allowed to exchange in basic solution. The recovered (90%) *o*-hydroxy-(benzylidene-α-C^{14})-acetophenone was isomerized to flavanone-2-C^{14} in 80% yield. Since future work will require more highly hydroxylated compounds rather than flavanone itself, no effort was devoted to finding the best conditions for complete exchange, nor in discovering the best recovery methods. It is obvious that the efficiency of the radioactivity transfer would be improved by use of a smaller molar proportion of the benzaldehyde-α-C^{14} and by carrying out the exchange under such conditions that by-product formation is minimized.

Experimental

2'-Hydroxy-(benzylidene-α-C^{14})-acetophenone.—A 0.5-g. portion of benzaldehyde-α-C^{14}, whose millimolar activity was 1.49 microcuries, was added to a cooled solution of 1.1 g. of 2'-hydroxybenzylideneacetophenone,[4a] 2 ml. of 20% sodium hydroxide and 20 ml. of ethanol. The solution was stirred for 60 hours at room temperature, diluted with water and acidified. The 2'-hydroxy-(benzylidene-α-C^{14})-acetophenone which separated was recrystallized twice from methanol to give 0.98 g. (90%) of recovered product, m.p. 86°, whose millimolar activity was 0.130 microcurie.[8]

Flavanone-2-C^{14}.—A 0.5-g. sample of the 2'-hydroxy-(benzylidene-α-C^{14})-acetophenone was dissolved in 30 ml. of ethanol containing 1 ml. of 1% sodium hydroxide. The solution was stirred at room temperature for 24 hours, adjusted to *p*H 6 with dil. hydrochloric acid, and diluted with water.

The product which precipitated from the chilled solution weighed 0.4 g. (80%), m.p. 74°,[3a] after five crystallizations from methanol; radioactivity, 0.130 μc./mmole.

(8) Radioactivity measurements were made by wet combustion of 10- to 20-mg. samples of organic compounds to carbon dioxide and determination of the ion current with a vibrating-reed electrometer; *cf.* O. K. Neville, THIS JOURNAL, **70**, 3501 (1948).

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2-Isopropyl-1-naphthol

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In 1929, Meyer and Bernhauer[1] reported the preparation of a compound which they described as 2-isopropyl-1-naphthol (m.p. 65–66°, benzoate ester, m.p. 121). This material was obtained by the potassium hydroxide fusion of a sulfonic acid prepared by the sulfonation of 2-isopropylnaphthalene.

We have recently had occasion to synthesize 2-isopropyl-1-naphthol by a less ambiguous method and obtained a product, m.p. 47–48°, which yielded a benzoate, m.p. 67–68°. The synthesis is also of interest in that several new compounds were prepared as intermediates.

Experimental

Diethyl Isopropyl-(β-phenylethyl)-malonate (I).—Two experiments were made to obtain an adequate supply of this compound. In the first batch, a sodium dispersion was prepared from 11.5 g. (0.5 mole) of sodium and 200 ml. of toluene. The dispersion was stirred and maintained at 25–35° while a solution of 101 g. (0.5 mole) of diethyl isopropylmalonate[2] in 200 ml. of toluene was added. To the resultant slurry was then added 92.5 g. (0.5 mole) of β-phenylethyl bromide. The mixture was heated and became homogeneous at 71° and began to precipitate sodium bromide at 99°. Titration of a sample with acid after heating for one hour at 100° indicated 65% reaction. The mixture was heated at reflux for an additional four hours. The product was washed with water, a few drops of acetic acid being used in the final wash to remove traces of base. The toluene and less volatile materials were distilled, the distillation being stopped when the pot temperature reached 140° (17 mm.). The residue was then distilled from a Claisen flask to yield 43 g. (0.14 mole, 28% theory), of I, b.p. 120–130° (1–2 mm.), n^{20}D 1.4857.

Anal. Calcd. for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.0; H, 8.51.

A second run using twice the quantities employed above yielded 65 g. (0.21 mole, 21% theory) of I.

Ethyl 2-Isopropyl-4-phenylbutyrate (II).—This compound was produced inadvertently by the partial hydrolysis and decarboxylation of I. A solution of 100 g. (0.33 mole) of I and 271 ml. of 2.66 *N* ethanolic potassium hydroxide was refluxed for seven hours. Water (150 ml.) was then added and the alcohol removed by distillation. The resulting aqueous solution was extracted with ether to remove traces of neutral organics, then acidified and the product separated by ether extraction. Fractionation through a helix-packed column yielded 34 g. (0.14 mole, 44% theory) of II boiling at 161° (17 mm.).

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.0; H, 9.28.

There was also obtained 23 g. of the corresponding acid III and 5 g. of a mixture of II and III.

2-Isopropyl-4-phenylbutyric Acid (III).—The 34-g. portion of II and the 5-g. fraction of acid–ester mixture obtained in the above experiment were combined and refluxed with 50 ml. of 5.0 *N* 95% ethanolic potassium hydroxide for eight hours. Water was then added and the alcohol removed by distillation. Acidification of the aqueous solution yielded 23 g. of III. This material was combined with the acid obtained in the above experiment and distilled from a claisen flask to yield 52 g. of III, m.p. 56–58.5°, b.p. 168–170° (6 mm.). Recrystallization from isoöctane yielded a product having a melting point of 59.5–60°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.4; H, 8.75.

The anilide of III was prepared and upon recrystallization from isoöctane obtained as white crystals, m.p. 111–112°.

Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.2; H, 8.49; N, 5.31.

2-Isopropyl-1-tetralone (IV).—The cyclization of III was effected by a procedure similar to that used by Adkins and Davis[3] for the synthesis of 2-methyl-1-tetralone.

The acid chloride of III was prepared by adding 52.2 g. (0.25 mole) of phosphorus pentachloride portionwise to 41.2 g. (0.2 mole) of III dissolved in 200 ml. of benzene. The mixture was refluxed for 30 minutes, cooled to and maintained at 25–30° while 104 g. (0.4 mole) of stannic chloride was added dropwise. After standing for 30 minutes the product was poured into 170 ml. of 12 *N* hydrochloric acid. The organic layer was washed three times with 4 *N* hydrochloric acid and then three times with 5% sodium carbonate solution. The product was dried by distilling off the benzene–water azeotrope and fractionated through a helix-packed column to yield 32 g. (0.17 mole, 85% theory) of 2-isopropyl-1-tetralone (IV), b.p. 162° (18 mm.), n^{20}D 1.4512.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.5; H, 8.50.

The 2,4-dinitrophenylhydrazone of IV was prepared and recrystallized from ethanol as orange-red needles, m.p. 149–150°.

Anal. Calcd. for $C_{19}H_{20}N_4O_4$: C, 61.94; H, 5.47. Found: C, 61.9; H, 5.57.

2-Isopropyl-1-naphthol (V).—A mixture of 7.44 g. (0.040 mole) of 2-isopropyl-1-tetralone and 1.27 g. (0.040 mole) of sulfur was heated to 300° over a 10-minute period and maintained at 300 to 310° for four minutes. At the end of this time hydrogen sulfide evolution was virtually complete.

(1) H. Meyer and K. Bernhauer, *Monatsh.*, **53**, 721 (1929).

(2) C. S. Marvel and V. du Vigneaud, "Organic Syntheses," Coll. Vol. II, edited by A. H. Blatt, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 94.

(3) H. Adkins and J. W. Davis, THIS JOURNAL, **71**, 2955 (1949).

The product was given a quick distillation (1–2 mm.) to yield 6.5 g. of a yellow oil. The oil was extracted with 1.1 *N* sodium hydroxide solution to separate the naphthol as the sodium salt. Acidification of the aqueous phase yielded 4 g. of crude V. Recrystallizations from isoöctane gave pure 2-isopropyl-1-naphthol (V), m.p. 47–48°.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.5; H, 7.58.

The benzoate of V was prepared by reaction with benzoyl chloride in the presence of pyridine (as described by Meyer and Bernhauer[1]) and after recrystallization from ethanol and isoöctane was found to melt at 67–68°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.4; H, 6.16.

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Polybenzyls from Benzyl Alcohol and Sulfuryl Chloride

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Gladstone and Tribe[2] noted the production of hydrocarbons of the formula $(C_7H_6)_n$ on pouring benzyl bromide over a copper–zinc couple. Friedel and Crafts[3] obtained similar material of the same empirical formula by the action of aluminum chloride upon benzyl chloride, a reaction which was studied further by Jacobson,[4] who noted that the substance formed with stannic chloride contained 1.4% chlorine. The products were considered to be essentially polybenzyls formed from the polymerizing unit —  —CH_2—.

What is probably a closely similar material was formed in an attempt to prepare benzyl chlorosulfonate by the action of sulfuryl chloride upon benzyl alcohol. The product was a green solid which slowly turned pink on exposure to air. Its analysis was in accord with the formula $H(C_7H_6)_{10}Cl$. The chlorine may be a chain terminal unit. Hydrogen chloride and sulfur dioxide were evolved in the reaction, the stoichiometry of which is not established.

Experimental

In an attempt to prepare benzyl chlorosulfonate, 21.6 g. (0.2 mole) of benzyl alcohol was added slowly to 27 g. (0.2 mole) of sulfuryl chloride at 0°, according to the general procedure described by Binkley and Degering.[5] During the addition of benzyl alcohol (about 90 min.), hydrogen chloride was evolved continuously. The resultant pale yellow viscous liquid (which sometimes contained a small amount of solid material) was stable provided that the temperature was maintained below 5°. On warming to room temperature, the mixture underwent a vigorous exothermic reaction. Hydrogen chloride and sulfur dioxide were evolved and a greenish mud was produced which solidified on cooling and slowly turned pink on exposure to air. The resin as obtained was contaminated by trapped gases and by a sulfur-containing material. Purification was complicated by the tendency of the material to form emulsions. The original resin was dissolved in benzene, washed with water, and precipitated from the benzene with methanol, a white "milk" being decanted from the pink resinous material. The resin was washed free of organic solvents in boiling water and on cooling a slightly brittle, pinkish-brown resin was obtained; yield 3–5 g., m.p. *ca.* 60° with preliminary softening. The resin was readily soluble in benzene, dioxane, N,N-dimethylformamide, pyridine, chloroform, carbon tetrachloride and benzaldehyde. It was insoluble in water, ethanol, formamide, hexane, 1-butanol and *t*-butyl alcohol. It swelled or was slightly soluble in ether, acetone, ethyl acetate, butanone, diethylamine and benzyl alcohol.

Anal. Calcd. for $H(C_7H_6)_{10}Cl$: C, 89.76; H, 6.46; Cl, 3.79. Found: C, 89.24; H, 6.25; Cl, 3.87.

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(1) Fellow of the Foreign Research Scientists Program of the Foreign Operations Administration.

(2) J. H. Gladstone and A. Tribe, *J. Chem. Soc.*, **47**, 448 (1885).

(3) C. Friedel and J. M. Crafts, *Bull. soc. chim.*, [2] **43**, 53 (1885).

(4) R. A. Jacobson, THIS JOURNAL, **54**, 1513 (1932); see also M. Kikkawa and S. Tsuruta, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **53**, 405 (1950); *C. A.*, **47**, 345 (1953).

(5) W. W. Binkley with E. F. Degering, THIS JOURNAL, **60**, 2810 (1938).

The Anticholinesterase Activity of Arylarsonic and Diarylarsinic Acids

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Certain aromatic phosphonic and phosphinic acids are active as inhibitors of plasma cholinesterase.[1] In the present note we are reporting on the anticholinesterase activity of a series of aromatic arsonic and arsinic acids.[2]

Experimental

p-Hydroxybenzenearsonic acid was Eastman Kodak White Label; *p*-arsanilic acid was obtained from the B. L.

TABLE I

ANTICHOLINESTERASE ACTIVITY OF ARYLARSONIC AND DIARYLARSINIC ACIDS

Compound	I_{50}[a] (moles/l.)
Arylarsonic acids	
$C_6H_5AsO_3H_2$	1.1×10^{-5}
m-$ClC_6H_4AsO_3H_2$	2×10^{-5}
p-$ClC_6H_4AsO_3H_2$	4×10^{-5}
p-$CH_3C_6H_4AsO_3H_2$	4×10^{-5}
p-$BrC_6H_4AsO_3H_2$	4×10^{-5}
o-$ClC_6H_4AsO_3H_2$	7×10^{-5}
p-$HOC_6H_4AsO_3H_2$	1.2×10^{-4}
p-$NH_2C_6H_4AsO_3H_2$	1.2×10^{-4}
o-$BrC_6H_4AsO_3H_2$	1.4×10^{-4}
m-$O_2NC_6H_4AsO_3H_2$	4×10^{-4}
p-$O_2NC_6H_4AsO_3H_2$	8×10^{-4}
p-$NH_2O_2SC_6H_4AsO_3H_2$	4×10^{-3}
Diarylarsinic acids	
(*o*-$BrC_6H_4)_2AsO_2H$	5×10^{-5} (2×10^{-4})[b]
(*o*-$ClC_6H_4)_2AsO_2H$	5×10^{-5} (2×10^{-4})[b]
(*o*-$BrC_6H_4)C_6H_5AsO_2H$	5×10^{-4}
(*m*-$ClC_6H_4)_2AsO_2H$	1×10^{-3} (1×10^{-3})[b]
(*p*-$ClC_6H_4)_2AsO_2H$	2×10^{-3}
(*m*-$O_2NC_6H_4)_2AsO_2H$	[c]
(*p*-$O_2NC_6H_4)_2AsO_2H$	[c]

[a] Concentration necessary for 50% inhibition when the enzyme and inhibitor were incubated for 20 minutes prior to the addition of the substrate solution. The value given is the final concentration after the addition of the substrate solution. [b] The value in parentheses was obtained with a second batch of the arsinic acid. [c] No significant inhibition at a concentration of 0.003 *M*.

(1) L. D. Freedman, H. Tauber, G. O. Doak and H. J. Magnuson, THIS JOURNAL, **75**, 1379 (1953).

(2) D. Vincent and P. Brygoo, *Bul. soc. chim. biol.*, **28**, 174 (1946), investigated the effect of a number of arsenical drugs on serum cholinesterase and noted that the few aromatic arsonic acids tested were inhibitors.