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Synthesis of 2,4-Di(*p*-formyl)-α-truxillic Acid by Crystal Engineering

Fusae Nakanishi,* Michiko Ishii, and Hachiro Nakanishi
Research Institute for Polymers and Textiles 1-1-4 Yatabe-Higashi, Tsukuba, Ibaraki 305

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Synopsis. *p*-Formycinnamic acid, which usually crystallizes in either the β-form or γ-form of packing, was converted into its diethyl acetal. The introduction of such bulky groups onto a benzene ring successfully provided us with the α-form of packing, from which the desired photodimer, 2,4-di(*p*-formyl)-α-truxillic acid (*c*-2, *t*-4-bis(*p*-formylphenyl)-*r*-1,*t*-3-cyclobutanedicarboxylic acid) was obtained with a yield of 85—90%.

We have previously reported[1)] the preparation of 3,4-di(*p*-formyl)-β-truxilic acid (*t*-3, *t*-4-bis(*p*-formylphenyl)-*r*-1, *c*-2-cyclobutanedicarboxylic acid) from *p*-formylcinnamic acid (*p*-FCA)crystals using irradiated light. Two polymorphic forms of *p*-FCA were found, each depending on recrystallization conditions: β-form; photo-reactive and γ-form; photostable. Attempted recrystallization using various kinds of solvents did not provide for the formation of α-form crystals, the photodimerization of which gives us 2,4-di(*p*-formyl)-α-truxillic acid **3** (*c*-2, *t*-4-bis(*p*-formylphenyl)-*r*-1-, *t*-3-cyclobutanedicarboxylic acid). The synthesis of **3** is of considerable interest since it might be converted into the same compound as the photodimer of diethyl 3,3′-(*p*-phenylene)diacrylate and the crystal structure and the photoreactivity of this dimer might provide us with crucial information on the mechanism of the four-center type photopolymerization,[2)] *i.e.*, a kind of crystal transition reaction from the monomer to the polymer.

This report is concerned with the successful formation of **3** by crystal engineering. The data on the crystal structure of cinnamic acid derivatives suggest that the introduction of a bulky group onto a benzene ring of cinnamic acid may lead to the formation of α-form crystals since the steric hindrance of a bulky group avoids the β-type packing. We have chosen a diethyl acetal group as an example of such a bulky group since it is easy to introduce and to retrieve.

First, preparation of **1** of *p*-FCA was attempted by the usual method, using various kinds of acids. The results are shown in Table 1. In the presence of a strong acid, such as conc. sulfuric acid, *p*-FCA was almost converted into **1**. However, the crystals of the diethyl acetal derivative, thus obtained, were unstable and were readily hydrolyzed by moisture in the air. Presumably the crystals were contaminated with acid residues. Even an attempted neutralization of the reaction mixture by washing was not effective in the interior of the crystals and an attempted improvement of the yield was unsuccessful. By means of acetic acid catalysis, the acetal formed was stable to moisture, but *p*-FCA still remained in a considerable amount and, moreover, separation of the acetal from the reaction mixture was rather difficult. Therefore, the following method was carried out in order to improve the preparation. After exposure to hydrogen chloride gas, acidified β-form crystals of *p*-FCA were suspended in ethanol at 15 °C. The UV spectrum of these suspended crystals gradually changed. The maximum of the UV absorption gradually shifted from 295 nm (*p*-FCA) to 276 nm. The crystals obtained at this stage were colorless with a mp of 142 °C, and were identified as **1** of *p*-FCA on the basis of elemental analysis and spectroscopic data (IR, UV, and NMR). This simple reaction proceeded under mild conditions, and side reactions, such as esterification, were not observed and quite pure **1** was obtained. It should be noted that the photostable γ-form of crystalline *p*-FCA was not converted into the acetal under the same conditions. These results suggest that the reaction was controlled by the crystal structure, that is, a topochemical reaction. The crystal structure of β-form of *p*-FCA[3)] showed that formyl groups were exposed on the well-developed crystal face. Though we can not establish the mechanism of this reaction in detail because of lack of the data on the crystal structure of γ-form of *p*-FCA, it seems that the reaction proceeds from a well-developed crystal face through an attack by an ethanol molecule, in a mechanism similar to that proposed for the solid-gas reaction of carboxylic acid with ammonia.[4)] The diethyl acetal crystals were found to be photoreactive. The absorption peak of the UV spectrum of irradiated diethyl acetal crystals in ethanol deceased gradually to a small peak with λ_{max} around 269 nm. At this stage, no absorption peak ascribed to double bonds was observed in the IR spectrum of irradiated crystals. In the NMR spectrum of irradiated crystals in DMSO-d_6, double bonds peaks disappeared and new peaks appeared at δ 3.7—4.6. The proton ratio of each peak in the NMR spectrum (benzene : methine : methylene and new peaks :

Table 1. Preparation of ethyl acetal of *p*-formylcinnamic acid (*p*-FCA)

Reactants	Acid	Reaction conditions	Yield/%
Acidified EtOH+*p*-FCA	Conc H_2SO_4	Reflux	Not isolated
	HCl Gas	Reflux	Mixture of *p*-FCA and diethyl acetal
	CH_3COOH	Reflux	
	HCl	Reflux	45
EtOH+Acidified *p*-FCA	HCl Gas	15 °C	88
Acidified EtOH+*p*-FCA	HCl Gas	15 °C	76

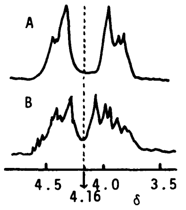
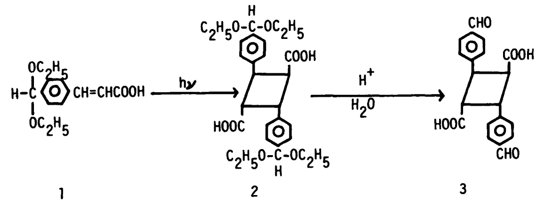


Fig. 1. Cyclobutane ring proton signals of (A) 3,4-di(*p*-formyl)-*β*-truxillic acid and (B) 2,4-di(*p*-formyl)-*α*-truxillic acid.

methyl) was found to be 8:2:12:12. New peaks (4 protons) were assingned as cyclobutane ring protons, based on a comparison with the reported data on cyclobutane rings.⁵⁾ These facts suggest that dimer **2** was formed by cycloaddition of **1**. In order to hydrolyze to a formyl derivative, diethyl acetal groups of the dimer **2** were treated with hydrochloric acid. Formation of dimer **3** was supported by elemental analysis, IR and NMR spectra. The configuration of the cyclobutane ring of **3** was determined by comparing the shape and the mid-point of symmetrical spin patterns of the cyclobutane rings in the NMR spectrum with those of reported cyclobutane rings. According to the report by Ben-Efraim *et al.*,⁵⁾ mid-points of cyclobutane ring proton patterns of *α*-truxillic acid, *β*-truxinic acid and *μ*-truxinic acid (*t*-3, *c*-4-diphenyl-*r*-1, *t*-2-cyclobutanedicarboxylic acid) have the same position. As shown in Fig. 1, the cyclobutane ring patterns of **3**, (B), were mirror-symmetrical but the shape was different from those of 3,4-di(*p*-formyl)-*β*-truxinic acid,¹⁾ (A). The mid-points of both spin patterns were the same value (4.16). These facts suggest that **3** was either *α*-truxillic acid or a *μ*-truxinic acid-type dimer. The cyclobutane ring patterns of **3** are similar to those of *α*-truxillic acid.⁵⁾ Based on these facts, it was certain that product **3** was an *α*-truxillic acid-type dimer. The over-all reaction is shown in Scheme 1. This is the first preparation of *α*-truxillic acid carrying formyl groups on benzene rings.



Scheme 1.

Experimental

p-FCA was prepared according to Wiely.⁶⁾ It crystallized into two different modifications, depending on the crystallization solvent. *β*-Form crystals were obtained from ethanol and *γ*-form from acetone. Both forms have the same melting point, 249 °C, but they have different X-ray diffraction patterns.

Preparation of Diethyl Acetal of p-*Formylcinnamic Acid.* *β*-Form crystals of *p*-FCA (2 g) were exposed to anhydrous hydrogen chloride gas for 30 min and the crystals were acidified. They were suspended in ethanol (30 ml) while stirring at 15 °C. At this temperature, 10% of the *p*-FCA crystals were dissolved in the ethanol. In order to determine the progress of reaction, the UV spectrum of the suspended crystals was occasionally measured while in the ethanol. When the absorption peak of the crystals ceased to shift, the crystals were collected by filtration. Some of diehyl acetal of *p*-FCA was further obtained by the evaporation of the mother liquor. The combined yield was 2.5 g. Found: C, 67.02; H, 6.93%. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25%. Mp 142 °C (from ethanol-hexane); UV$_{max}$ (EtOH) 276 nm; ^{1}H NMR (DMSO-d_6); δ=1.2 (6H, t, -CH$_3$) 3.3—3.7 (4H, q, -CH$_2$-), 5.5 (1H, s, -CH), 6.4—7.9 (2H, d, -CH=CH-), 7.3—7.8 (4H, m, aromatic proton).

Photodimerization of Diethyl Acetal of p-*FCA in the Crystalline State.* Diethyl acetal crystals (100 mg) of *p*-FCA were suspended in hexane (100 ml) and irradiated with a 500 W xenon lamp at 15—20 °C. After 6 h diethyl acetal of *p*-FCA was changed to the dimer in the yield of 85—90%. Mp 230—232 °C; ^{1}H NMR (DMSO-d_6); δ=1.15 (12H, t, -CH$_3$), 3.3—3.7 (8H, q, -CH$_2$-), 5.5 (2H, s, -CH), 3.7—4.6 (4H, m, cyclobutane proton), 7.3 (8H, m, aromatic proton).

Dimer **2** (100 mg) was suspended in dil HCl (50 ml) for a few hours while stirring. By this treatment dimer **3** was obtained. Mp 273—275 °C (from ethanol-water); UV$_{max}$ (EtOH) 264 nm; Found: C, 68.17; H, 4.68%. Calcd for $C_{20}H_{16}O_6$: C, 68.18; H, 4.58%. ^{1}H NMR (DMSO-d_6); δ=3.7—4.6 (4H, m, cyclobutane proton), 7.4—8.0 (8H, m, aromatic proton), 10.0 (2H, s, -CHO).

References

1) F. Nakanishi, H. Nakanishi, T. Tsuchiya, and M. Hasegawa, *Bull. Chem. Soc. Jpn.*, **49**, 3096 (1976).

2) F. Suzuki, Y. Suzuki, H. Nakanishi, and M, Hasegawa, *J. Polym. Sci.*, A-1, **7**, 2391 (1969).

3) H. Nakanishi, Unpublished data.

4) R. S. Miller, D. Y. Curtin, and I. C. Paul, *J. Am. Chem. Soc.*, **96**, 6329 (1974).

5) D. A. Ben-Efraim and B. S. Green, *Tetrahedron*, **30**, 2357 (1974).

6) R. H. Wiley and P. H. Hobson, *J. Am. Chem. Soc.*, **71**, 2429 (1949).