and the temperature was lowered in an attempt to detect the ester rather than the oxime. In reaction of alkyl halides with salts of nitrocyclohexane the procedure employed differs from the reference,[1] in that the salt was first prepared by shaking an equivalent amount of base with a methanolic solution of the nitroparaffin until reaction was complete. The alkyl halide was then added in stoichiometric quantity and the mixture was stirred for several hours while controlling the temperature with a bath of ice, Dry Ice, or other coolant around the vessel.

Titrations. The titrimetric experiments employed about 0.01 mole of nitrocyclohexane or its salt, dissolved or suspended in 50 ml. or more of solvent (methanol or ethanol; a few runs were also tried in water). 1 *N* HCl and NaOH were used as titrating reagents. A Leeds and Northrup electronic *p*H recording titrator was used.

Nitrocyclohexane does not interfere with titration. In methanolic media it does not react at an appreciable rate with base until the *p*H reading exceeds 11. Since hydrochloric acid makes little contribution to the titration curve above *p*H 3 in either water or methanol the bulk of the measured *p*H range is free of obstacles to titrating *aci*-nitrocyclohexane or its salt. The curves obtained in methanol are displaced toward higher *p*H than in water. Neither are symmetric because of the disappearance of the free *aci* form. Therefore the exact strength of *aci*-nitrocyclohexane is not readily determined from the titration curves. *Aci*-nitrocyclohexane appears to be comparable in strength to acetic acid—perhaps slightly stronger. This is similar to the reported ionization of *aci*-nitroethane.[11]

Mass spectrometer analysis. The mass spectrum of cyclohexanone dimethyl acetal, a frequent component of the reaction mixtures in this work, is presented elsewhere.[12] The mass spectra of the other important compounds involved in these reactions are shown in Table I. Peaks below *m/e* 35 were not used for analytical purposes and have been omitted here.

All analyses were performed on a modified 90° sector type mass spectrometer.[13] The sample inlet system temperature was 100° and the ion source temperature was 160°.

Calculation of the mass spectra of the samples was done by the usual stepwise subtraction of component spectra[14] in the conventional manner and needs no further explanation here.

Acknowledgment. The authors wish to thank Oscar Daniels for obtaining polarographic data, Alvin W. Baker, William J. Potts, Jr., Richard A. Nyquist, and Duncan S. Early for infrared analyses, A. W. Baker for Raman analyses, H. W. Rinn and R. F. Bremer for x-ray analyses, E. R. Hopke for ultraviolet analyses, R. F. Lind, R. F. Hamilton, and associates for laboratory distillation services, and Union Oil Co. of California and E. I. du Pont de Nemours and Co. Inc., for supplying samples of nitrocyclohexane.

---

(11) Maron and Shedlovsky, *J. Am. Chem. Soc.*, **61**, 753 (1939).

(12) McCoy, Baker, and Gohlke, to be published.

(13) The instrument has been described by Caldecourt, ASTM Committee E-14 Mass Spectrometer Conference, New Orleans, May 1954.

(14) Washburn, Wiley, and Rock, *Ind. Eng. Chem., Anal. Ed.*, **15**, 541 (1943).

[CONTRIBUTION FROM THE INSTITUTE FOR CHEMICAL RESEARCH, KYOTO UNIVERSITY]

Nitration of Desoxybenzoin

MICHIYASU SUGII AND RISABURO NAKAI

Received July 3, 1956

The action of nitric acid (*d* 1.30) on desoxybenzoin-carbonyl-C^{14} has been investigated. The reaction routes have been elucidated from radio assay of the reaction products and their fission products.

In the nitration of desoxybenzoin to nitrobenzil reported by Zinin,[1] it is not possible to decide which benzene nucleus of desoxybenzoin is nitrated. The nitration of the benzyl nucleus seems to be more probable, since Ney[2] found that desoxybenzoin gave *p*-nitrodesoxybenzoin by treating with fuming nitric acid at low temperatures. A decision as to the reaction route, however, is possible by using desoxybenzoin labeled in the carbonyl with isotopic carbon, since the different routes of reactions will lead to isotopically distinguishable products.

The syntheses and the reaction routes are shown in Fig. 1. The measured specific activities of the products at each step are also shown under the formulas. For the determination of specific radioactivity, the labeled compounds were burned in a wet combustion apparatus described by Claycomb *et al.*,[3] and converted to barium carbonate. The activity was counted at infinite thickness with a Geiger-Müller counter tube and compared with the count of a standard barium carbonate.

By the nitration of desoxybenzoin-carbonyl-C^{14} (I), prepared from phenylacetic acid-carboxyl-C^{14}, there were obtained benzoic acid-carboxyl-C^{14} (VI), inactive *p*-nitrobenzoic acid (V) and a mixture of *p*-nitrobenzil-carbonyl-C^{14} (II) and benzil-carbonyl-C^{14} (III). As the nitrating agent more concentrated nitric acid (*d* 1.30) than Zinin's nitric acid (*d* 1.20) was used, because the former gave better yield of pure II. The crude mixture of the two benzils was purified by means of chromatography

---

(1) N. Zinin, *Ann.*, Supplementbandes **3**, 154 (1864). The position of nitro group of nitrobenzil obtained by him was obscure and he reported that when nitrobenzil was treated with alcoholic potassium hydroxide, he obtained oxybenzoic acid and azobenzoic acid.

(2) E. Ney, *Ber.*, **21**, 2448 (1888).

(3) C. K. Claycomb, T. T. Hutchens, and J. T. Van Bruggen, *Nucleonics*, **7**, No. 3, 38 (1950).

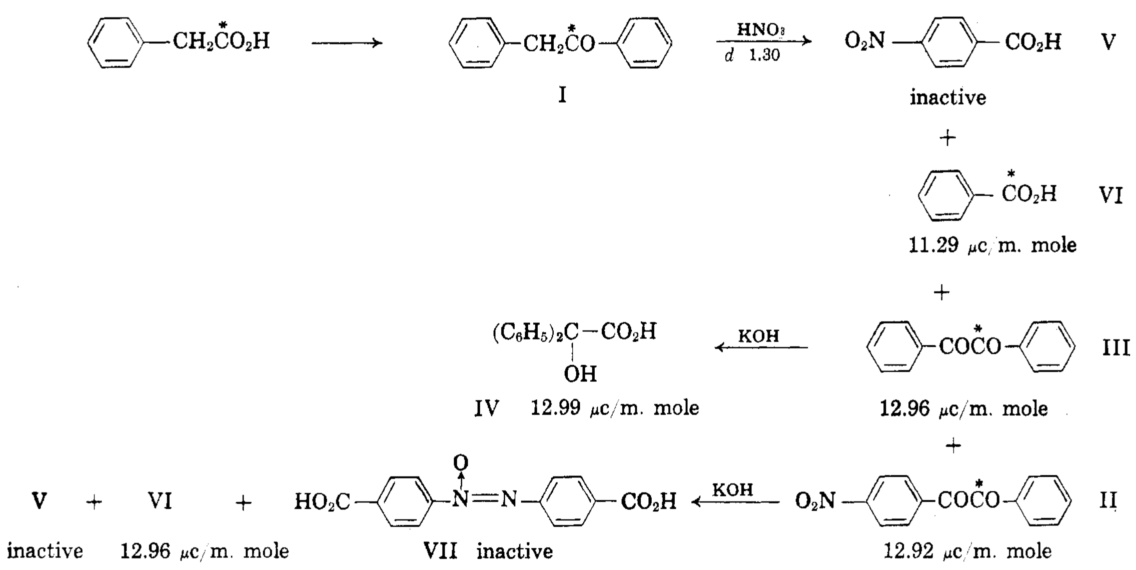

FIG. 1

and separated into each component, II and III, by fractional crystallization; compound II gave yellow minute scales, m.p. 141–142° and III gave yellow needles, m.p. 93–94°. Compound III was identified by conversion into benzilic acid-1-C^{14} or -2-C^{14} (IV).

When treated with alcoholic potassium hydroxide, II decomposed easily into inactive *p,p'*-azoxydibenzoic acid (VII), benzoic acid-carboxyl-C^{14} (VI) and inactive *p*-nitrobenzoic acid (V). The nitro derivatives of the decomposition products showed no activity and the specific activity of VI was equal to that of II. These facts indicate that in the nitration of I, the nitro group enters a *para* position to the methylene group of desoxybenzoin-carbonyl-C^{14}.

The nonlabeled specimens of *p*-nitrodesoxybenzoin, *p*-nitrobenzil, and benzil were synthesized and treated with the nitric acid, respectively, in the same manner as mentioned above. *p*-Nitrodesoxybenzoin gave benzoic acid, *p*-nitrobenzoic acid, and *p*-nitrobenzil. Benzil and *p*-nitrobenzil, however, were resistant to nitration and oxidation and were recovered quantitatively. These results would lead to the following conclusions. In the course of the action of the nitric acid on desoxybenzoin-carbonyl-C^{14}, the *p*-nitrodesoxybenzoin-carbonyl-C^{14} is formed as an intermediate product, and its methylene group is oxidized to a carbonyl group, and produces *p*-nitrobenzil-carbonyl-C^{14}. The oxidative disruption of the same intermediate, which occurs simultaneously with the above oxidation, gives benzoic acid-carboxyl-C^{14} and inactive *p*-nitrobenzoic acid. A similar oxidation prior to the nitration of desoxybenzoin-carbonyl-C^{14} also takes place and yields benzil-carbonyl-C^{14}, which undergoes no reaction with the nitric acid. On the other hand, oxidative disruption prior to nitration of desoxybenzoin-carbonyl-C^{14} will produce both inactive and active benzoic acid and cause some decrease in the specific activity of the isolated benzoic acid-carboxyl-C^{14}. This concept was confirmed by the fact that the specific activity of benzoic acid-carboxyl-C^{14}, which had been produced through the two reaction routes of desoxybenzoin-carbonyl-C^{14}, was comparatively lower (11.29 μc/mmol.) than the theoretical value (12.95 μc/mmol.) expected from the specific activity of starting material.

The essential reaction routes of the reaction of desoxybenzoin-carbonyl-C^{14} with nitric acid is shown in Fig. 2.

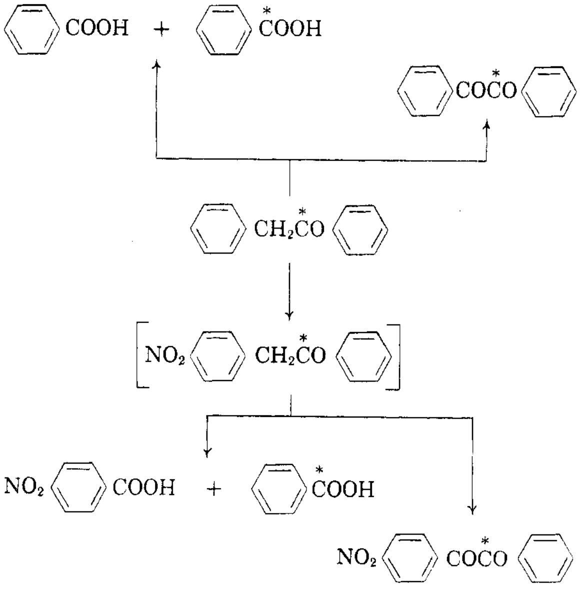

FIG. 2

EXPERIMENTAL

Desoxybenzoin-carbonyl-C^{14} (I). To 8.05 g. of phenylacetic acid-carboxyl-C^{14} (12.87 μc/m.mol.) in a 200 ml. two-neck flask fitted with a reflux condenser was added 15 g. of thionyl chloride. The mixture was heated on a water bath for 20 min. The thionyl chloride was removed under vacuum and after the residue was allowed to cool, 50 ml. of dry benzene and 9 g. of anhydrous aluminum chloride were added. The mixture was refluxed for 1 hr. on a water bath, then cooled, and poured onto a mixture of 100 g. of cracked ice and 5 ml. of concentrated hydrochloric acid. The benzene layer was separated, and the aqueous layer was extracted with a mixture of 25 ml. of benzene and 25 ml. of ether. The ether-benzene solution was washed with 20 ml. of water, and dried over calcium chloride. The solvent was removed under reduced pressure. The residue was recrystallized twice from methanol; yield, 6.95 g.; m.p. 54–55°. It had a specific activity of 12.95 μc per mmol. On further cooling of the mother liquor, 2.01 g. of crystals was obtained. The total yield of product was 8.96 g. (77.5%).

Nitration of desoxybenzoin-carbonyl-C^{14}. (a) *p-Nitrobenzil-carbonyl-C^{14}* (II). To 68 g. of nitric acid (*d* 1.30) was added 8.46 g. of I and the mixture was gently refluxed for 40 min. The cooled mixture was poured into 800 ml. of water and boiled. The heavy yellow oil was separated from the hot aqueous liquor by means of hot funnel. This oil layer solidified and 6 g. of yellow crystals was obtained, m.p. 60–80°. The benzene solution of crude crystals was passed through the alumina-column. The eluted residue was recrystallized thrice from ethanol. The final pure product formed yellow minute scales (m.p. 141–142°) and was obtained in a yield of 1.74 g. (15.8%). It had a specific activity of 12.92 μc per mmol.

Anal. Calcd. for $C_{14}H_9O_4N$: C, 65.88; H, 3.55; N, 5.49. Found: C, 66.10; H, 3.64; N, 5.32.

(b) *Benzil-carbonyl-C^{14}* (III). The mother liquor (ethanol) separated from II was evaporated and 3.87 g. of yellow residue was obtained. The residue was redissolved in 50 ml. of ethanol and allowed to stand overnight at room temperature. The long yellow needles were collected and weighed, 1.48 g. (16.4%), m.p. 89–94°. The benzene solution of crystals was passed through the alumina column. The eluted residue was recrystallized twice from ethanol and yielded 0.79 g. (8.75%) of yellow needles, m.p. 93–94°. No depression in melting point occurred, when mixed with an authentic sample of benzil. It had a specific activity of 12.96 μc per mmol.

(c) *Benzilic acid-1-C^{14} or-2-C^{14}* (IV). From 0.738 g. of III, 0.613 g. (76.6%) of crude benzilic acid (m.p. 146–148°) was prepared, by the method of Liebig.[4] The crude product was recrystallized twice from benzene and yielded 0.508 g. (63.5%) of fine needles; m.p. 149–150°. It had a specific activity of 12.99 μc per mmol. When mixed with an authentic sample of benzilic acid, no depression in melting point occurred.

(d) *p-Nitrobenzoic acid* (V). The hot aqueous liquor described in (a), from which the yellow oil layer was separated, was allowed to stand overnight. The pale yellow crystals which were filtered and dried, weighed 1.49 g. (20.8%); m.p. 190–200°: The product was recrystallized five times from boiling water, and sublimed at a temperature of 140–150° and a pressure of 7 mm. The sublimate, when recrystallized from boiling water, yielded 0.3 g. (4.15%) of pale yellow scales, m.p. 238–239°. When mixed with an authentic sample of *p*-nitrobenzoic acid, no depression in melting point occurred. A 2.855 mg. sample contained an activity indistinguishable from the background.

(e) *Benzoic acid-carboxyl-C^{14}* (VI). The aqueous filtrate separated from crude V, described in (d) was combined with the mother liquor of V and the mixed aqueous solution was extracted with ether. After washing the ether solution with water, the ether was distilled off. The residue was sublimed at a temperature of 60–65° and a pressure of 7 mm. It formed almost white needles; m.p. 115–119°; yield, 0.916 g. (17.4%). After three sublimations, white needles, m.p. 120–121°, were obtained; yield, 0.765 g. (14.5%). It had a specific activity of 11.29 μc per mmol. When mixed with an authentic sample of benzoic acid, no depression in melting point occurred.

Decomposition of p-nitrobenzil-carbonyl-C^{14}. (a) *p,p'-Azoxydibenzoic-acid* (VII). To a solution of 1.7 g. of potassium hydroxide in a mixture of 7 ml. of water and 10 ml. of ethanol was added 1.66 g. of II and the mixture was refluxed for 20 min. on a water bath. After cooling, the precipitated crystalline product (potassium salt of VII) was filtered and washed with ethanol. The crystals were redissolved in 80 ml. of hot water and filtered. The filtrate was acidified with dilute hydrochloric acid. The gelatinous substance was precipitated, centrifuged and washed well with hot water. The yield was 0.784 g. (42%). This product was further boiled with ethanol, filtered, washed with hot ethanol, dissolved in dilute ammonia, and then reprecipitated with dilute hydrochloric acid. Reprecipitation was repeated five times to remove the other adsorbed radioactive compounds. The yield was 0.641 g. (34.3%). The purified product was a yellow, amorphous powder, insoluble in all solvents and did not melt below 300°. Its analytical data corresponded to *p,p'*-azoxydibenzoic acid, and the ultraviolet absorption spectrum was also identical with that of the authentic specimen.[5] A 2.585 mg. sample contained an activity indistinguishable from the background. λ_{max} 262 mμ (0.1*N* NaOH) log ϵ 4.06; 335 mμ, log ϵ 4.24.

Anal. Calcd. for $C_{14}H_{10}N_2O_5$: C, 58.74; H, 3.51; N, 9.79. Found: C, 58.52; H, 3.51; N, 9.73.

(b) *Benzoic acid-carboxyl-C^{14}* (VI). The filtrate separated from the potassium salt of VII was treated with 5 ml. of water and acidified with hydrochloric acid. After evaporating the solvent (ethanol), the residual aqueous solution was allowed to stand overnight at room temperature. The crystalline product was filtered, washed with 4 ml. of water, and sublimed at a temperature of 60–65° and a pressure of 7 mm. Almost colorless needles, m.p. 114–118°, were obtained; yield, 0.566 g. (71%). After three sublimations white needles, m.p. 120–121°, were obtained; yield, 0.406 g. (51%). It had a specific activity of 12.96 μc per mmol. When mixed with an authentic sample of benzoic acid, no depression in melting point occurred.

(c) *p-Nitrobenzoic acid* (V). The residual part from sublimation of VI was further sublimed at a temperature of 140–50° and a pressure of 7 mm. Yellow needles were obtained; yield, 0.145 g. (13.3%); m.p. 192–200°. The sublimate was recrystallized thrice from boiling water and pale yellow scales were obtained, yield 0.046 g. (4.2%), m.p. 238–239°. When mixed with an authentic sample of *p*-nitrobenzoic acid, no depression in melting point occurred. A 1.633 mg. sample contained an activity indistinguishable from the background.

Action of nitric acid on p-nitrodesoxybenzoin. To 30 g. of nitric acid (*d* 1.30) was added 4.0 g. of *p*-nitrodesoxybenzoin which was prepared from *p*-nitrophenylacetic acid by the method of Petrenko-Kritschenko.[6] The mixture was treated in the same manner as that described in the nitration of desoxybenzoin-carbonyl-C^{14} and gave 2.03 g. (47.7%) of *p*-nitrobenzil, 0.39 g. (14.0%) of *p*-nitrobenzoic acid, and 0.3 g. (14.7%) of benzoic acid.

Action of nitric acid on p-nitrobenzil and benzil. A mixture of 2 g. of *p*-nitrobenzil and 16 g. of nitric acid (*d* 1.30) and a mixture of 5 g. of benzil and 40 g. of nitric acid (*d* 1.30) were treated, respectively, in the same manner as described in the above. In these cases, no reaction was recognized. *p*-Nitrobenzil and benzil were recovered quantitatively; 1.99 g. (99.5%); 4.97 g. (99.5%).

TAKATSUKI, OSAKA-FU, JAPAN

---

[4] H. V. Liebig, *Ber.*, 41, 1644 (1908).

[5] F. Meyer and K. Dahlem, *Ann.*, **326**, 334 (1903).

[6] P. Petrenko-Kritschenko, *Ber.*, **25**, 2242 (1892).