

compounds should form anhydrides or imides and no direct separation is possible by this method.⁴

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THE α,β,γ -TRIMETHYLGLUTARIC ACIDS

Sir:

In the preceding Communication F. E. Ray expresses the opinion that in our recent paper [THIS JOURNAL, 52, 4598 (1930)] (a) certain compounds described were impure and (b) that the method of separation of the α,β,γ -trimethylglutaric acids was not valid.

With respect to his first objection, we would draw attention to the fact that the compounds we described were analytically pure and, in the cases where crystalline, were unchanged in melting points after the third crystallization.

Ray prepared his tiglic ester through methylethylmalonic ester, obtained apparently by methylation and ethylation of sodium enol malonic ester. Besides the methylethylmalonic ester, the reaction product would contain monomethyl or ethyl and dimethyl or diethyl malonic esters, which cannot be completely separated by fractional distillation [Michael, *J. prakt. Chem.*, 72, 537 (1905)]. Ray finally obtained a product which boiled at 100° (30 mm.), which is clearly too high for tiglic ester (b. p. 156° (760 mm.)). The addition compound he prepared from this product through sodium enol cyanacetic ester boiled at 150–170° (30 mm.) and this obviously impure material was methylated. By hydrolysis the product gave a solid acid from which by repeated crystallization, a 145° melting acid was isolated. This was considered to be α -carboxy α,β,γ -trimethylglutaric

⁴ Since writing this Note, Michael and Ross in a footnote contained in the following Communication to the Editor, p. 1175, have kindly called my attention to a transposition of an analysis in my paper⁵ [THIS JOURNAL, 50, 562 (1928)]. The silver salt of α,β,γ -trimethyl- α -carboxyglutaric acid was analyzed and found correct (page 562, line 15). Following this is given the titration of the α,β,γ -trimethylglutaric acid, $C_8H_{14}O_4$. This should, of course, have followed the paragraph which describes the preparation of this acid from the malonic acid derivative for which the analysis of the silver salt is given.

In the hope of identifying this α,β,γ -trimethylglutaric acid (m. p. 134°) as the racemic form I have attempted its resolution by means of the brucine and strychnine salts but without success. It may thus be one of the meso forms. As a check to previous work the silver salt of the acid was prepared and analyzed with the following results:

Anal. Subs., 0.0450: Ag, 0.0248. Calcd. for $C_8H_{12}O_4Ag_2$: Ag, 55.6. Found: Ag, 55.1.

This leaves no doubt that the acid melting at 134° is α,β,γ -trimethylglutaric acid.

acid but the formula was not proved by analysis.¹ No yield was given of this acid and it was not clear from the description in his paper that the 145° melting acid was used for pyrogenic decomposition. In his preparation of the tribasic acid through tiglic and sodium enol malonic esters, Ray obtained it as a sirup from which apparently he could obtain the 134° melting dicarboxylic acid more readily than from the 145° melting acid. It is therefore difficult to understand the reference in his letter of "necessity to purify before decomposition." The acid melting at 134° was described as α,β,γ -trimethylglutaric acid, although no analyses of this material are given. We, therefore, cannot attach the importance that Ray does to this substance of unknown composition, obtained from an impure source.

With respect to the second objection, the validity of the method is a well established fact. The stereomeric poly-alkyl dicarboxylic acids do not form anhydrides with equal facility, or of equal stability, and we refer Dr. Ray to the literature of these acids [Perkin and Bone, *J. Chem. Soc.*, **69**, 264 (1896); Thorpe and Young, *ibid.*, **83**, 358 (1903), and others].

Since we used this method in the separation of the α,β,γ -trimethylglutaric acids, our products were described as *cis* and *trans* to indicate their origin and relative ease of anhydride formation. It was not relevant to our investigation to separate the possible stereomeric forms of α,β,γ -trimethylglutaric acid; it was sufficient for us to obtain a pure imide, m. p. 90°, and an acid, m. p. 125°, as reference compounds and to indicate further the existence of a *trans* acid form.

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ARTHUR MICHAEL
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STEREOCHEMISTRY OF DERIVATIVES OF DIPHENYL AND ANALOGS

Sir:

Apparently the first suggestion that stereoisomerism of the type observed in the diphenyl series might also occur among binuclear heterocyclic aromatic substances is due to Kermack and Slater,¹ who attempted the resolution of 3-*o*-nitrophenyl-indole-2-carboxylic acid. A recent publication by Steele and Adams² describes the attempted resolution of certain phenylpyridine compounds.

¹ Ray gives no C and H analysis of this acid. Using very small quantities of material he showed by analysis of the silver salt that the silver content agreed with the formula of a tricarboxylic acid $C_8H_{14}O_6$, but titration with 0.1 *N* alkali indicated a dicarboxylic acid $C_8H_{14}O_4$. Analysis of the silver salt and titration could only indicate the equivalent of the acid. These conflicting analyses cannot indicate whether the acid was methylated; that is, whether the acid was $C_8H_{14}O_6$ or $C_8H_{12}O_6$.

¹ Kermack and Slater, *J. Chem. Soc.*, 36 (1928).

² Steele and Adams, *THIS JOURNAL*, **52**, 4528 (1930).