

The 1-acylated hydantoin were prepared by a method hitherto unreported for this class of compounds. The reaction time for the synthesis of the acylated hydantoin is much less by using an acid chloride as the acylating agent and carrying out the reaction in pyridine than by the usual method of heating the hydantoin directly with an acid anhydride.⁵ A solution of 0.02 mole of the hydantoin in 10 ml. of pyridine was cooled and 0.02 mole of the acid chloride was added slowly. The mixture then was refluxed for 20–30 minutes. The reaction mixture was poured onto crushed ice and the granular material which separated out was filtered off and recrystallized. The position of the acyl group in the products is inferred from their solubility in alkali.

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The Synthesis of Radioactive Diazinon Using P³²

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Investigations of the mode of action of O,O-diethyl-O-(2-isopropyl-6-methyl-4-pyrimidinyl) thiophosphate (Diazinon) have been difficult because of the lack of suitable analytical techniques. The use of a radioactive label in the Diazinon molecule offers a partial solution to the problems of investigating its distribution and metabolism in both mammals and insects.

It is possible to label Diazinon with C¹⁴, S³⁵, or P³². Since the later isotope offers an easy synthetic route and is more readily measured radiometrically, elemental red phosphorus was selected as a starting material. This material was submitted to Oak Ridge National Laboratories for service irradiation to a specific activity of approximately 50 mc. per gram. The synthesis of phosphorus trichloride is based on the method of Forbes, *et al.*² The two step chlorination and the use of the powdered antimony³ were utilized to increase the specific activity and yield of phosphorus trichloride.

No physical constants were obtained on the active products. The *n*^{25D} of Diazinon from repeated practice runs with inactive materials was 1.4978. The values reported in the literature are 1.4978–1.4881.⁴ The specific activity of the product of two

active runs ranged from 1.51 to 1.62 mc./g. Bioassays using the common housefly gave an LD₅₀ of 2.4 μ g./g. of flies for the active product compared with a value of 2.5 for a sample of the inactive product. Paper chromatographic analyses of the labeled product, using the methods of Kaplanis, *et al.*⁵ gave an *R*_f of 0.86 using a polar stationary phase and 0.43 using an apolar stationary phase as contrasted with *R*_f's of 0.86 and 0.42, respectively, for samples of the inactive product. No radioactive contamination of the Diazinon was detected using either system. Determination of the *R*_f of the labeled O,O-diethyl chlorothiophosphate by radiometric means gave values of 0.87 for the polar stationary system and 0.79 for the apolar stationary system. Paper chromatographic analyses of unreacted diethyl chlorothiophosphate distilled from the final reaction mixture indicated two radioactive spots from the apolar stationary system. The second spot had a value corresponding to that of Diazinon. More careful purification of the unreacted diethyl chlorothiophosphate indicated that some Diazinon was actually being distilled over, under the conditions outlined here.

EXPERIMENTAL

Phosphorus trichloride. Two g. of the irradiated elemental red phosphorus was added to a 25-ml. two-necked flask equipped with a chlorine bubbler, water-cooled condenser, and drying tube. Then 2.5 g. of redistilled phosphorus trichloride was added as a solvent for the chlorination. The flask was heated on an oil-bath to reflux. Dry chlorine then was introduced through the bubbler at a rate sufficient to minimize clogging. After approximately one-half hour of chlorination, the reaction was stopped and cooled in an ice-bath. The remaining 2 g. of irradiated red phosphorus was added, the reaction brought to reflux, and chlorination continued until white specks of phosphorus pentachloride began to appear. The reaction was cooled in an ice-bath and 6.5 g. of powdered antimony was added to convert the phosphorus pentachloride to phosphorus trichloride. After the addition of the antimony, the reaction was allowed to come slowly to room temperature to avoid the violent conversion of phosphorus pentachloride to phosphorus trichloride. The phosphorus trichloride then was distilled (73–75°) into a second reaction vessel at atmospheric pressure. Yields on two active runs ranged from 31 to 62% conversion of P₄ to PCl₃.

Thiophosphoryl trichloride. This compound was synthesized by the method of Knotz.⁶ The product was distilled (122–126°) at atmospheric pressure. The yields on two active runs were 87%.

O,O-Diethyl chlorothiophosphate. The method for the synthesis of this intermediate was essentially that of Fletcher, *et al.*,⁷ modified to minimize radiological hazards. The compound was distilled at 42–45° at 0.25 mm. The yields on two runs ranged from 72–79%.

Diazinon. Benzene (90 ml.) containing 13.03 g. of 2-isopropyl-6-methyl-4-hydroxypyrimidine and 11.92 g. of anhydrous potassium carbonate was placed in a round-bottom flask equipped with a water separator and condenser.

(1) Part of a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Kansas State College.

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The mixture was heated on an oil-bath until water started to collect in the water separator. The reaction then was cooled to 50–60° and 16.1 g. of O,O-diethyl chlorothiophosphate was added from a dropping-funnel. The dropping-funnel was rinsed with 10 ml. of dry benzene and refluxing was resumed. After 15 hours of refluxing, the reaction was cooled and 100 ml. of cold water was used to transfer the reaction mixture to a 250 ml. separatory-funnel. The benzene layer was separated and washed with 30 ml. of 10% NaOH and then with 30-ml. portions of water until the water was neutral to litmus. The benzene extract was dried over calcium chloride for 15 minutes, then was transferred to a 100-ml. separatory-funnel and dried over fresh calcium chloride for 1½ hours.

Aliquots of the benzene extract then were filtered into a 50-ml. round-bottom flask attached to a distilling head and the benzene was stripped off with a stream of dry air under reduced pressure. After most of the benzene had been removed in this manner, the system was placed under a vacuum of 0.25 mm. and heat was applied. The unreacted O,O-diethyl chlorothiophosphate and other low-boiling materials were distilled off (42–45°). The oil-bath temperature then was raised to a temperature of 120° for ½ hour. The residue in the flask contained crude Diazinon. The yield on the final step was 62%.

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2-Pyrones. XX. Carboxydehydroacetic Acid and Its Derivatives

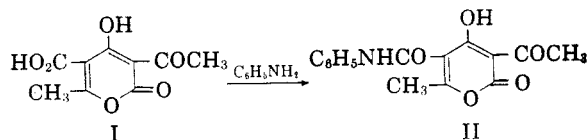
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In re-examining some details of the structure and reactions of dehydroacetic acid in terms of its 4-hydroxy-2-pyrone structure,¹ our attention was directed to the compound 5-carboxydehydroacetic

acid² (I) which was first described in 1893³ by von Pechman and Neger. This compound shows infrared absorption characteristics similar to those of dehydroacetic acid itself and of triacetic lactone which has been established⁴ as having a 4-hydroxy-2-pyrone structure. Some important points for comparison are summarized in Table II. There is a narrow absorption band in the O—H stretching range at 3.30 μ , similar to that observed with dehydroacetic acid, rather than the broad absorption indicative of extensive hydrogen-bonding observed with triacetic lactone. There is another absorption band not observed with dehydroacetic acid. This is at 5.66 μ and, even though not at the customary carboxyl carbonyl position, is attributed to the carbonyl of the carboxyl group since this is the only difference in the two structures.

The most unusual feature of the chemical behavior of this acid is the ease with which it has been reported³ to form its anilide (5-phenylcarbonyl-dehydroacetic acid, II). This reaction is said to take place on heating the acid with aniline in acetic acid for 10 minutes on the water-bath. This is the only example known to the authors in which amide formation takes place under such conditions. Since previous studies⁵ have shown that there are many possible reactions which might take place between 2-pyrones and aniline, it seemed desirable to provide additional information about this reaction and additional data establishing the structure of this product. We have observed that the anilide is also formed on refluxing the reactants in benzene or toluene. The anilinium salt, which first precipitates and can be isolated and identified as such, is converted under these conditions to the anilide. To substantiate the hypothesis that the product of this reaction is in fact the anilide we have prepared the acid chloride from thionyl chloride and the carboxydehydroacetic acid and observed that on reaction with aniline it gives the same product. The infrared absorption spectra shows a general similarity to the spectra of related compounds. The disappearance of the absorption band at 5.66 μ on converting the carboxylic acid to the amide is significant evidence for the phenylcarbonyl structure. Furthermore, both of the bands in the range commonly associated with the two amide carbonyl bands (at 6.0 and 6.45) are much more strong in the anilide than they are in the acid. The synthetic data and infrared absorption characteristics appear



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(2) The Chemical Abstracts systematic name for this structure is 3-acetyl-5-carboxy-6-methyl-2H-pyran-2,4(3H)-dione. Since dehydroacetic acid is indexed as dehydroacetic acid the carboxy derivative may be indexed as a pyrandione or as a derivative of the acid.

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