The potassium salt does not crystallize readily.

Three general methods were used to prepare the esters, as follows: the Schotten–Baumann reaction, the action of thionyl chloride or other condensing agents, and the action of acid chlorides upon the dry alkali phenolates.

The cyclohexylresorcinol and cyclohexylphenol used in preparing the following esters were supplied through the courtesy of Dr. R. R. Read, of Sharpe and Dohme, Baltimore, to whom the thanks of the authors are due.

## Experimental Part

**Cyclohexylresorcinol Dibenzoate,** $(C_6H_3)(C_6H_{11})\cdot(C_7H_5O_2)_2(1,2,4)$.—To 100 cc. of 10% potassium hydroxide was added 10 g. of cyclohexylresorcinol, which dissolved to a red wine color. Fifteen and three-tenths grams of benzoyl chloride was added gradually, the reaction mixture being stirred vigorously during the course of the reaction, which was complete within twenty minutes. A heavy yellow oil formed which settled to the bottom. The supernatant liquid was decanted and the heavy oily product repeatedly washed with water. This oil did not deposit crystals, so it was dissolved in a small quantity of hot alcohol, from which the solid product readily separated on cooling. After two recrystallizations from alcohol the white plate crystals melted sharply at 88°. The crystals have a pleasant aromatic odor; yield, 60%.

*Anal.* Calcd. for $C_{26}H_{24}O_4$: C, 78.00; H, 6.00. Found: C, 77.81, 77.96; H, 5.51, 6.19.

***p*-Cyclohexylphenol Salicylate,** $C_6H_4(C_6H_{11})\cdot(HOC_6H_4COO)(1,4)$. **Method I.**—Eight grams of well dried sodium *p*-cyclohexylphenolate and 12 g. of sodium salicylate together with 30 cc. of phosphorus oxychloride and 10 g. of finely powdered sodium chloride were heated in a balloon flask[5] on a sand-bath for an hour at 130°. The heat was then removed and the flask allowed to cool to room temperature. The reaction mixture was extracted with an equal mixture of ethyl and methyl alcohols. White crystals separated from the alcoholic solution, which melted at 103.5°. Results by this method are very uncertain and usually the yield is very small.

**Method II.**—Twenty grams of cyclohexylphenol and the theoretical amount of salicylic acid were refluxed with an excess of thionyl chloride on a water-bath for two hours. The excess thionyl chloride was decomposed with cold water, the residue well washed and dissolved in alcohol. The crystalline product after further purification melted at 103.5°. A mixed melting point of the products from Methods I and II gave 103°; yield, 25%.

*Anal.* Calcd. for $C_{19}H_{20}O_3$: C, 77.03; H, 6.75. Found: C, 77.09, 76.94; H, 7.10, 6.91.

---

[5] U. S. Patent 1,606,171.

**p-Cyclohexylphenol Hydrocinnamate,** $C_6H_4(C_6H_{11})\cdot(C_6H_5CH_2CH_2COO)(1,4)$.—The acid chloride of hydrocinnamic acid was prepared by the method of McMaster and Ahmann.[6] Hydrocinnamic acid was refluxed with an excess of thionyl chloride for two hours, the excess thionyl chloride distilled off, and the acid chloride purified by vacuum distillation. (Other acid chlorides used in this investigation were prepared in a similar manner.)

Twenty grams of sodium cyclohexylphenolate and 17 g. of hydrocinnamoyl chloride were well stirred for ten minutes and at the same time gently warmed. The product was repeatedly washed with water and the residue dissolved in hot alcohol. On cooling, fine needle-like crystals rapidly separated out. On recrystallization the product melted at 74°; yield, 33%.

*Anal.* Calcd. for $C_{21}H_{24}O_2$: C, 81.82; H, 7.79. Found: C, 81.39, 81.57; H, 7.88, 7.84.

**p-Cyclohexylphenol *m*-Nitrobenzoate,** $C_6H_4(C_6H_{11})(O_2NC_6H_4COO)(1,4)$.—The acid chloride of *m*-nitrobenzoic acid and the calculated amount of well dried sodium cyclohexylphenolate were warmed together for ten minutes, the reaction mixture washed repeatedly with water and dissolved in hot alcohol. The crystals on further purification melted at 114°. Analysis was by the method of Knecht and Hibbert.[7]

*Anal.* Calcd. for $C_{19}H_{19}O_4N$: N, 4.31. Found: N, 4.50, 4.32.

**p-Cyclohexylphenol p-Nitrobenzoate,** $C_6H_4(C_6H_{11})(O_2NC_6H_4COO)1,4$.—Three grams of *p*-cyclohexylphenol and the calculated amount of *p*-nitrobenzoic acid were heated with 10 g. of thionyl chloride and 5 g. of phosphorus trichloride for an hour on a water-bath. The excess acid chlorides were decomposed with water and the residue was crystallized from alcohol. The first crop of crystals was rejected and the second portion after repeated recrystallizations melted at 137°; yield, 15%.

*Anal.* Calcd. for $C_{19}H_{19}O_4N$: N, 4.31. Found: 4.37, 4.41.

## Summary

The following salol type esters of cyclohexylresorcinol and *p*-cyclohexylphenol have been prepared and described: (1) cyclohexylresorcinol dibenzoate, (2) *p*-cyclohexylphenol salicylate, (3) *p*-cyclohexylphenol hydrocinnamate, (4) *p*-cyclohexylphenol *m*-nitrobenzoate and (5) *p*-cyclohexylphenol *p*-nitrobenzoate.

MORGANTOWN, WEST VIRGINIA

---

[6] McMaster and Ahmann, THIS JOURNAL, **50**, 145 (1928).

[7] "New Reduction Methods in Volumetric Analysis," Longmans, Green, 1910, and *J. Soc. Chem. Ind.*, **39**, 87 (1920).