nitrophenol while β-6-nitro-3-arsonophenoxyethanol gave 3-hydroxy-4-nitrophenylarsonic acid and *o*-nitrophenol.

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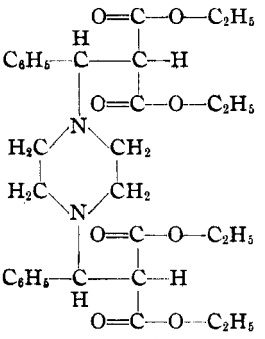
[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF FLORIDA]

Derivatives of Piperazine. X. Reactions with Unsaturated Esters. Part 2[1]

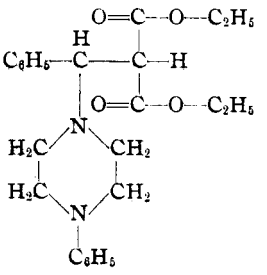
BY J. P. BAIN AND C. B. POLLARD

In the first paper[2] of this series, the addition of piperazine to esters of maleic and fumaric acids was reported. Further work in this field by the present authors has led to a study of the reactions of piperazine and monophenylpiperazine with a number of arylidene malonic esters. Other investigators have reported the addition of aniline,[3] phenylhydrazine,[4] piperidine[5] and other primary and secondary amines to benzalmalonic ester. The reactions proceed as expected with addition of the amine to the conjugate system.

Piperazine and benzalmalonic ester yielded tetraethyl (α,α′-diphenyl-1,4-piperazylene-dimethylene)-dimalonate (I). Monophenylpiperazine and benzalmalonic ester yielded diethyl α-(4-phenyl-1-piperazyl)-benzylmalonate (II).



(I)



(II)

The desired products may be formed in two ways: (a) the addition of the secondary amine to the arylidene malonic ester in alcoholic solution, and (b) addition of the secondary amine to the aromatic aldehyde and malonic ester in alcoholic solution. Heating is not necessary but serves to complete the reaction in a shorter time.

Arylidene malonic esters may be prepared by heating a mixture of aromatic aldehyde and malonic ester with a trace of an amine as a catalyst. It is probable that in the alternative procedure the secondary amine catalyzes the formation of the arylidene malonic ester and then adds to the conjugate system. On mixing equivalent quantities of piperazine, an aromatic aldehyde, and cyanoacetic ester, good yields of the arylidene cyanoacetic ester were obtained but no addition products were detected.

On refluxing (I) with a slight excess of alcoholic potassium hydroxide, long needles of a nitrogen-free potassium salt were obtained. This was surprising as another investigator[4,5] obtained the expected potassium salts from his amine addition products with benzalmalonic ester. The potassium salt was identified tentatively as potassium α-ethoxybenzylmalonate,[6] which would be formed by splitting out piperazine, adding alcohol to the conjugate system, and hydrolyzing. Piperazine was recovered in good yield from the mother liquor.

Acid hydrolysis of (I) with 3 *N* hydrochloric acid yielded piperazine hydrochloride and benzalmalonic ester which on prolonged hydrolysis yielded benzaldehyde and malonic acid. From one hydrolysis a small amount of cinnamic acid was identified.

The stability of (I) is also shown by hydrogenolysis experiments. Dibenzylpiperazine and malonic ester are produced by cleavage of the C–C bond and benzylmalonic ester and piperazine are produced by cleavage of the C–N bond. Toluene might be produced by simultaneous cleavage of the two bonds in the same molecule, but has not been identified as yet.

Experimental

Materials.—Piperazine hexahydrate, aldehydes and malonic ester were purchased from Eastman Kodak Co. The arylidene malonic esters were prepared by the method of Knoevenagel.[7] N-Monophenylpiperazine was prepared by the method of Pollard and MacDowell.[8]

(1) Presented at the Chapel Hill meeting of the American Chemical Society, April 14, 1937.

(2) Pollard, Bain and Adelson, THIS JOURNAL, **57**, 199 (1935).

(3) Blank, *Ber.*, **28**, 145 (1895).

(4) Goldstein, *ibid.*, **28**, 1450 (1895).

(5) Goldstein, *ibid.*, **29**, 813 (1896).

(6) Claisen and Crismer, *Ann.*, **218**, 141 (1883).

(7) Knoevenagel, *Ber.*, **31**, 2585 (1898).

(8) Pollard and MacDowell, THIS JOURNAL, **56**, 2199 (1934).

TABLE I

TETRAETHYL (α,α'-DIARYL-1,4-PIPERAZYLENE DIMETHYLENE) DIMALONATES

Aryl	M. p., °C.	Recryst. solvent	Analyses, % Calcd. C	H	N	Found C	H	N
Phenyl	151–152	Toluene	65.9	7.3	4.8	66.1	7.2	4.9
3,4-Methylenedioxyphenyl	150–151	Toluene	60.9	6.3	4.2	61.0	6.5	4.2
o-Chlorophenyl	156–157	Benzene	..	...	4.3	..	...	4.3
p-Methoxyphenyl	146–147	95% ethanol	63.5	7.2	4.4	63.7	7.2	4.3
2-Furyl	126–127	95% ethanol	59.8	6.8	5.0	59.8	6.8	5.0

TABLE II

DIETHYL α-(4-PHENYL-1-PIPERAZYL) R MALONATES

R	M. p., °C.	Recryst. solvent	Analyses, % Calcd. C	H	N	Found C	H	N
Benzyl	144–145	95% ethanol	70.2	7.4	6.8	70.3	7.4	6.7
3,4-Methylenedioxybenzyl	144–145	95% ethanol	66.0	6.7	6.2	65.8	6.8	6.2
p-Methoxybenzyl	146–147	95% ethanol	68.1	7.3	6.4	68.2	7.4	6.4
2-Furfuryl	103–104	50% ethanol	66.0	7.1	7.0	66.1	7.1	6.9

Preparation of the Condensation Products. Method A.—One equivalent of the secondary amine was added to 1 mole of the arylidene malonic ester in 500 cc. of 95% ethanol. The mixture was heated to boiling and allowed to stand. Separation of the product usually began within an hour. After standing overnight the solid cake was broken up, filtered, washed with 100 cc. of cold ether, and recrystallized from the appropriate solvent. The yields were from 70 to 90%.

Method B.—One equivalent of the amine was added to a mixture of 1 mole of aldehyde and 1 mole of malonic ester in 500 cc. of 95% ethanol. The mixture was heated to boiling and allowed to stand overnight. Isolation and purification of the products were carried out as in Method A.

Attempted Condensation with Ethyl Cyanoacetate.—Piperazine hexahydrate, 19.4 g., was added to a mixture of 21.2 g. of benzaldehyde and 22.6 g. of ethyl cyanoacetate in 100 cc. of 95% ethanol. The mixture was heated to boiling and allowed to stand overnight. The product on recrystallization from 95% ethanol melted at 50–51°. There was no melting point depression when mixed with an authentic specimen of ethyl α-cyano-β-phenylacrylate.

Saponification of (I).—Ten grams of (I) was dissolved in 400 cc. of hot absolute ethanol and a solution of 5 g. of potassium hydroxide in 100 cc. of absolute ethanol was added. The mixture was refluxed for two hours. On cooling, 5.5 g. of a nitrogen-free salt separated in long needles. It was recrystallized from 95% ethanol and dried in a desiccator over phosphorus pentoxide. One gram of the salt was dissolved in 10 cc. of water and 1 cc. of 6 *N* hydrochloric acid added. No precipitate formed even after standing in the ice-chest for several days. Two grams of the salt was heated to 120°, a loss in weight of 10% taking place. A small amount of distillate was collected and identified as ethanol by conversion into its naphthyl urethan, m. p. 79–79.5°. The heated portion of the potassium salt was dissolved in 15 cc. of water and treated with 2 cc. of 6 *N* hydrochloric acid. After standing overnight crystals were obtained, melting at 196–197°, and were identical with an authentic sample of benzalmalonic acid. According to these reactions the original potassium salt was probably potassium α-ethoxybenzyl malonate.[6]

The alcoholic mother liquor was treated with 15 cc. of concd. hydrochloric acid. A precipitate formed immediately and was filtered off. The precipitate was dissolved in water, treated with 5 g. of sodium nitrite, excess hydrochloric acid, and then heated to boiling. On cooling, 1,4-bis-nitrosopiperazine, m. p. 158°, was deposited. The amount obtained accounted for 75% of the piperazine in the original molecule.

Acid Hydrolysis of (I).—Ten grams of (I) was added to 200 cc. of 3 *N* hydrochloric acid. The white, finely crystalline ester gradually disappeared and a light oil appeared which was mainly benzalmalonic ester with some benzaldehyde. After four hours of refluxing the mixture was cooled and the oil separated. The oil yielded a semicarbazone, melting at 212°, identical with an authentic sample of benzaldehyde semicarbazone. The mother liquor was concentrated to about 20 cc. and 5 g. of sodium nitrite dissolved in 30 cc. of water was added. 1,4-Bis-nitrosopiperazine, m. p. 158°, was deposited on cooling.

Hydrogenolysis of (I).—One hundred grams of (I) was placed in a hydrogenation bomb with 250 cc. of dioxane and 6–8 g. of Raney nickel. Hydrogen at 1000 lb./sq. in. (68 atm.) pressure was used. No absorption of hydrogen took place at room temperature even after shaking for ten hours. The temperature was raised gradually to 100° where hydrogen absorption was fairly rapid. After approximately 2 moles of hydrogen per mole of (I) had been absorbed the shaking was stopped and the apparatus allowed to cool. From the dioxane solution, after filtration from the nickel, the following products were isolated and converted to suitable derivatives for identification: 3 g. of piperazine, 4.5 g. of malonic ester, 5 g. of dibenzylpiperazine and 31 g. of benzylmalonic ester.

Acknowledgments.—The authors wish to express their gratitude to Dr. Austin M. Patterson for suggestions concerning the nomenclature of the condensation products, and to Mr. G. A. Barber for some of the nitrogen analyses.

Summary

1. A number of new additions of amines

to conjugate systems have been reported.

2. Several reactions have been carried out to determine the stability of these products.

3. The methods used in separating the hydrogenolysis products of these compounds are being improved and further work in this field will be reported at an early date.

GAINESVILLE, FLORIDA RECEIVED JULY 2, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

Sulfur Studies. XII. Thioaldehydes in the Naphthalene and Anthracene Series

BY J. H. WOOD AND R. W. BOST

In a previous paper[1] it was shown that thioaldehydes of the benzene series either polymerize or undergo the Cannizzaro reaction immediately upon formation. This work has been extended into the naphthalene and anthracene series with the idea that the increased molecular weight might retard polymerization reactions to the extent that the monomer could be isolated and studied.

α-Thionaphthaldehyde and β-ethoxythionaphthaldehyde are much more resistant to polymerization than thiobenzaldehyde and we have been able to keep dilute solutions of these thioaldehydes from twenty-four to thirty-six hours before complete polymerization occurred. They exhibit the condensation reactions characteristic of oxo-aldehydes such as the elimination of hydrogen sulfide with 2,4-dinitrophenylhydrazine with the formation of the hydrazone. They give color reactions with Grote's reagent and form precipitates with mercuric chloride. In the presence of much acid, immediate polymerization occurs with the formation of the cyclic trimer.

The cyclic trimer, β-ethoxytrithionaphthaldehyde, is formed in a quantitative yield upon passing hydrogen sulfide in solutions of the aldehyde which have been saturated previously with dry hydrogen chloride. Upon being vacuum distilled, the trimer is mainly decomposed into the new stilbene analog, *sym*-di-β-ethoxynaphthylethylene. This furnishes an excellent synthesis of *sym*-dinaphthyl substituted ethylenes. If the distillation is carried out in the presence of a few crops of concentrated sulfuric acid, some depolymerization also occurs and we have isolated from the distillate a few drops of monomeric β-ethoxythionaphthaldehyde as a red oil. Alcoholic solutions of the oil give the characteristic reactions mentioned above. Polymerization occurs in a few hours.

(1) J. H. Wood and R. W. Bost, THIS JOURNAL, **59**, 1011 (1937).

Thioanthracene-aldehyde-9 polymerizes immediately upon formation into linear polymers and we have been unable to prepare the cyclic trimer. This is no doubt due to the large anthranyl groups which prevent ring closure. Further evidence of this is the fact that both geometrical isomers of trithiobenzaldehyde are formed in the same reaction, but the *trans* form is produced in a much greater quantity. On the other hand, only one of the two possible geometrical isomers of β-ethoxytrithionaphthaldehyde is formed in the reaction similar to that by which the trithiobenzaldehydes are produced, and it is logical to assume that it is the *trans* form. That is, the β-ethoxynaphthyl group does not permit ring closure when all are on the same side of the ring and only the *trans* form is produced. With anthracene-thioaldehyde-9, ring closure is not possible even with two groups on one side and the other on the opposite side.

The aldehydes used in this investigation are not on the market and considerable time was consumed in finding satisfactory methods by which fairly large quantities could be made readily. The general syntheses of aldehydes which give fair yields in the benzene series were found to give none, or at best only poor yields in the naphthalene and anthracene series. The methods described below were found to be the most satisfactory of those tried for the preparation of the aldehydes used.

Experimental

α-Naphthaldehyde.—α-Naphthylcarbithioic acid was prepared by the method of Bost and Mattox.[2] The semicarbazone of the aldehyde was prepared from the carbithioic acid by the method of Wuyts, Berman and Lacourt.[3] Hydrolysis of the semicarbazone gave the aldehyde. Purification was accomplished by means of the bisulfite reaction followed by distillation.

(2) R. W. Bost and W. J. Mattox, *ibid.*, **52**, 332 (1930).

(3) H. Wuyts, L. Berman and A. Lacourt, *Bull. soc. chim. Belg.*, **40**, 665 (1931).