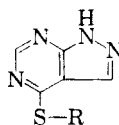


TABLE II  
4-ALKYLTHIOPYRAZOLO[3,4-*d*]PYRIMIDINES



R	Meth. of Synth.	M.P.	Yield, %	pH 1		pH 11		Calcd. N	Found N
				$\lambda_{\max}$ , $M\mu$	$\epsilon$	$\lambda_{\max}$ , $M\mu$	$\epsilon$		
C <sub>2</sub> H <sub>5</sub>	A	163	58	300	14,400	287	14,400	31.1	31.2
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	A	107	55	300	14,500	287	15,500	28.8	28.8
<i>iso</i> -C <sub>3</sub> H <sub>7</sub>	A	116	50	300	13,900	287	14,500	28.8	28.8
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	A	97-98	61	300	13,500	288	14,500	26.9	26.8
<i>n</i> -C <sub>5</sub> H <sub>11</sub>	B	86-87	54	301	12,400	289	10,400	25.2	24.9
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	B	82	47	300	16,000	289	13,200	23.7	23.4
<i>n</i> -C <sub>7</sub> H <sub>15</sub>	B	68-69	49	301	14,000	287	14,000	22.4	22.2
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	B	64	45	301	10,000	287	14,800	21.5	21.5

overnight and the crude product filtered, washed with ligroin, and recrystallized from an ethylacetate-heptane mixture.

*Method (C).* To 6 g. of 6-purinethiol,<sup>11</sup> dissolved in 100 ml. of 5% potassium hydroxide, was added 7 g. of the appropriate alkyl iodide. The mixture was refluxed and stirred until only one phase was present. The pH of the solution was adjusted to 7 with dilute hydrochloric acid and the solution cooled. The crude product was filtered, washed with ligroin, and thoroughly dried. The dried product was placed in the thimble of a soxhlet extractor and extracted continuously with benzene from 4 to 10 hr. The benzene extract was cooled and filtered and the product recrystallized from an ethylacetate-heptane mixture.

*Preparation of the 4-alkylthiopyrazolo[3,4-*d*]pyrimidines listed in table II. Method (A).* This method is essentially that of method (A) used for the preparation of the 6-alkylthiopyrimidines. The only change in procedure was that 4-chloropyrazolo[3,4-*d*]pyrimidine<sup>8</sup> was employed instead of 6-chloropurine. The crude product was recrystallized from an ethylacetate-heptane mixture.

*Method (B).* This method is similar to that of method (B) above using 4-chloropyrazolo[3,4-*d*]pyrimidine<sup>8</sup> instead of 6-chloropurine. 4-Octylthiopyrazolo[3,4-*d*]pyrimidine was recrystallized from *n*-heptane rather than a mixture of ethylacetate and *n*-heptane.

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(11) G. B. Elion, E. Burgi, and G. H. Hitchings, *J. Am. Chem. Soc.*, **74**, 411 (1952).

### Use of Acetone Dimethyl Acetal in Preparation of Methyl Esters

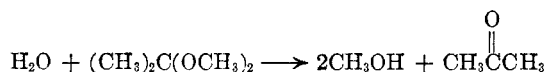
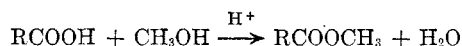
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When an ester is prepared by the reaction of an alcohol with an acid, the reaction is usually driven to completion by removing the water as an azeotrope with an inert solvent. In the preparation of methyl esters the use of an inert solvent which

forms an azeotrope with water is unattractive because of the low water content of azeotropes which boil below methanol. In the preparation of dimethyl oxalate, Bowden<sup>1</sup> used 0.65 mole of concentrated sulfuric acid per mole of oxalic acid. The large amount of sulfuric acid apparently acted as a catalyst and also as a drying agent for the reaction. Clinton and Laskowski<sup>2</sup> reported that "the use of either methylene dichloride or ethylene dichloride as a solvent removes the necessity for continuous drying and gives very high yields of methyl esters." However, in their procedure for each mole of organic acid present there was used three moles of methanol and 300 ml. of solvent.

We have found that by using acetone dimethyl acetal, methyl esters can be prepared conveniently in nearly quantitative yields. The primary function of the acetal appears to be that of a water scavenger and the preparation can be represented by the following two reactions:



For each mole of water formed during the esterification reaction, two moles of methanol are introduced into the reaction solution by the hydrolysis of the acetone dimethyl acetal. As a result the process is self-accelerating. When methanol is present in the initial reaction mixture in excess of 20 mole % of the carboxylic acid groups present, the reaction rate is high throughout the preparation. In the absence of methanol, acetone dimethyl acetal reacts very slowly, if at all, with a carboxylic acid at temperatures up to 75°. (The acetone dimethyl acetal will crack to isopropenyl methyl ether and methanol in the presence of a

(1) E. Bowden in *Org. Syntheses*, Coll. Vol. II, 414 (1943).

(2) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **70**, 3135 (1948).

strong acid esterification catalyst as the temperature is raised above 65 to 75°.)

When acid hydrates such as oxalic acid dihydrate are to be esterified, no methanol is needed to initiate the reaction as the acetone dimethyl acetal is readily hydrolyzed by the water of hydration. To insure complete conversion of the acid, the amount of acetone dimethyl acetal used should be in slight mole excess (up to 10%) of the total water present and/or expected. The advantages of this method for preparing methyl esters are: (1) there is no need for a water azeotrope trap, (2) a high reaction rate is maintained during the entire esterification reaction, (3) acid hydrates can be readily esterified, and (4) the acid is completely converted to its methyl ester.

#### EXPERIMENTAL

*Effect of acetone dimethyl acetal on the reaction rate during esterification.* In Fig. 1 the results of four experiments on the

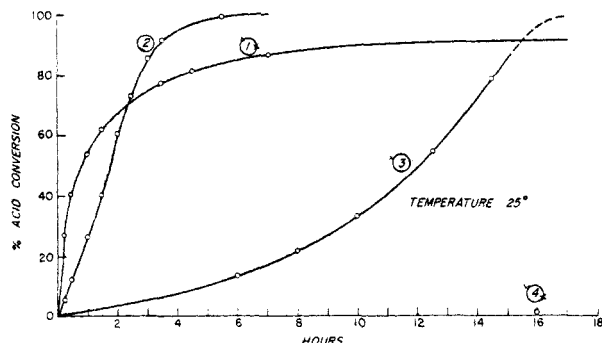


Fig. 1. Rate of esterification of propionic acid.

MOLES OF	1	2	3	4
Propionic acid	0.25	0.25	0.25	0.25
Methanol	0.75	0.25	0.075	0.00
Acetone dimethyl ketal	0.00	0.25	0.25	0.25
Hydrogen chloride	0.006	0.006	0.006	0.006

esterification of propionic acid are plotted. The quantity of each reactant used is as given plus sufficient anhydrous dioxane to make the total volume in each experiment 100 ml. The unreacted propionic acid was determined periodically by titrating an aliquot with standard ethanolic sodium hydroxide solution.

In experiment 1 the initial reaction rate was high but soon decreased and finally reached equilibrium where 94% of the propionic acid was converted. In experiment 2, two thirds of the methanol was present as a part of the acetone dimethyl acetal. The initial rate of this reaction was lower than in experiment 1; however, a high rate was maintained through almost all of the reaction period. In the early hours of experiment 3 the rate was low because the concentration of methanol was low. As the esterification proceeded, the concentration of the methanol increased as a result of the hydrolysis of the acetone dimethyl acetal and this effected a corresponding increase in the reaction rate. At 20 hr. all of the propionic acid in experiment 3 was converted and although no checks were made between 14 and 20 hr., the course of the reaction was probably as indicated. After 16 hr. there was no detectable conversion of the propionic acid in experiment 4. At 50 hr., 5% of the propionic acid was converted and from that point the reaction rate increased

and all of the acid was converted. This experiment was repeated several times and each time there was essentially no reaction until 35 to 50 hr. and then there was a rapid conversion of the propionic acid. No special effort was made to exclude all atmospheric moisture or to use acetone dimethyl acetal that was absolutely free of methanol. Trace amounts of methanol and/or water would act as initiators for the reaction.

*Esterification of dehydrated castor oil acids.* A mixture of 200 ml. of dehydrated castor oils (1 ml. = 30.4 ml. *N*/10 NaOH), 0.60 mole of acetone dimethyl acetal, 0.3 mole of methanol and 0.012 mole of HCl was allowed to stand at room temperature. When checked 39 hr. later, more than 99% of the acids were esterified.

*Preparation of dimethyl adipate.* Four moles (585 g.) of adipic acid was added to a solution of 5 g. of *p*-toluenesulfonic acid dissolved in 5 moles (200 ml.) of methanol. This mixture was stirred in a 2 l. flask and maintained at 40° to 60°. As the reaction progressed, acetone dimethyl acetal was added in increments. By the end of 0.5 hr., 200 ml. had been added, by the end of 1 hr., 600 ml. total had been added (at this point all adipic acid was in solution), and by the end of 1.5 hr., a total of 1 l. (8 moles) of the acetone dimethyl acetal had been added. At the end of 2 hr. only 10% of the acid remained unreacted. After 4 hr. the reaction was 99% complete. One half of the crude solution was then distilled at a rate such that by the end of 3 hr. all of the acetone and methanol had been removed. This left a 98.8% yield of crude, straw colored dimethyl adipate,  $n_D^{25}$  1.4275. On further distillation a 94% yield of pure dimethyl adipate ( $n_D^{25}$  1.4263;  $b_{10}$ , 109°C.; lit.<sup>3</sup>  $n_D^{20}$  1.4281;  $b_{20}$ , 122°C.) was recovered.

A similar experiment in which all of the reactants were mixed at one time and left overnight at room temperature (with stirring) resulted in 100% conversion of the adipic acid.

*Preparation of dimethyl oxalate.* One mole of oxalic acid dihydrate, 2 g. of *p*-toluenesulfonic acid and 2 moles of acetone dimethyl acetal were combined with stirring. Heat was applied so that a temperature of 50–55° was maintained. After 1.25 hr. another mole of acetone dimethyl acetal was added. After an elapsed reaction time of 2 hr. the final mole of acetone dimethyl acetal (4 mole total) was added. The reaction was 98% complete after 5 hr. at which time the methanol and acetone were distilled until only 175 ml. of the product-methanol solution remained. By cooling, filtering out the white crystalline product, and reworking the mother liquor, 107 g. of dimethyl oxalate (91% theory), m.p. 51–53° (lit.<sup>1</sup> m.p. 52.5–53.5°), was recovered.

*Acknowledgment.* The authors wish to thank Mr. Bernis Self for his aid in these experiments.

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(3) A. I. Vogel, *J. Chem. Soc.*, 333–341 (1934).

### Heterocyclic Vinyl Ethers XIV. Photochemical Dimerization of 2-Nitrobenzo-1,4-dithiadene and Reactions of Benzo-1,4-dithiadene with Mercuric Salts<sup>1</sup>

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When 2-nitrobenzo-1,4-dithiadene (m.p. 105–107°), which is red in color, is exposed to light, it is