

**Methyl Ester of Indene-2-carboxylic Acid.**—Indene-2-carboxylic acid was prepared by hydrolysis of diethyl indene-2,3-dicarboxylate, obtained by treatment of diethyl benzyloxalacetate with cold sulfuric acid.<sup>16</sup> The acid (3 g.) was esterified with diazomethane in ethereal solution. The solid (2.9 g.), obtained by evaporation of the organic solvent, was purified by crystallization in petroleum ether (b.p. 60–80°) and by sublimation *in vacuo*, m.p. 82–83.5°. The product was homogeneous by gas chromatography and could be separated from methyl indene-3-carboxylate on the above mentioned column.

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>O<sub>2</sub>: C, 75.84; H, 5.79. Found: C, 75.73; H, 5.76.

The n.m.r. and double resonance spectra in deuteriochloroform were obtained on a Varian Associates H. R. 100 spectrometer using the method of Johnson.<sup>17</sup>

(16) J. Bougault, *Compt. rend.*, **159**, 745 (1914).

(17) L. F. Johnson, "Varian Technical Information Bulletin," Vol. III, No. 3, 5, 1962.

## A Convenient Preparation of Methanol-*d*<sup>1</sup>

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*Received August 6, 1964*

The  $\alpha$ -hydrogens of esters are conveniently exchanged with methanol-*d* (CH<sub>3</sub>OD) as the solvent, but a good preparation of this alcohol has been lacking.

Among the methods used previously are the hydrolysis of dimethyl oxalate with D<sub>2</sub>O and sodium carbonate,<sup>3</sup> the exchange of methanol with D<sub>2</sub>O,<sup>4</sup> the hydrolysis of trimethyl borate with D<sub>2</sub>O,<sup>5</sup> and the reaction of sodium methoxide or magnesium methoxide with D<sub>2</sub>O.<sup>6</sup> We have used most of these methods and have also utilized the acid-catalyzed hydrolysis of 2,2-dimethoxypropane.<sup>7</sup>

None of these methods is really satisfactory, especially for the preparation of reasonable quantities of methanol-*d* of high isotopic purity. Such objections do not apply to the preparation described below.

This method involves the hydrolysis of commercially available dimethyl carbonate. However, in one experiment a mixture of 800 g. of dimethyl carbonate, 20 g. of D<sub>2</sub>SO<sub>4</sub> and 196 g. of D<sub>2</sub>O required 3 weeks of refluxing for complete reaction. The reaction rate could undoubtedly be increased by using more acid, but a separate preparation of D<sub>2</sub>SO<sub>4</sub> is an important limitation. This inconvenience was avoided by an *in situ* preparation of the acid catalyst using dimethyl sulfate since hydrolysis of this ester is rapid. The experimental procedure below uses quantities such that reaction is complete in 3 days of refluxing. A somewhat larger ratio of dimethyl sulfate could undoubtedly be used but a too rapid hydrolysis rate should be avoided because of the evolution of CO<sub>2</sub>.

(1) This research was supported in part by a grant from the National Science Foundation.

(2) (a) National Institutes of Health Postdoctoral Fellow, 1963–1964; (b) National Science Foundation Summer Cooperative Predoctoral Fellow, 1964.

(3) H. O. House and V. Kramer, *J. Org. Chem.*, **28**, 3362 (1963).

(4) K. Wiberg, *J. Am. Chem. Soc.*, **77**, 5987 (1955).

(5) C. G. Swain and M. M. Labes, *ibid.*, **79**, 1084 (1957).

(6) C. G. Swain, J. T. McKnight, and V. P. Kreiter, *ibid.*, **79**, 1088 (1957).

(7) F. R. Jensen, unpublished results.

Since diethyl carbonate and diethyl sulfate are also available commercially, a similar preparation of ethanol-*d* should be feasible.<sup>8</sup>

## Experimental

Dimethyl carbonate (Eastman White Label), 400 g. (4.44 moles), and deuterium oxide (Bio-rad Labs., Richmond, Calif.), 100 g. (5.00 moles), were placed in a carefully dried 1-l. one-necked flask. Dimethyl sulfate (Eastman practical grade), 16 g. (0.13 mole), was added and the flask was attached to two reflux condensers arranged in series (initial rapid evolution of carbon dioxide may entrain some liquid). The flask contents were heated to reflux with provision for moisture exclusion. After 72 hr. the disappearance of the carbonyl stretching frequency of dimethyl carbonate in the infrared indicated that the reaction was complete. The methanol-*d* was distilled directly from the reaction flask through a 30-cm. Vigreux column. One further distillation from a small amount of sodium sufficed to yield 275 g. (8.34 moles, 94% yield) of gas chromatographically pure (Carbowax 20M column) methanol-*d*, b.p. 66–66.5°.

The amount of deuterium substitution was obtained conveniently from the n.m.r. spectrum<sup>9</sup> of methanol-*d*. The area under the hydroxyl peak was compared with one of the two peaks due to C<sup>13</sup> splitting. From the relative intensities, the methanol-*d* was found to contain 98.6 ± 0.4% deuterium.

(8) NOTE ADDED IN PROOF.—This preparation has now been carried out successfully. Because of a slower hydrolysis rate, double the quantity of diethyl sulfate is convenient.

(9) A Varian A-60 nuclear magnetic resonance spectrometer was used.

## Stability of the Carbon-Phosphorus Bond in Trichloromethylphosphonate Esters. Ether Formation in Reactions with Alcohols and Phenols

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Esters of phosphonic acids containing a trichloromethyl group attached to phosphorus are sensitive to alkali, liberating chloroform,<sup>1</sup> but it is now generally accepted that in the absence of alkali the C–P bond is stable. The reaction of trichloromethylphosphonate esters with primary amines was believed at first to be a case of C–P bond scission,<sup>2</sup> but later work,<sup>3</sup> which has been amply substantiated,<sup>4</sup> showed that the products were not amides but amine salts, the esters behaving in this reaction as alkylating agents. The products of the reaction of diethyl trichloromethylphosphonate with aniline, for example, were N-ethylaniline and the aniline salt of ethyl hydrogen trichloromethylphosphonate.<sup>3,4</sup>

More recently, the reaction of diethyl trichloromethylphosphonate with ethanol was examined to determine

(1) I. S. Bengelsdorf, *J. Am. Chem. Soc.*, **77**, 6611 (1955).

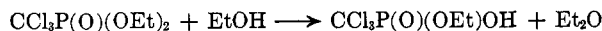
(2) G. Kamai, *Dokl. Akad. Nauk SSSR*, **55**, 219 (1947); *Chem. Abstr.*, **41**, 5863 (1947). A similar behavior was implied for ethyl phenyltrichloromethylphosphonate by G. Kamai, *Zh. Obshch. Khim.*, **18**, 443 (1948); *Chem. Abstr.*, **42**, 7723 (1948).

(3) (a) A. Ya. Yakubovich and V. A. Ginsburg, *Dokl. Akad. Nauk SSSR*, **82**, 273 (1952); *Chem. Abstr.*, **47**, 2685 (1953); (b) A. Ya. Yakubovich and V. A. Ginsburg, *Zh. Obshch. Khim.*, **24**, 1465 (1954); *Chem. Abstr.*, **49**, 10834 (1955).

(4) (a) K. C. Kennard and C. S. Hamilton, *J. Am. Chem. Soc.*, **77**, 1156 (1955); (b) C. E. Griffin, *Chem. Ind. (London)*, 415 (1958); (c) Tzeng-Shou Tung and Shyh-Tsong Chern, *Hua Hsueh Hsueh Pao*, **24**, 30 (1958); *Chem. Abstr.*, **53**, 3113, 2114s (1959).

whether the ester was a possible intermediate in the formation of triethyl phosphate and chloroform from triethyl phosphite, carbon tetrachloride, and ethanol.<sup>5</sup> The ester was recovered unchanged after being boiled in ethanol for 4 hr.<sup>5</sup>

In the present work it is shown that a reaction *does* take place on prolonged boiling, though not in the sense indicated above. Prolonged boiling of a solution of diethyl trichloromethylphosphonate in ethanol produced a low-boiling material identified as **diethyl ether**. The residue, which was strongly acidic, was identified as **ethyl hydrogen trichloromethylphosphonate**. The reaction therefore took the following path.



The ester behaved in this reaction as an alkylating agent, as in the reaction with amines. The mildness of the reaction, however, was remarkable because such alkylations usually require a catalyst and temperatures of the order of 200°.<sup>6</sup>

No alkylation was observed when diethyl ethylphosphonate or diethyl acetylphosphonate was refluxed with ethanol for the same length of time. The strong  $-I$  inductive effect of the trichloromethyl group appears to be necessary.

The alkylation of phenol by diethyl trichloromethylphosphonate produced an 85% yield of phenetole in 4.5 hr. at 150°.

#### Experimental

**Reaction with Ethanol.**—A solution of 25.6 g. (0.1 mole) of diethyl trichloromethylphosphonate<sup>7</sup> in 100 ml. of anhydrous ethanol was heated at total reflux in a small distillation assembly which included a K-head and a 3-in. column packed with glass helices. The vapor temperature dropped over an 8-hr. period from 79.5 to 54°, while the liquid temperature remained constant at 80°. A test for chloroform with pyridine and 5 *N* sodium hydroxide<sup>8</sup> was negative. The low-boiling material was then drawn off from time to time as required to keep the vapor temperature above 78°, and fresh ethanol was added to the boiling solution as required to maintain the original volume. The distillation was stopped after 26 hr. when it was evident that no more low-boiling material was being formed. The distillate (200 ml.) was redistilled, giving 2.0 g., b.p. 36°,  $n_D^{25}$  1.34, and 2.5 g., b.p. 43–74°,  $n_D^{25}$  1.3580. Both fractions contained diethyl ether, identified by its odor and infrared spectrum.

The undistilled portion of the reaction proper was stripped of solvent under vacuum, leaving 26.6 g. of strongly acidic residue,  $n_D^{25}$  1.4631. Titration with 0.1 *N* sodium hydroxide gave a curve with inflections at 32.0 and 33.9 ml./g., corresponding to 0.080 mole of ethyl hydrogen trichloromethylphosphonate and 0.005 mole of trichloromethylphosphonic acid. Together they accounted for 72.3% of the residue, the remainder being neutral, presumably ethanol. A portion of the product was dissolved in benzene and treated dropwise with aniline, giving the known aniline salt of ethyl hydrogen trichloromethylphosphonate, m.p. 186.5° dec. (cor.) after recrystallization from ethanol.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{13}\text{Cl}_3\text{NO}_3\text{P}$ : N, 4.37. Found: N, 4.35.

The literature<sup>3,4</sup> gives melting points ranging from 174° dec. to 198° dec. for this salt.

Neither diethyl ethylphosphonate nor diethyl acetylphosphonate showed any evidence of reaction with ethanol under these conditions, save for a small increase in acidity. The refractive indices of the recovered esters were unchanged.

(5) P. C. Crofts and I. M. Downie, *J. Chem. Soc.*, 2559 (1963).

(6) Y. Runavot, P. Schneebeli, D. Chabrier, and R. Ramain, *Compt. rend.*, **253**, 1573 (1961).

(7) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **69**, 1002 (1947).

(8) F. Feigl, "Spot Tests in Organic Analysis," 5th Ed., Elsevier Publishing Co., Amsterdam, 1956, p. 313.

**Reaction with Phenol.**—A solution of 51.2 g. (0.2 mole) of diethyl trichloromethylphosphonate and 18.8 g. (0.2 mole) of phenol was heated at 150° for 4.5 hr. and then distilled, giving 20.7 g. (85%) of a fraction, b.p. 68–70° (18 mm.),  $n_D^{25}$  1.5056, identified by its infrared spectrum as phenetole.

### The Dehydrative Dimerization of 2- and 4-Methyl-5-imidazolecarboxylic Acids

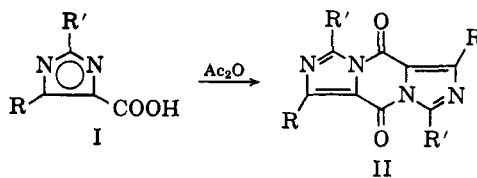
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Received January 28, 1964

In connection with our imidazole studies we have had occasion to treat a number of imidazolecarboxylic acids with acetic anhydride.

4-Methyl-5-imidazolecarboxylic acid (Ia), upon refluxing in acetic anhydride, deposited on cooling a crystalline product, m.p. 238–239°. Infrared examination revealed the absence of carboxylic acid absorption and the appearance of a carbonyl band at 1690  $\text{cm}^{-1}$ . Loss of a molecule of water was indicated from analytical results, with titration data furnishing a molecular weight of ca. 215. The material reacted readily with aniline, giving 4-methyl-5-imidazolecarboxanilide. These data led us to believe that the compound in question was, in fact, a dehydrated dimer of Ia, corresponding to structure IIa.



a, R = CH<sub>3</sub>; R' = H  
b, R = H; R' = CH<sub>3</sub>

Structures of this type are not entirely unknown. For example the action of thionyl chloride on 2-benzimidazolecarboxylic acid has been reported to yield dibenzimidazo[1,2-*a*:1',2'-*d*]tetrahydropyrazine-6,13-dione.<sup>1</sup> Likewise thionyl chloride is known to effect a comparable dehydrative dimerization of 4,5-diphenyl-2-imidazolecarboxylic acid.<sup>2</sup> Pyman,<sup>3</sup> however, failed to get any reaction between 4-imidazolecarboxylic acid and thionyl chloride, an observation which was subsequently confirmed by Weidenhagen.<sup>4</sup> Our own observations, as seen in the light of the cited literature reports, led us to investigate the effect of thionyl chloride on Ia. Upon refluxing a suspension of these reagents, only 4-methyl-5-imidazolecarboxylic acid hydrochloride was obtained. However, addition of DMF to the reaction mixture initiated an exothermic reaction, leading not to the formation of IIa, but giving instead the acid chloride hydrochloride, identified by transformation to the carboxanilide.

(1) R. A. Copeland and A. R. Day, *J. Am. Chem. Soc.*, **65**, 1072 (1943).

(2) R. Gompper, E. Hoyer, and H. Herlinger, *Ber.*, **92**, 550 (1959).

(3) F. L. Pyman, *J. Chem. Soc.*, 109 (1916).

(4) R. Weidenhagen and H. Wegner, *Ber.*, **70**, 2309 (1937).