sodium, and is an interesting variation of the lateral metalation of toluene by ethylsodium which was first examined by Schorigin.[2]

Incidental to studies on interconversions by organometallic compounds, we have investigated procedures for the preparation of organoalkali compounds, particularly the benzylmetallic types.[3] One of the more interesting results is the conversion of *m*-tolylsodium to benzylsodium. *m*-Chlorotoluene and sodium in petroleum ether first give *m*-tolylsodium, as evidenced by the formation of *m*-toluic acid (free of phenylacetic acid) on carbonation. On refluxing the mixture, the *m*-tolylsodium is converted to benzylsodium. In the Bachmann–Clarke[1] migration with *p*-tolylsodium one may be dealing with an allylic rearrangement of the kind frequently observed with a variety of organometallic compounds. However, with *m*-tolylsodium it is difficult to account for the migration on the basis of an allylic rearrangement. Although mechanisms have not been proposed for the migrations cited, it is probable that the meta and para transformations proceed by different routes, if the relative rates of migration are criteria.

Experimental

A mixture of 12.7 g. (0.1 mole) of *m*-chlorotoluene, 5.7 g. (0.25 g. atom) of sodium sand and 100 cc. of petroleum ether (b. p., 85–100°) was heated to reflux temperature and then promptly cooled to room temperature. The reaction then proceeded spontaneously, and the temperature was kept between 35–40°. After two hours, the reaction mixture was black, and the evolution of heat ceased. Carbonation of an aliquot of the mixture by solid carbon dioxide yielded *m*-toluic acid as the only acid.[4] The remaining mixture was refluxed for six hours and then carbonated by pouring upon crushed solid carbon dioxide. From the resulting acids there was isolated a 5.3% yield of phenylacetic acid (mixed m. p.), but no *m*-toluic acid or phenylmalonic acid. A small quantity of clear, oily acidic material has not yet been identified.

With a twenty-hour period of refluxing, the yield of phenylacetic acid was 4.7%. However, with only a one-hour period of refluxing the yield of phenylacetic acid was 8.3%. It should be stated that carbonation after heating a mixture of *p*-chlorotoluene, sodium and petroleum ether yielded 65% of phenylacetic acid.[3]

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(2) Schorigin, *Ber.*, **41**, 2723 (1908).

(3) A detailed report on these studies by the authors together with Dr. Ogden Baine will be published shortly. An account of the reactions and their mechanisms was presented at the Eighth National Organic Symposium, St. Louis, Dec. 30, 1939.

(4) In a separate experiment where carbonation of the entire mixture was effected at this point, the yield of *m*-toluic acid was 84%.

Preparation of Borneol Glucuronide

BY HARVEY K. MURER AND LATHAN A. CRANDALL, JR.

We have had good success in the isolation of the zinc salt of borneol glucuronide by the method of Quick[1] and Pryde and Williams[2] from the urine of dogs fed borneol provided care is taken in the proper adjustment of acidity previous to the lead clarification of the urine.

In their preparation of the free glucuronide the zinc salt was dissolved in hot 3.4 *N* sulfuric acid, filtered and allowed to crystallize from the hot solution. The glucuronide was filtered off and washed with ice water and recrystallized from hot water for further purification. It is difficult to filter and wash this product in water, and several recrystallizations are necessary to obtain a pure product with subsequent loss in yield. Also uronic acids are destroyed by hot acid of this strength and some hydrolysis of the glucuronide takes place, giving rise to the difficulty of removing borneol from the product.

To avoid these difficulties the removal of the zinc was first attempted with hydrogen sulfide. The zinc salt was suspended in acetone. A slow but fairly good removal of zinc was accomplished but the product retained a strong odor of sulfide after several purifications from acetone.

The above use of acetone led to a simple method which has given good results in the preparation of large quantities of borneol glucuronide of good purity.

Two hundred grams of dry zinc borneol glucuronide is added with stirring to 800 ml. of warm acetone containing 14.7 ml. of concentrated sulfuric acid. The zinc sulfate and any unreacted zinc salt are easily centrifuged down and the clear acetone solution decanted. The centrifuge flasks and precipitate are washed once with 50 to 100 ml. of warm acetone, centrifuged and the clear solution added to the original. Fifty ml. of water is added to the acetone solution to allow for crystallization of the hydrate and to keep traces of zinc sulfate in solution. Crystals of fine needles will set the solution almost solid at room temperature. The product is filtered with suction, washed with cold acetone, and vacuum dried at 40°. The filtrate is easily concentrated and again cooled for crystallization without further addition of water, filtered and washed as before. A still

(1) A. M. Quick, *J. Biol. Chem.*, **74**, 331–341 (1927).

(2) J. Pryde and R. T. Williams, *Biochem. J.*, **27**, 1197–1204 (1933).

further small amount of pure product may be obtained by a third crystallization of the filtrate. Unreacted zinc salt and remaining glucuronide in the washings may be recovered by dissolving the sludge in hot acidified water, adding an excess of zinc acetate and recovering the insoluble salt by filtration.

Attempts to find some more suitable method for the hydrolysis of borneol glucuronide than the acid hydrolysis suggested by Quick for the preparation of glucuronic acid have not been successful. B-Emulsin will hydrolyze considerable quantities of glucuronide; however, the reaction rate is slow, the equilibrium poor for preparation purposes, and the high acidity produced by the free glucuronic acid destroys emulsin, necessitating continued addition of the enzyme. This last step therefore is the limiting one in the preparation of glucuronic acid by Quick's method.

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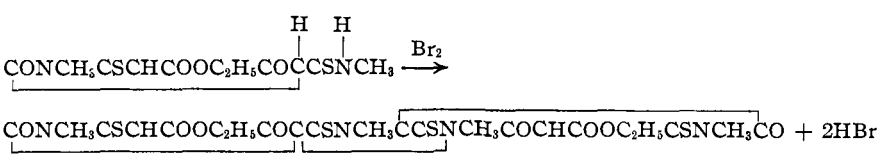
The Action of Methyl Isothiocyanate on Ethyl Acetonedicarboxylate

BY DAVID E. WORRALL

The highly substituted derivatives of piperidine obtained ultimately by the action of aryl isothiocyanates on the sodium enolate of ethyl acetonedicarboxylate undergo further cyclization, in the presence of bromine, into piperidyl benzothiazoles.[1] An examination of similar reactions with an alkyl isothiocyanate has shown that a piperidine is formed which also loses a molecule of hydrogen. Thiazole formation is impossible, therefore the assumption has been made that a spiro piperazine is obtained as the result of a bimolecular condensation.



(1) Worrall, THIS JOURNAL, **61**, 2967 (1939).

Abenius[2] found that a reaction of this type occurs with the bromoacetyl derivative of aniline.

Experimental

1 - Methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfopiperidine-3-thioformomethylamide.—Using the customary technique, 0.1 g. mole of the ester was changed into the disodium derivative and mixed with two equivalents of methyl isothiocyanate. The mixture, after the spontaneous reaction subsided, was heated for an hour and decomposed in the usual manner. The pasty product was extracted with cold alcohol and the residue crystallized from alcohol. Bright yellow platelets resulted, m. p. 98°, yield 4–5 g.

Anal. Calcd. for $C_{11}H_{14}N_2O_4S_2$: C, 43.7; H, 4.6. Found: C, 43.6; H, 4.5.

The substance, soluble in sodium carbonate solution is reprecipitated unchanged by a strong acid. Hot acid changes it into an intractable tar, while boiling with alcoholic potash produces methylamine, hydrogen sulfide and other decomposition products. The original material contained an insoluble portion (0.3 g.) that separated from a large volume of alcohol in slender pale yellow needles, m. p. 235–236°. An analysis indicated the formula $C_{18}H_{14}N_4O_5S_4$, but it was not identified.

1 - Methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfomethoxypiperidine-3-thioformomethylamide.—The product, obtained by heating 1 g. of the amide with methyl iodide–ethyl alcohol mixture for thirty minutes, separated on cooling as slender colorless needles, m. p. 110°.

Anal. Calcd. for $C_{12}H_{16}N_2O_4S_2$: C, 45.6; H, 5.1. Found: C, 45.3; H, 5.0.

Di - spiro - 3,3' - di - (1 - methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfopiperidine) - 3'',3''' - (1,4 - dimethyl - 2,5-disulfopiperazine).—Bromination of 1 g. of the amide in glacial acetic acid formed a precipitate that, after heating on a water-bath for a short time, was crystallized from alcohol. Cream colored needles separated, m. p. 180°.

Anal. Calcd. for $C_{11}H_{12}N_2O_4S_2$: C, 44.0; H, 4.0. Found: C, 43.6; H, 3.9.

It is dissolved by cold concd. sulfuric acid, forms a gelatinous substance with hot alcoholic potash (probably the corresponding carboxy derivative) and is only slightly attacked by long heating with concd. hydrochloric acid.

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(2) Abenius, *J. prakt. Chem.*, (2) **40**, 431 (1889).