fractions were pale greenish-yellow and had a sweet, oily, alcoholic odor; total yield 85.5%.

Anal. Calcd. for $C_7H_{10}O$: C, 76.30; H, 9.15. Found (main fraction): C, 76.40; H, 9.27.

The absorption spectrum of the purer "tail" fraction consisted of a sharp triplet system: $\lambda\lambda_{max}$ 252, 261.2, 271.7 mμ in 95% ethanol, ϵ_{max} 26,500, 34,300, 25,800. No diene was present. The bulk fraction gave a curve of identical shape, but lower ϵ_{max} (30,600).

This preparation was probably sterically heterogeneous (variation in ϵ) and in any case was not the pure *trans–trans* isomer, for which a melting point of 79–80° has been reported.[14]

1-Bromo-2,4,6-heptatriene.—With stirring and cooling, 3.9 ml. (0.041 mole) of phosphorus tribromide was dropped into a mixture of 11 g. (0.1 mole) of heptatrienol with 2.7 ml. (0.035 mole) of dry pyridine. The viscous mixture, intermittently stirred, was kept in a −10° bath for 30 min., at room temperature for 30 min., and in a 45° bath for 15 min.; then poured into 30 ml. of ice and water and thrice extracted with ether–petroleum ether. (Considerable tar remained undissolved.) The water-washed extract, dried over magnesium sulfate, was distilled through a 15-cm. center-rod column, giving a single fraction, b.p. 48–49° (0.8 mm.), $n^{25}D$ 1.5983, d^{25} 1.295, m.p. 2–6.2°. The light-yellow, fragrant, rather lachrymatory liquid weighed 8.2 g. (51% yield). Stored at −70° under nitrogen, it remained unchanged for nearly a year.

Anal. Calcd. for C_7H_9Br: C, 48.58; H, 5.24; Br, 46.18; *MR*D, 39.0. Found: C, 49.04; H, 5.19; Br, 46.15, 45.75; *MR*D, 45.7.

The absorption spectrum consisted of a smooth peak entirely devoid of fine structure; λ_{max} 272 mμ (isoöctane), ϵ 31,200.

The steric configuration of this bromide would be expected to be the same as that of the starting material, or approximately so.

1,3,5,7,9,11,13-Tetradecaheptaene.—When bromoheptatriene was coupled with sodamide as previously described, the expected heptaene peaks appeared, but only a minute trace of the compound was formed. A better yield (though still well below 1%) was obtained by quickly adding the bromide (2.2 g., in 10 ml. of ether) to a liquid ammonia solution of slightly less than one equivalent of potassamide, prepared *in situ* from potassium. A transient dark-violet color was observed. The final orange extract, in 50% methylene dichloride–hexane, was dried, filtered, and immediately chromatographed on a 3 × 25-cm. alumina column, precooled to 5°, developing with the same solvent. The main, red-fluorescent zone required 750 ml. of solvent for substantially complete elution. It was sterically inhomogeneous, the first λ_{max} (isoöctane) ranging from 388.1 mμ early in the fraction to 390.4 mμ at its end. This eluate was considerably richer in a triene, λ_{max} 264 mμ, than in the desired heptaene. The first two-thirds (A) and the final third (B) were separately vacuum-concentrated to dryness with a trace of hydroquinone; nitrogen was admitted, and 10 ml. of 10% ether–alcohol was added to dissolve the non-heptaene constituents. After 12 hours at −40°, filtration with cold alcohol rinses gave 7.5 mg. (vacuum-dry weight) of minute golden-yellow flakes from (A) and 2 mg. from (B). The material from (B) was dissolved in a little ether (not all was soluble) and diluted with isoöctane. The resulting absorption spectrum (Fig. 1) showed an ϵ_{max} of only 36,000; the compound was therefore still very impure. The 255-265-275 triplet system in this spectrum is no doubt attributable in large measure to persisting triene contamination rather than to the true *cis*-peak.

In isoöctane, the absorption peaks appeared at 332.3, 349.7, 367.9 and 390.0 mμ. In 95% ethanol, the long wave length peak occurred at 391.4 mμ; the shape was identical.

The solid from fraction (A) gave a curve of substantially identical shape, though much higher at 265 mμ, with the $\lambda\lambda_{max}$ occurring at 331.1, 348.4, 366.4 and 388.5 mμ (isoöctane). A catalytic amount of iodine was added, and the solution was illuminated with a 100-watt bulb. After 80 minutes, all of the $\lambda\lambda_{max}$ had increased by 1.0 mμ; and although the height of the main absorption peaks had scarcely altered, that of the 265-mμ peak had decreased by 50%. These changes indicate the presence of a *cis* isomer (or isomers) in fraction (A).

Tetradecaheptaene had no detectable odor. The Carr–Price reagent gave a faint greenish-blue, which was stronger in the specimens richer in the triene contaminant. (Tetradecahexaene gives an indigo-blue.[10])

Apparatus.—The spectrophotometer used was a Beckman model DU, whose wave length scale, above 250 mμ, had been calibrated to the nearest 0.05 mμ against a mercury lamp.

Acknowledgment.—For the analyses, I am indebted to Mr. Joseph Grodsky of this Laboratory.

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Diaryloxyalkane Derivatives. Some Miscellaneous Diphenoxypropanes[1]

BY FREEMAN H. MCMILLAN[2]

RECEIVED MAY 15, 1952

As part of a program leading to the preparation of some moderately high molecular weight compounds several new derivatives of 1,3-diphenoxypropane have been prepared.

It has been found that by substituting ethylene glycol for ethanol as the solvent for the reaction between trimethylene bromide and the potassium salt of a phenol and heating to 130° the time required for the reaction is materially shortened. For example, potassium *p*-nitrophenoxide was condensed with trimethylene bromide in ethylene glycol at 130° for one hour giving a 61% yield of *p,p'*-dinitro-1,3-diphenoxypropane[3] whereas the same reaction in refluxing ethanol for three hours gave only a 22% yield. An additional advantage of this procedure is that even the more difficultly soluble potassium salts, *e.g.*, potassium *p*-nitrophenoxide, are more soluble in this solvent than in ethanol. Either the anhydrous potassium salt of the phenol may be used or the theoretical amount of 85% potassium hydroxide may be dissolved in the ethylene glycol with the phenol and the trimethylene bromide.

p,p'-Dinitro-1,3-diphenoxypropane was reduced with Raney nickel in quantitative yield to the corresponding diamine. This in turn was converted to the N,N'-dibenzyl derivative by reduction with Raney nickel in the presence of benzaldehyde. The intermediate Schiff base was also isolated and characterized. Treatment of *p,p'*-diamino-1,3-diphenoxypropane with hydrogen chloride and phosgene in refluxing toluene gave 1,3-diphenoxypropane *p,p'*-diisocyanate.

Two carboxylic acid derivatives of 1,3-diphenoxypropane were prepared. Ethyl *p*-hydroxybenzoate was condensed with trimethylene bromide in a solution of potassium hydroxide in ethylene glycol. The resulting diester was hydrolyzed to 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid

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[14] I. N. Nazarov and L. B. Fisher, *Zhur. Obshchei Khim.*, **20**, 1107 (1950) [*C. A.*, **44**, 9460 (1950)]. These authors prepared heptatrienol by an allylic rearrangement, which by analogy with pentadienol (I. M. Heilbron, *et al.*, reference 8) would undoubtedly furnish a *trans–trans* product.

[1] For previous papers *cf.* J. A. King, THIS JOURNAL, **66**, 2076 (1944), and J. A. King and F. H. McMillan, *ibid.*, **67**, 336 (1945).

[2] Warner Institute for Therapeutic Research, 113 West 18th Street, New York 11, N. Y.

[3] J. A. Goodson, *et al.*, *Brit. J. Pharmacol.*, **3**, 62 (1948), report m.p. 132°.

with aqueous sodium hydroxide. *m*-Hydroxyacetophenone similarly gave *m,m'*-diacetyl-1,3-diphenoxypropane which underwent the Willgerodt reaction with sulfur and morpholine[4] giving 1,3-diphenoxypropane-*m,m'*-diacetic acid.

Experimental[5,6]

***p,p'*-Dinitro-1,3-diphenoxypropane.**—A mixture of potassium *p*-nitrophenoxide (35.4 g., 0.20 mole), trimethylene bromide (20.2 g., 0.10 mole) and ethylene glycol (60 ml.) was stirred and heated at 130° for one hour. The cooled mixture was poured into cold water (600 ml.) giving 19.5 g. (61%) of product melting at 122–125°; after two crystallizations from ethanol it melted at 129.5–130.5°.

***p,p'*-Diamino-1,3-diphenoxypropane.**—When the above dinitro compound (120 g., 0.375 mole), dissolved in ethyl acetate (1 liter), was shaken with Raney nickel and hydrogen at 60° and 500 p.s.i., the theoretical amount of hydrogen was taken up in two hours. The residue, after removal of catalyst and solvent, weighed 97 g. (100%) and melted at 102–105°. An analytical sample, after two crystallizations from Skellysolve C, melted at 104.5–105.5°.

Anal. Calcd. for $C_{15}H_{18}N_2O_2$: N, 10.93. Found: N, 10.89 (by titration with acetous perchloric acid).

***p,p'*-Dibenzalamino-1,3-diphenoxypropane.**—*p,p'*-Diamino-1,3-diphenoxypropane (12.9 g., 0.05 mole) and benzaldehyde (10.6 g., 0.10 mole) were mixed and heated until a uniform melt was obtained (internal temperature about 130°). The cooled mixture was crystallized from ethanol giving 17.5 g. (80%) of product melting at 120–125°. An analytical sample, after two more crystallizations from ethanol, melted at 125–126.5°.

Anal. Calcd. for $C_{29}H_{26}N_2O_2$: N, 6.45. Found: N, 6.40 (Kjeldahl).

***p,p'*-Dibenzylamino-1,3-diphenoxypropane.**—The above dibenzal compound was hydrogenated over Raney nickel in ethyl acetate at 60°. After one crystallization from ethanol the diamine was obtained in 70% yield melting at 88–89°. An analytical sample, after an additional crystallization from ethanol, melted at 88.5–89.5°.

Anal. Calcd. for $C_{29}H_{30}N_2O_2$: N, 6.38. Found: N, 6.25 (by acetous perchloric acid titration).

This compound was also obtained in 82% yield melting at 83–87° by direct hydrogenation of a solution of *p,p'*-diamino-1,3-diphenoxypropane and benzaldehyde in ethyl acetate.

1,3-Diphenoxypropane *p,p'*-Diisocyanate.—*p,p'*-Diamino-1,3-diphenoxypropane (25.0 g., 0.10 mole) was suspended in dry toluene (100 ml.). This mixture was heated to reflux with stirring and then saturated with hydrogen chloride. Phosgene was then bubbled into the mixture with continued refluxing and stirring for three hours at which time there was no further evidence of clearing of the mixture. The hot mixture was filtered through Filter-cel and the toluene was removed from the filtrate by distillation *in vacuo*. The residue on cooling crystallized; it weighed 21.7 g. (70%) and melted at 100–105°. An analytical sample, after crystallization from Skellysolve C, melted at 103–105°.

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: N, 9.03. Found: N, 8.71 (micro-Dumas).

***p,p'*-Dicarbethoxy-1,3-diphenoxypropane.**—A mixture of ethyl *p*-hydroxybenzoate (83 g., 0.50 mole), trimethylene bromide (50.5 g., 0.25 mole) and 85% potassium hydroxide (33 g., 0.50 mole) was heated at 130° with stirring for three hours. The cooled mixture was poured into water (1500 ml.) giving a solid which after crystallization from ethanol (500 ml.) weighed 58 g. (63%) and melted at 93–100°. An analytical sample, after two more crystallizations from ethanol, melted at 102–105°.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.74; H, 6.45. Found: C, 67.70; H, 6.39.

1,3-Diphenoxypropane-*p,p'*-dicarboxylic Acid.—The above diester (7.4 g., 0.02 mole) was refluxed with 20% sodium hydroxide solution (175 ml.) for three hours. Chilling gave 6.5 g. (90%) of the disodium salt of 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid. This solid was boiled with ethanol (250 ml.) to remove any unhydrolyzed ester, then taken up in water (30 ml.) and reprecipitated by pouring into ethanol (250 ml.). The product weighed 5.9 g. (82%).

Anal. Calcd. for $C_{17}H_{14}O_6Na_2$: Na, 12.78. Found: Na, 12.90.

This disodium salt was taken up in water (50 ml.) and the solution was acidified by slow addition of dilute hydrochloric acid. The 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid which separated weighed 4.9 g. (77% based on ester used) and melted at 305–309°. The compound is extremely insoluble in water and no suitable recrystallization solvent could be found.

Anal. Calcd. for $C_{17}H_{16}O_6$: neut. equiv., 158. Found: neut. equiv., 163.

***m,m'*-Diacetyl-1,3-diphenoxypropane.**—A mixture of *m*-hydroxyacetophenone (272 g., 2.0 mole), trimethylene bromide (202 g., 1.0 mole) and 85% potassium hydroxide (132 g., 2.0 mole) in ethanol (1.0 liter) was refluxed with stirring for 14 hours. The solid which formed when the cooled mixture was poured into water was so fine it filtered with great difficulty; consequently it was filtered with the aid of Filter-Cel from which it was subsequently removed by extraction with chloroform. The residue, after removal of the chloroform by distillatin *in vacuo*, rapidly crystallized, weighed 221 g. (71%) and melted at 71–80°. An analytical sample, after two crystallizations from ethanol, melted at 91–93°.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.00; H, 6.41. Found: C, 72.97; H, 6.66.

1,3-Diphenoxypropane-*m,m'*-diacetic Acid.—A mixture of *m,m'*-diacetyl-1,3-diphenoxypropane (15.6 g., 0.05 mole), sulfur (8.0 g., 0.25 mole) and morpholine (17.4 g., 0.20 mole) was heated at reflux for one hour. The reaction mixture was taken up in chloroform (250 ml.) and the chloroform solution was washed with dilute hydrochloric acid. The chloroform was removed under vacuum and the residue was hydrolyzed by refluxing with 50% (by weight) sulfuric acid (200 ml.). The crude diacid was removed from the cooled hydrolysis mixture by filtration and after crystallization from water (4 l.) it weighed 4.8 g. (28%) and melted at 168–170°. An analytical sample, after crystallization from methanol, melted at 171–172.5°.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.28; H, 5.81. Found: C, 66.15; H, 5.72.

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(4) E. Schwenk and E. Bloch, THIS JOURNAL, **64**, 3051 (1942); J. A. King and F. H. McMillan, *ibid.*, **68**, 2335 (1946).

(5) Melting points are uncorrected.

(6) Analyses were performed in the analytical laboratories of this Institute under the direction of Mr. Morris E. Auerbach.

Condensations of Cinchoninaldehyde. V.[1] With Phenylacetonitriles

BY ARTHUR P. PHILLIPS

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Cinchoninaldehyde reacted rapidly with a variety of substituted phenylacetonitriles to produce the α-(substituted phenyl)-β-(4-quinolyl)-acrylonitriles (see Table I).

When an alcohol solution of the reactants was treated with alkali the mixture turned first yellow, then orange, and finally deep red and the colorless product separated, all within less than a minute. The intense color changes may be associated with anionic intermediates.

The condensation of the *p*-nitrophenylacetonitrile, expected to be more reactive because of activation by the *p*-nitro, gave a poor yield of IV (Table I) in the usual procedure with alkali catalyst. When a more weakly basic catalyst, such as diethylamine or piperidine, was used the reaction gave good yields of IV. Apparently with the more reactive nitrile the stronger base catalyst is detrimental.

In the condensation with *o*-methoxyphenyl-

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(1) Paper IV, THIS JOURNAL, **70**, 452 (1948).