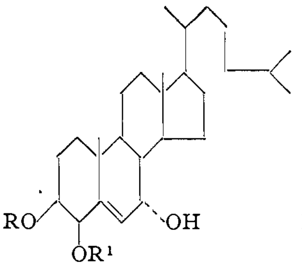

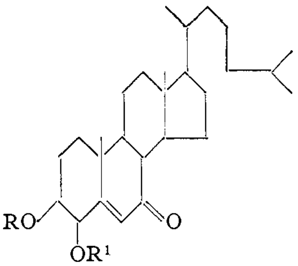

Ia, R = CH_3CO
R^1 = H
b, R = H
R^1 = CH_3CO

IIa, R = CH_3CO R^1 = H
b, R = H R^1 = CH_3CO
c, R = CH_3CO R^1 = C_6H_5CO
d, R = C_6H_5CO R^1 = CH_3CO

IIa or IIb. Benzoylation of the unoxidized hydroxyl group in IIa or IIb resulted in the acetoxybenzoxy-unsaturated-7-ketone (IIc or IId). This compound could not be obtained in crystalline form even after purification by chromatography and vacuum sublimation. All attempts at crystallization resulted in a gel which gave an amorphous white powder on drying. Formation of gels in this series of compounds has been found to occur frequently.[4] 3β,4β-Dihydroxy-Δ^5-cholesten-7-one acetate benzoate thus obtained melted at 194–197°, $[\alpha]^{23}_{D}$ −58.3° (chloroform), $\epsilon_{233 m\mu}$ 23,000. In order to prove the structure of this compound, both isomers, IIc and IId were prepared by unequivocal methods.

Chromic acid oxidation of the known 3β-acetoxy-4β-benzoxy-Δ^5-cholestene[5] yielded 3β-acetoxy-4β-benzoxy-Δ^5-cholesten-7-one (IIc) which in contrast to the amorphous product described above readily crystallized, m.p. 163–164°, $[\alpha]^{23}_{D}$ −58.1° (chloroform), $\epsilon_{233 m\mu}$ 24,400. Its m.p., crystalline form and especially its characteristic infrared spectrum in the region of 1185–875 cm.$^{-1}$[6] definitely established its non-identity with the amorphous ketone obtained from the triol monoacetate I.

Similar oxidation of 3β-benzoxy-4β-acetoxy-Δ^5-cholestene[5] gave 3β-benzoxy-4β-acetoxy-Δ^5-cholesten-7-one (IId) which could not be obtained crystalline. The product on drying gave an amorphous powder,[7] m.p. 185–188°, $[\alpha]^{23}_{D}$ −57.1° (chloroform), $\epsilon_{233 m\mu}$ 23,000.

These physical constants together with the infrared spectrum (1185–875 cm.$^{-1}$), identical in every respect with that of the product obtained from I, proved that the latter was the 3β-benzoxy-4β-acetoxy derivative (IId). It is evident from these results that the reaction of cholesterol acetate with N-bromosuccinimide followed by chromatography gave rise to the 4-acetoxy derivative Ib rather than Ia as previously formulated.

Experimental[8]

Benzoylation of 7-Keto-Δ^5-cholestene-3β,4β-diol Monoacetate (IIb).—One hundred and eighty-six mg. of 7-keto-Δ^5-cholestene-3β,4β-diol monoacetate (IIb) was benzoylated overnight at room temperature with pyridine and benzoyl chloride. The benzoylated product was chromatographed on alumina and the petroleum ether eluates gave 139 mg. of amorphous material. Attempts to crystallize the product from a number of solvents always led to the formation of a gel. Sublimation in a high vacuum yielded a hard glassy material and attempts at crystallization of this product also failed. The acetate–benzoate was finally purified by allowing a concentrated methanol solution to gel, filtering with vacuum and washing the gel with cold methanol. This procedure was repeated three times to give an amorphous powder of IId, m.p. 194–197° with previous sintering at 190°, $[\alpha]^{23}_{D}$ −58.3 ± 1° (chloroform), $\epsilon_{233 m\mu}$ 23,000 (ethanol).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 76.10; H, 8.69.

3β-Acetoxy-4β-benzoxy-Δ^5-cholesten-7-one (IIc).—To 600 mg. of 3β-acetoxy-4β-benzoxy-Δ^5-cholestene[5] in 12 cc. of glacial acetic acid was added portionwise, a solution of 0.48 g. of chromic oxide, 0.4 cc. of water and 1.8 cc. of glacial acetic acid over a period of 2 hours. The oxidation mixture was maintained at 60° during this time and for an additional 2 hours. The excess chromic oxide was destroyed with ethanol and the solvent removed *in vacuo*. The residue was taken up in ether and washed with dilute hydrochloric acid, sodium carbonate solution and water. The ether solution was dried and the solvent evaporated to give 267 mg. of crystalline product. This material was chromatographed on silica gel and the petroleum ether–ether (4:1) eluates gave 188 mg. of crystalline 3β-acetoxy-4β-benzoxy-Δ^5-cholesten-7-one (IIc). Recrystallizations from methanol and acetone gave IIc, m.p. 163–164°, $[\alpha]^{23}_{D}$ −58.1 ± 1° (chloroform), $\epsilon_{233 m\mu}$ 24,400 (ethanol).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 77.09; H, 8.72.

The infrared spectrum in the region 1185–875 cm.$^{-1}$ was different from that of its isomer 3β-benzoxy-4β-acetoxy-Δ^5-cholesten-7-one (IId) and the product obtained by the benzoylation of 7-keto-Δ^5-cholestene-3β,4β-diol monoacetate.

3β-Benzoxy-4β-acetoxy-Δ^5-cholesten-7-one (IId).—A suspension of 190 mg. of 3β-benzoxy-4β-acetoxy-Δ^5-cholestene[5] in 4 cc. of glacial acetic acid was oxidized in the same manner as above with 1.1 cc. of a solution containing 0.48 mg. of chromic oxide, 0.4 cc. of water and 1.8 cc. of glacial acetic acid. Upon chromatographic separation on silica gel, the petroleum ether–ether eluates gave 87 mg. of amorphous material. All attempts at crystallization were unsuccessful.[7] The oxidation product was purified by allowing a concentrated solution in methanol to gel, filtering with vacuum and washing the amorphous material with cold methanol. This process was repeated three times to give an amorphous powder of 3β-benzoxy-4β-acetoxy-Δ^5-cholesten-7-one (IId), m.p. 185–188° with previous sintering at 179.5°, $[\alpha]^{23}_{D}$ −57.1 ± 1° (chloroform), $\epsilon_{233 m\mu}$ 23,000 (ethanol), Petrow and Starling[4] reported m.p. 217–218°, $[\alpha]_{D}$ −59.4° (chloroform).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 76.85; H, 8.92.

The infrared spectrum in the region 1185–875 cm.$^{-1}$ was identical in every respect to the benzoylation product of 7-keto-Δ^5-cholestene-3β,4β-diol monoacetate.

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[4] V. A. Petrow and W. W. Starling, *J. Chem. Soc.*, 749 (1946).

[5] V. A. Petrow, O. Rosenheim and W. W. Starling, *ibid.*, 135 (1943).

[6] We wish to express our gratitude to the late Dr. K. Dobriner and to Mrs. P. Humphries for their help in determining and interpreting the infrared spectra.

[7] Petrow and Starling[4] have reported the preparation of this compound in crystalline form, m.p. 217–218°, $[\alpha]_{D}$ −59.4° (chloroform). However, attempts to crystallize IId by their methods were unsuccessful.

[8] All melting points are corrected.

The Heat of Fusion of Lithium

BY SCOTT B. KILNER

RECEIVED MAY 12, 1952

The heat of fusion of lithium has been variously reported as 0.15,[1] 0.23,[2] 0.76[3] and 1.1[4] kcal./gram

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[1] J. Sherman, *Chem. Revs.*, **11**, 93 (1932).

[2] A. Thum, Dissertation, Zurich, 1906.

[3] F. R. Bichowsky and F. D. Rossini, "The Thermochemistry of the Chemical Substances," Reinhold Publishing Corp., New York, N. Y., 1936.

[4] K. K. Kelley, U. S. Bur. Mines, Bull., No. 393, 166 p. (1936).

atom. We have determined the heat of fusion calorimetrically and find it to be 0.69 ± 0.07 kcal./gram atom. The value agrees, within the rather large uncertainty of our measurements, with that of Bichowsky and Rossini,[3] which was calculated from the (calorimetric) entropies of fusion of the other alkali metals. Kelley's value[4] of 1.1 kcal./gram atom was calculated from freezing point–composition data for several binary alloys; his calculations for sodium gave values in agreement with those obtained calorimetrically, whereas for potassium the calorimetric value was less than the alloy value by approximately the same factor that we find for lithium. The melting point, which has been reported as 179 and 186°,[3] was found to be 179 ± 1°.

The heat of fusion was calculated from the heat content *vs.* temperature curve of an ampoule of $^{3}/_{4}$-in. o.d. stainless steel tubing containing slightly more than 13 g. of lithium. The lithium (99.5%) was handled in an atmosphere of argon, and the ampoule closed by heliarc welding. The heat content of the ampoule was measured by an adaptation of the method of mixtures for temperatures between 164 and 191°. The calorimeter was calibrated with pure copper for the same range of temperatures. Values for the heat capacity of copper were taken from the National Bureau of Standards compilation.[5]

(5) F. D. Rossini, D. D. Wagman, W. H. Evans, E. J. Blau and S. Levine, "Selected Values of Chemical Thermodynamic Properties," U. S. National Bureau of Standards, Washington, D. C., 1947.

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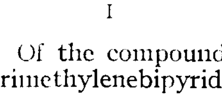
The Synthesis of 2,2'- and 4,4'-Polymethylenebipyridines

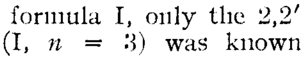
BY L. M. JAMPOLSKY, M. BAUM, S. KAISER, L. H. STERNBACH AND M. W. GOLDBERG

RECEIVED MAY 16, 1952

The present paper describes the preparation of several new 2,2'- and 4,4'-polymethylenebipyridines of the general structures I and II. They were required as intermediates for the synthesis of the corresponding polymethylene-bipyridinium compounds,[1] some of which were found to have interesting curare-like properties.[2]



I



II

Of the compounds of formula I, only the 2,2'-trimethylenebipyridine (I, $n = 3$) was known. It was obtained by Michael addition of 2-picoline to 2-vinylpyridine.[3] We have now prepared the corresponding pentamethylene (I, $n = 5$), hexamethylene (I, $n = 6$), heptamethylene (I, $n = 7$) and octamethylene (I, $n = 8$) homologs by treating 2-picolyllithium with the appropriate polymethylene dibromide. All four compounds were high boiling oils and gave crystalline dimethobromides.

The only known member of the 4,4'-polymethylenebipyridine series (II) was the dimethylene compound (II, $n = 2$). It was obtained by heating 4-picoline with sulfur.[4] We used the same method for its preparation, and synthesized the missing members of this series from the monomethylene to the octamethylene compound by a variety of other reactions. The monomethylene compound (II, $n = 1$) was made by treating 4-chloropyridine with 4-picolylpotassium in liquid ammonia. The trimethylene compound (II, $n = 3$) was prepared by condensing 4-picoline with 4-vinylpyridine in the presence of potassium (sodium was unsuitable for this purpose), and the tetramethylene compound (II, $n = 4$) was obtained by condensing 3-(4-pyridyl)-1-bromopropane with 4-picolylpotassium in liquid ammonia. We also attempted to prepare the tetramethylene compound by reacting ethylene dibromide with 4-picolylpotassium in liquid ammonia. However, the only product obtained in this case was the known 4,4'-dimethylenebipyridine (25% yield). The unexpected course of this reaction can best be explained by assuming a simultaneous formation of ethylene from the ethylene dibromide. Similar, but not completely analogous reactions are known, for example, the formation of bromobenzene, ethylene and lithium bromide from phenyllithium and ethylene dibromide.[5]

The 4,4'-pentamethylenebipyridine (II, $n = 5$) and the corresponding hexamethylene (II, $n = 6$), heptamethylene (II, $n = 7$) and octamethylene (II, $n = 8$) compounds were all prepared by reacting 4-picolylpotassium in liquid ammonia with the appropriate polymethylene dibromide. The lower members of the 4,4'-polymethylenebipyridine series crystallize readily. The hexamethylene compound was isolated in form of its crystalline dimethobromide and the hepta- and octamethylene homologs in form of their crystalline dihydrobromides.

Experimental[6]

2,2'-Polymethylenebipyridines.—The compounds of this series were prepared by treating 2-picolyllithium in ether with the appropriate polymethylene dibromide. The 2,2'-pentamethylenebipyridine was obtained in 40% yield using trimethylene dibromide, the 2,2'-hexamethylenebipyridine in 62% yield using tetramethylene dibromide, the 2,2'-heptamethylenebipyridine in 46% yield using pentamethylene dibromide, and the 2,2'-octamethylenebipyridine in 41% yield using hexamethylene dibromide. All data on these new compounds and their derivatives are summarized in Table I. The reaction conditions were identical in all cases, and we describe, therefore, in detail only the preparation of the **2,2'-hexamethylenebipyridine**: To a stirred solution of phenyllithium, prepared from 31 g. (4.4 g. atoms) of lithium and 345 g. (2.2 moles) of bromobenzene in 1 liter of absolute ether, was added 186 g. (2 moles) of dry 2-picoline. This was followed by the dropwise addition of 152 g. (0.7 mole) of tetramethylene dibromide. The reaction mixture was refluxed for 2 hours. Ice and about 275 ml. of concentrated hydrochloric acid were then added and the aqueous phase separated. It was made strongly alkaline by the addition of 50% potassium hydroxide solution and extracted with ether. The ether extract was concentrated and the residue fractionated in high vacuum. The main fraction, b.p. 160–165° (0.5 mm.), gave a crystalline **dimethobromide**

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(1) To be reported in subsequent papers.

(2) See L. O. Randall, *Ann. N. Y. Acad. Sci.*, **54**, 460 (1951), and *J. Pharmacol. Exptl. Therap.*, **105**, 7 (1952).

(3) N. J. Leonard and J. H. Boyer, THIS JOURNAL, **72**, 4818 (1950).

(4) H. I. Thayer and B. B. Corson, *ibid.*, **70**, 2330 (1948).

(5) G. Wittig and G. Harborth, *Ber.*, **77**, 306 (1944).

(6) All melting points are corrected.