both the stable and metastable methylethylacetic modifications is highly specific of this compound.

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Summary

1. Optical crystallographic data and melting points of the *p*-bromoanilides of nine lower aliphatic acids have been determined.
2. Metastable crystalline modifications of the *n*-valeric, isovaleric, *d,l*-methylethylacetic, and methacrylic derivatives have been obtained from the molten material.
3. The unsaturated methacrylic derivative was successfully prepared by the regular procedure, without formation of the chloroisobutyric derivative.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Method of Garelli and Racciu for the Preparation of Piperazine: A Criticism

BY DEAN B. ROLLINS AND H. N. CALDERWOOD[1]

With regard to a paper[2] describing a simple and inexpensive dehydration method for obtaining piperazine disulfate by heating monoethanolamine with sulfuric acid, we wish to call attention to the fact that the authors do not prove that the reaction product obtained by them is piperazine disulfate. The solubilities reported and the percentages of nitrogen and sulfate, their only analytical data for the product they designate as piperazine disulfate, hold also for β-aminoethylsulfuric acid. Their only other description, the rhombohedral crystals from dilute ethanol, is characteristic of β-aminoethylsulfuric acid,[3,4] the crystals of piperazine disulfate from dilute ethanol being monoclinic.

The interaction of monoethanolamine and fuming sulfuric acid to form β-aminoethylsulfuric acid was reported in 1918.[4] Believing that Garelli and Racciu might have developed conditions leading to the formation of piperazine disulfate, we attempted to prepare the compound according to the method sketched by them, but in twenty-three experiments, under various time and temperature conditions and with different amounts and concentrations of sulfuric acid, we were unable to obtain even a trace of piperazine, the resulting product in every case being β-aminoethylsulfuric acid.

Our reagents were monoethanolamine, 99.54% purity, from the Carbide and Carbon Chemicals Corporation, and C. P. grade sulfuric acid in concentrations from 88.3 to 20% fuming. Samples of both our crude and recrystallized products analyzed for nitrogen by the semi-micro Dumas method and for sulfur by both wet and dry oxidation gave the results recorded in Table I. These values being valid for both β-aminoethylsulfuric acid and piperazine disulfate, other properties of our purified product were compared with the corresponding properties of an authentic sample of piperazine disulfate.

TABLE I

ANALYSES OF CRUDE AND PURIFIED PRODUCTS

Material	Crude I	Crude II	Purified I	Purified II	Calcd. $C_2H_7NO_4S$
Sample, g.	0.07025	0.07753	0.07117	0.07054	
Nitrogen, %	9.96	9.94	10.13	10.05	9.93
Sample, g.	0.2710	0.2652	0.2745	0.2714	
Sulfur, % Wet			22.40	22.48	22.68
Sulfur, % Dry	22.34	22.37			

Our product purified by recrystallization from dilute ethanol formed rhombohedral crystals sintering at 230°, as recorded in the literature for β-aminoethylsulfuric acid,[3,4] whereas piperazine disulfate from dilute ethanol gave white monoclinic crystals which began to darken at 325° and charred at 330°. Our purified product gave no precipitate with barium chloride, even after standing at room temperature for ten hours, nor with benzenesulfonyl chloride, whereas piperazine disulfate gave immediately after the addition of barium chloride a copious precipitate of barium sulfate, and with benzenesulfonyl chloride gave a copious white crystalline precipitate melting at 281°.[5] The molecular weight of our purified

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[2] Garelli and Racciu, *Atti. accad. sci. Torino*, **69**, 162–165 (1934).

[3] Gabriel, *Ber.*, **21**, 1056 and 2667 (1888).

[4] Frankel and Cornelius, *ibid.*, **51**, 1660 (1918).

[5] Hans T. Clarke, "A Handbook of Organic Analysis," Edward Arnold and Company, London, 4th ed., 1926, p. 207.

product determined by neutralization was 141.2 and 142.5, and by cryoscopy 140.5 and 141.5, values in excellent agreement with the theoretical 141 for β-aminoethylsulfuric acid, whereas piperazine disulfate would have given values at least twice as large.

In case of a remote possibility that β-aminoethylsulfuric acid might under favorable conditions decompose to form piperazine which Garelli and Racciu[6] claim to have isolated from their product, our purified product was treated with an equivalent amount of potassium hydroxide and steam distilled. The pale yellow viscous liquid obtained by evaporating the steam distillate to dryness yielded no piperazine, contained nitrogen but not sulfur, and did not form insoluble derivatives with reagents for either amino or alcohol groups. The use of small and large excesses of potassium and sodium hydroxides failed to yield piperazine or any other definite product. With large excesses of the hydroxides steam distillation was always accompanied by a volatile imine, probably ethyleneimine.[7]

Garelli and Racciu state that they obtained the pure base as a crystalline hydrate, m. p. 44°, to which they assign a formula approximating that of the monohydrate, but incorrect, as printed, for any piperazine hydrate. Since the literature[8] reports that it is piperazine hexahydrate which melts at 44°, this statement of Garelli and Racciu is surprising. Our examination of an authentic sample of piperazine corroborated Berthelot's findings.

It would be interesting to know in detail the method by which Garelli and Racciu isolated the free base from the product which they designate as piperazine disulfate and which had the crystalline form not of piperazine disulfate but of β-aminoethylsulfuric acid, and also in detail the conditions under which they obtained piperazine hydrate, from the base so isolated, by cooling over sulfuric acid the residue obtained by evaporating to dryness on a water-bath the condensate formed in isolating the free base by steam distillation. We found that piperazine hexahydrate when stored at room temperature over sulfuric acid volatilized completely and was absorbed by the acid.

We wish to express our gratitude to Messrs. G. E. Bernard, J. M. Hogrefe, and A. L. Wilson of the Carbide and Carbon Chemicals Corporation for their interest and assistance in this investigation.

Summary

1. The only product that can be isolated from the reaction of monoethanolamine and either concentrated or fuming sulfuric acid by the method of Garelli and Racciu is β-aminoethylsulfuric acid.[9]

2. β-Aminoethylsulfuric acid does not form an insoluble derivative with benzenesulfonyl chloride.

3. Both piperazine disulfate and piperazine hexahydrate form the same insoluble derivative with benzenesulfonyl chloride.

4. From dilute ethanol piperazine disulfate forms monoclinic crystals which begin to darken at 325° and char at 330°. This crystalline form and its behavior upon heating are reported for the first time here.

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[6] Ref. 2, p. 164.

[7] Wenker, THIS JOURNAL, **57**, 2328 (1935).

[8] Berthelot, *Compt. rend.*, **129**, 688 (1899), and *Ann. chim. phys.*, [7] **20**, 471 (1900).

[9] We have just received a letter written on August 5, 1938, by Prof. G. Bruni, lifelong friend of Prof. Garelli, who allows us to quote him as authority for the fact that after the departure of Dr. Racciu from his Institute, Professor Garelli had occasion to repeat his preparation, recognized the product as β-aminoethylsulfuric acid and was planning a short paper rectifying the mistake, when illness and death overtook him.