The Preparation of Tetramethylphthalic Anhydride[1)]

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The alkaline hydrolysis of bis(nitromethyl)prehnitene (**1**) with aqueous sodium hydroxide gave almost quantitatively disodium tetramethylphthalate (**11**). Under milder conditions the sodium salts of tetramethylphthalimide (**8**), *N*-hydroxytetramethylphthalimide (**10**), and 2-hydroxy-3-hydroxyimino-4,5,6,7-tetramethylphthalimide (**9**) were formed, probably as intermediate products of the above reaction. But, pentamethylphenylnitromethane (**14**) and bis(nitromethyl)isodurene (**15**) were not hydrolyzed in an aqueous base. From the above results, it is recognized that the sodium nitronate from **1** is unstable in a different way from general nitronates such as the sodium salt of **14** or **15**. It appears that the instability of **1** arises from the two adjacent nitromethyl groups on the benzene ring.

Phthalic anhydride is used chiefly in the manufacture of alkyd resins, plasticizers, dyes, and pigments. Also, tetrachlorophthalic anhydride is commercially available in heat-stable alkyd resins, dye intermediates, *etc.* Similarly, if polymethylphthalic anhydride could be easily prepared, it would have many uses. But phthalic anhydride is a very unreactive compound with respect to alkylation. Also, tetramethylphthalic anhydride (**13**) or acid is hard to obtain from hexamethylbenzene by the selective oxidation.[2)]

We have previously reported that bis(nitromethyl)-prehnitene (**1**) was obtained by the nitration of hexamethylbenzene with benzoyl nitrate by Willstätter's method.[3,4)] In the present paper, the reaction of **1** with an aqueous base was studied, and a useful procedure for preparing **13** was found.

Hitherto, many studies of the acid hydrolysis of nitroalkanes have been reported. For example, the acid hydrolysis of a salt of a primary or secondary nitroalkane affords an aldehyde or a ketone, respectively, and nitrous oxide (Nef reaction).[5,6)] Closely related to the Nef reaction is the hydrolysis of free primary nitroalkanes with concentrated mineral acid to the corresponding carboxylic acids and hydroxylamine salts.[7)] It is considered that the above reactions of nitroalkanes require an initial acid-catalyzed isomerization to nitronic acid.[8)] But no reports of the alkaline hydrolysis of a salt of a nitroalkane or free nitroalkane seem to have been made.

Results and Discussion

1 was treated with 5% sodium hydroxide at 75 or 100 °C. By addition of silver nitrate solution to the resulting solution, the products were isolated as their silver salts, which were treated with methyl iodide. From the methylated reaction mixture, *N*-methyltetramethylphthalimide (**8′**), 2-methoxy-3-methoxyimino-4,5,6,7-tetramethylphthalimidine (**9′**), *N*-methoxytetramethylphthalimide (**10′**), and dimethyl tetramethylphthalate (**11′**) were isolated by column chromatography. Further, from the reaction mixture in an early stage a trace of methyl 2-cyano-3,4,5,6-tetramethylbenzoate (**12′**) was also isolated.

Table 1. Reaction of bis(nitromethyl)prehnitene with an aqueous sodium hydroxide

Expt. No.	Conditions Temp (°C)	Time (min)	Yields (mol %)[a)] **8′**	**9′**	**10′**	**11′**	Unknowns (wt %)
1	75	10	14	2	13	49	8
2	100	15	2	—	15	64	10
3	100	30	—	—	10	77	—
4	100	5 h	—	—	—	97	—

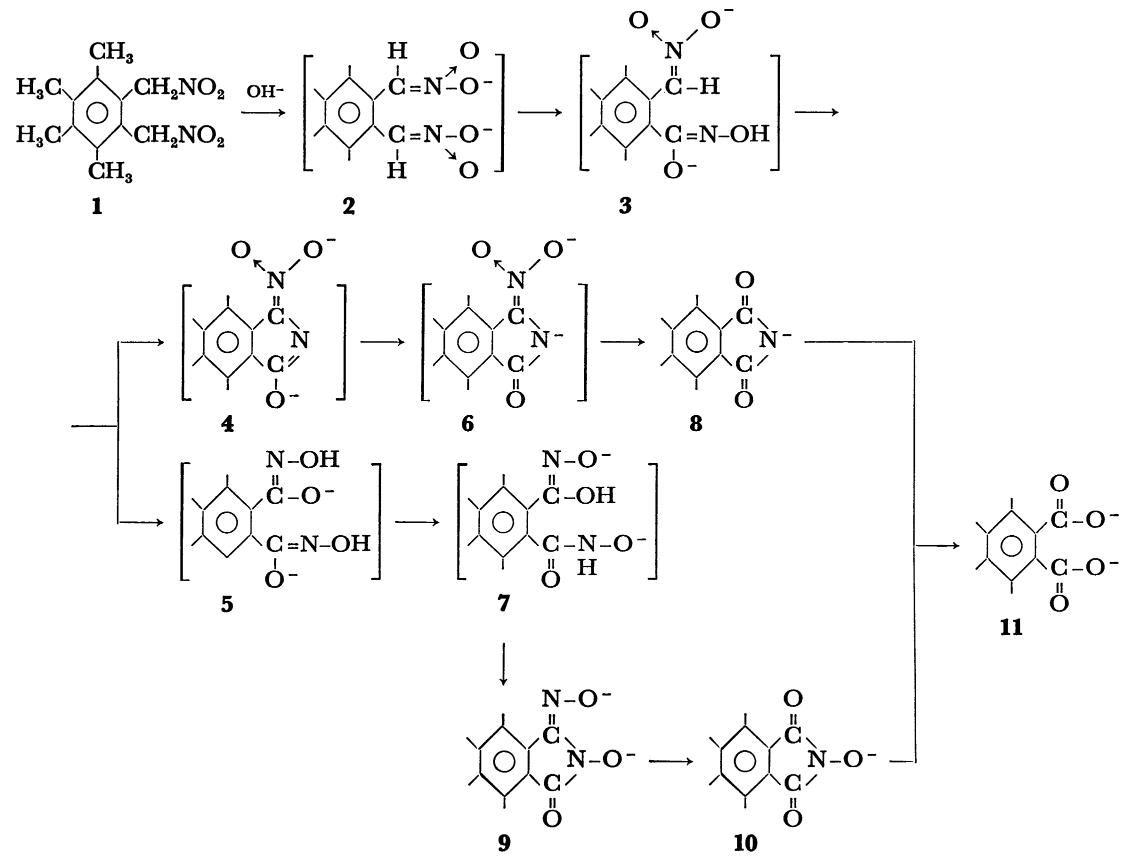
a) The yields were determined by GLC after the products were methylated by warming their silver salts in methyl iodide.

The reaction was followed by measuring the yields of these products. The results are given in Table 1. Under milder conditions **8′**, **9′**, and **10′** were obtained (Expt. No. 1). But, on continued warming, they rapidly decreased, whereas **11′** increased. Finally, an almost quantitative yield of **11′** was obtained.

On the other hand, after **1** was treated with 5% sodium hydroxide at 100 °C for 9.5 h, the acidification of the hydrozate with diluted hydrochloric acid gave almost quantitatively tetramethylphthalic anhydride (**13**). The filtrate reduced Fehling's solution. This fact suggested that the hydroxylamine salt was produced, but further investigations were not carried out. Also, when **1** was treated with 10% sodium hydroxide, almost similar results were obtained. But, when pentamethylphenylnitromethane (**14**) or bis(nitromethyl)isodurene (**15**) was treated with 5% sodium hydroxide at 100 °C for 10 h, the acidification of the resulting solution with hydrochloric acid gave unreacted **14** or **15** only. Moreover, upon treatment with 35% hydrochloric acid at 100 °C for 5 h in a sealed tube, **1** was recovered unchanged.

From the above results, it is recognized that the sodium nitronate (**2**) from **1** is unstable in a different way from general nitronates such as the sodium salt of **14** or **15**, and so the conversion of **1** to the phthalate (**11**) does not require the initial isomerization to the free nitronic acid. It appears that the instability of **1** arises from the two adjacent nitromethyl groups on the benzene ring.

A plausible reaction path is shown in the following scheme. But there is no evidence pertaining to the mechanism of conversion of nitronate to hydroxamate.



Scheme 1.

Disodium tetramethylphthalate (**11**) is easily converted to **13** by acidification, probably since the steric repulsion of four methyl groups on the benzene ring facilitates the cyclization between two carboxyl groups. The phthalic acid could not be isolated. Similarly, the hydroxamate **3** or **7** would be easily converted to the cyclized product **4** or **9**, respectively, which is finally hydrolyzed to produce **11**. But it is not clear which is chosen more preferentially as an intermediate, sodium tetramethylphthalimide (**8**) or sodium *N*-hydroxytetramethylphthalimide (**10**).

Experimental

Analyses. All melting points are uncorrected. IR spectra were recorded by means of a Hitachi EPI-S2 spectrometer, while NMR spectra were obtained by a Hitachi R-22 NMR spectrometer at 90 MHz, using tetramethylsilane as an internal standard. The GLC analyses were carried out on a Hitachi 063 apparatus, using Silicone DC 550 (25%)-Celite 545 (4 mm × 1 m) columns (Temp: 215 °C; Carrier gas: H_2 40 ml/min).

Materials. **1**, **14**, and **15** were obtained by the nitration of hexamethylbenzene with acetyl nitrate according to the following method.

Fuming nitric acid (30 g, $d=1.5$) was added over a period of 0.5 h to vigorously stirred acetic anhydride (150 ml), keeping the temperature between 15 and 20 °C by the use of an ice bath. The resulting solution was added to a solution of hexamethylbenzene (14.0 g) in carbon tetrachloride (150 ml), and stirred at about 5 °C for 2 h. The reaction mixture was poured into water (450 ml). The organic layer was separated and washed with dilute sodium carbonate and then with water. Concentration and cooling of the solution yielded a white crystalline solid. Its chromatography (7.2 g) on silica gel gave **14** (0.2 g, mp 85—87 °C; lit,[10] 86—88 °C) from the light petroleum eluates; **1** (6.5 g, mp 139—140 °C; lit,[3] 139 °C) and **15** (0.2 g) from the benzene elutes. **1** and **4** were identified by comparison of these IR and NMR spectra with those of authentic samples. The structure of **15** was deduced from elemental analysis and spectral data.

15: colorless needles, mp 146—147 °C. Found: C, 56.83; H, 6.57; N, 10.96%. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10%. IR (KBr, cm^{-1}): 1542 and 1386 ($-NO_2$). NMR ($CDCl_3$, δ ppm): 2.29 (s, Ar–CH_3, 3H), and 5.75 (s, $-CH_2-$, 4H).

General Procedures. **1** (0.100 g) was treated with 5% sodium hydroxide (15 ml) at 75 or 100 °C in a sealed tube. The resulting solution was cooled to room temperature, and treated with a large excess of silver nitrate solution (4.0 g/20 ml). After cooling, the precipitate was collected by filtration, dried, and refluxed with methyl iodide (1 g) in benzene (50 ml) for 6 h. An insoluble material was filtered off, and the filtrate was evaporated to dryness under reduced pressure.

Isolation of the Products. The following example shows a typical experimental procedure (Expt. No. 1, Table 1).

The residue (0.1 g) obtained by the evaporation of the above filtrate was chromatographed on a column (1 × 12 cm) of alumina (10 g, 200—300 mesh) and eluted successively with petroleum ether (50 ml), petroleum ether–benzene (1: 1, 100 ml), benzene (50 ml), benzene–diethyl ether (1: 1, 100 ml), diethyl ether (50 ml), and diethyl ether–methanol (100 ml). Each fraction was evaporated, and the residue was recrystallized from methanol to afford the following products successively: *N*-methyltetramethylphthalimide (**8′**), dimethyl tetramethylphthalate (**11′**), 2-methoxy-3-methoxyimino-4,5,6,7-tetramethylphthalimidine (**9′**), and *N*-methoxytetramethylphthalimide (**10′**). **8′**, mp 180—181 °C, was identified by comparison with the IR and NMR spectra of an authentic sample.[9] The structures of **9′**, **10′**, and **11′** were deduced from their elemental analyses and spectral data.

9′: colorless prisms, mp 156—158 °C. Found: C, 64.61; H, 7.06; N, 10.73%. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68%. IR (KBr, cm^{-1}): 1725 (C=N), 1637 (C=N), 1265, 1146, 1121, 1037, 994, and 932 (C–N, C–O or N–O). NMR ($CDCl_3$, δ ppm): 2.15 (d, Ar–CH_3, 6H), 2.50 (d, Ar–CH_3, 6H), and 4.04 (d, O–CH_3, 6H).

10′: colorless needles, mp 203—204 °C. Found: C, 67.15; H, 6.32; N, 6.18%, mol wt (Rast), 236. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01%; mol wt, 223. IR (KBr, cm^{-1}): 1760, 1719 (C=O), 1254, 1146, 1102, 998, and 905 (C–N, C–O, or N–O). NMR ($CDCl_3$, δ ppm): 2.24 (s, Ar–CH_3, 6H), 2.56 (s, Ar–CH_3, 6H), and 4.00 (s, O–CH_3, 3H).

11′: colorless plates, mp 127.5—128.5 °C. Found: C, 66.95; H, 7.33%. Calcd for $C_{14}H_{18}O_4$: C, 67.10; H, 7.25%. IR (KBr, cm^{-1}): 1724 (C=O), 1233, and 1162 (C–O–C). NMR ($CDCl_3$, δ ppm): 2.25 (Ar–CH_3, 6H), 2.35 (Ar–CH_3, 6H), and 3.85 (–OCH_3, 6H).

Further, from the reaction mixture in an early stage (Expt. No. 1) a trace of **12′**, mp 75—76 °C, was also isolated; it was identified by comparing its retention time in GLC and its IR spectrum with those of an authentic sample.[9]

The progress of the reactions was followed by GLC. The results are shown in Table 1. The yields of products were caculated by assuming that the ratio of the peak areas was identical with the weight ratio of the products. Here, the peak of **8′** overlapped with that of **11′**, and so, if necessary, the ratio of **8′** to **11′** was derived from the result of the column chromatography.

Preparation of Tetramethylphthalic Anhydride (13). To 5% sodium hydroxide (50 ml), **1** (1.00 g) was added, and the mixture was stirred at 100 °C for 9.5 h. The reaction mixture was cooled to room temperature, and acidified by the addition of 2M hydrochloric acid. The resulting white precipitate was collected by filtration, dried (0.77 g, 95 mol % as **13**), and recrystallized from benzene: colorless needles, mp 238—239 °C. Found: C, 70.70; H, 5.81%; mol wt (Rast), 200. Calcd for $C_{12}H_{12}O_3$: C, 70.61; H, 5.88%; mol wt, 204. IR (KBr, cm^{-1}): 1834, 1767 (C=O), 1200, and 910 (C–O). NMR ($CDCl_3$, δ ppm): 2.3 (Ar–CH_3, 6H) and 2.6 (Ar–CH_3, 6H).

Further, **13** (0.4 g) was dissolved in 2 M sodium hydroxide (30 ml), and the solution was treated with excess silver nitrate solution. The resulting precipitate was collected by filtration, dried, and refluxed with excess methyl iodide (1.5 ml) in benzene (30 ml) for 4 h. After filtration of the insoluble materials, the filtrate was evaporated, and the residue was recrystallized from methanol to afford **11′** (0.3 g) as colorless plates.

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