(m, 3 H), 1.35 (sextet, J = 7 Hz, 2 H), 0.88 and 0.89 (two t, J = 7 Hz, 3 H), 0.00 and -0.01 (two s, 9 H). Anal. Calcd for $C_{14}H_{26}O_2Si$: 254.1702. Found: 254.1711.

7, 8 (R = CN) (R_f 0.45, 4:1 hexane-ether): IR ($CHCl_3$) 2210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.87 and 5.98 (two bs, 1 H), 2.7-2.9 (m, 1 H), 1.8-2.8 (m, 6 H), 0.03 (s, 9 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 146.5, 137.7, 134.6, 130.8, 122.4, 29.8, 29.6, 25.7, 25.2, 24.9, 24.6, 24.5, -2.4. Anal. Calcd for $C_{10}H_{17}NSi$: 179.1130. Found: 179.1128.

7, 8 (R = $CONH_2$): mp 85 °C (R_f 0.50, 7:3 hexane-ethyl acetate); IR ($CHCl_3$) 1680, 1540 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.38 (bs, 1 H), 5.93 (bs, 1 H), 5.52 (bs, 1 H), 1.8-2.5 (m, 6 H), 1.5-1.7 (m, 1 H), 0.01 and 0.03 (two s, 9 H). Anal. Calcd for $C_{10}H_{19}NOSi$: 197.1235. Found: 197.1225.

9 (R_f 0.50, 4:1 hexane-ether): IR ($CHCl_3$) 1750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.92 (bs, 1 H), 3.70 (s, 3 H), 3.68 (s, 3 H), 2.80 (m, 2 H), 2.43 (m, 2 H), 2.17 (m, 2 H), 0.045 (s, 9 H). Anal. Calcd for $C_{13}H_{22}O_4Si$: 270.1287. Found: 270.1273.

Preparation of 3-(Trimethylsilyl)-1,3,7-octatriene (5). Stirring 9 mg (5 mol %) of palladium acetate, 52 mg (25 mol % of triphenylphosphine, and 0.053 mL (10 mol %, 1.5 M in hexane) of n-butyllithium in 2 mL of THF at room temperature for 1 h generates a yellow solution. At the same temperature, 150 mg (0.80 mmol) of acetate **3a** and 81 mg (0.81 mmol) of triethylamine were added sequentially and the resulting solution was refluxed overnight. Following the same workup as above gave, after flash chromatography eluting with hexane, 45 mg (62% yield) of the triene **5**: IR ($CHCl_3$) 1635 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 6.63 (ddd, J = 17.5, 11.0, 1.1 Hz, 1 H), 5.80 (m, 2 H), 5.12 (dd, J = 17.5, 1.2 Hz, 1 H), 5.10 (dd, J = 11.0, 1.2 Hz, 1 H), 5.00 (dd, J = 17.0, 1.5 Hz, 1 H), 4.95 (dd, J = 12.0, 1.5 Hz, 1 H), 2.30 (m, 2 H), 2.10 (m, 2 H), 0.10 (s, 9 H). Anal. Calcd for $C_{11}H_{19}Si$: 180.1290. Found: 180.1182.

Acknowledgment. We thank the National Science Foundation and Rhone-Poulenc for their generous support of this program.

Registry No. **1**, 13683-41-5; **2a**, 66374-47-8; **2b**, 103202-40-0; **3a**, 103202-20-6; **3b**, 103202-21-7; **5**, 103202-37-5; **6**, 14221-01-3; **7** (R = CH_3), 103202-22-8; **7** (R = CH_2CH_3), 103202-24-0; **7** (R = CO_2CH_3), 103202-26-2; **7** (R = $CO_2C_2H_5$), 103202-28-4; **7** (R = $CO_2C_4H_9$-n), 103202-30-8; **7** (R = CN), 103202-32-0; **7** (R = $CONH_2$), 103202-34-2; **8** (R = CH_3), 103202-23-9; **8** (R = CH_2CH_3), 103202-25-1; **8** (R = CO_2CH_3), 103202-27-3; **8** (R = $CO_2C_2H_5$), 103202-29-5; **8** (R = $CO_2C_4H_9$-n), 103202-31-9; **8** (R = CN), 103202-33-1; **8** (R = $CONH_2$), 103202-35-3; **9**, 103202-36-4; BSA, 10416-59-8; $(bpy)Mo(CO)_3(CH_3CN)$, 26748-33-4; $Mo(CO)_6$, 13939-06-5; $Pd(OAc)_2$, 3375-31-3; acetaldehyde, 75-07-0; propanal, 123-38-6; methyl vinyl ketone, 78-94-4; ethyl vinyl ketone, 1629-58-9; methyl acrylate, 96-33-3; ethyl acrylate, 140-88-5; n-butyl acrylate, 141-32-2; acrylonitrile, 107-13-1; acrylamide, 79-06-1; dimethyl maleate, 624-48-6; diethyl fumarate, 624-49-7; 4-acetyl-3-methyl-1-(trimethylsilyl)cyclohexene, 103202-38-6; 5-acetyl-3-methyl-1-(trimethylsilyl)cyclohexene, 103202-39-7; toluene, 108-88-3.

Regioselective Side-Chain Nitration of Polymethylbenzenes Directed by an Acyl Function and Its Application to the Synthesis of Polysubstituted Phthalic Acid Derivatives

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Received January 15, 1986

Nitration of three types of tetramethylacetophenones and pentamethylacetophenone with fuming nitric acid in acetic anhydride was carried out. The product distributions were compared with those estimated from substituent effects. A variety of acylpentamethylbenzenes including pentamethylbenzoic acid were reacted with the nitrating system to give regioselectively 2-(nitromethyl)-3,4,5,6-tetramethylacylbenzenes. The selective nitrations of some benzoic acid derivatives followed by an alkaline treatment have been found to provide the N-hydroxyphthalimide derivatives, which are readily converted to the phthalic anhydrides and the phthalazines.

Electrophilic nitration of polysubstituted benzenes has been extensively studied with respect to the problem of the ipso substitution mechanism.[1] Most of these studies have focused their attention on the mechanistic details with very little interest in the synthetic aspects of the reaction.[2] This is because ipso substitution generally gives a complex mixture of products (due to various modes of decomposition of the resulting Wheland intermediate (W_i)).

In anticipation that an acyl function, with a strong electron-withdrawing ability, would direct the decomposition of the Wi, we have undertaken nitration of acylpolymethylbenzenes with fuming nitric acid in acetic anhydride. First, the nitrations of 2,3,4,6-, 2,3,5,6-, and 2,3,4,5-tetramethylacetophenones (**1-3**) and pentamethylacetophenone (**4**) were carried out to establish the product distributions. Based on the results, our preparative work has been extended to the nitration of a variety of acylpentamethylbenzenes **5** and benzoic acid derivatives **7** substituted with a methyl group at the 2-, 3-, and 6-positions. The nitration of **5** and **7** has been found to give products selectively nitrated on the methyl group ortho to the acyl and carboxyl moieties. The regioselective side-chain nitration of the benzoic acids **7** followed by an alkaline treatment has resulted in the N-hydroxyphthalimides **10** which were easily converted to the phthalic anhydrides **11** and phthalazines **12**. Our paper also reports a convenient procedure for the preparation of the polysubstituted phthalic acid derivatives which are not accessible by usual methods.[3]

Results

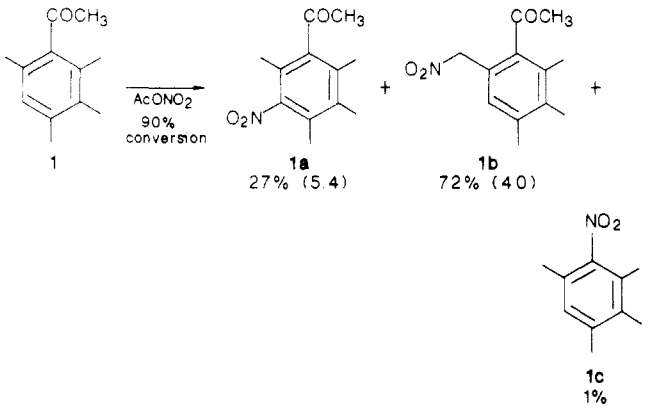
Nitration of Polymethylacetophenones. Nitration of polymethylacetophenones **1-4** with 2 equiv of fuming

(1) (a) Schofield, K. In *Aromatic Nitration*; Cambridge University Press: London, 1980; p 171. (b) Hartshorn, S. R. *Chem. Soc. Rev.* **1974**, *3*, 169. (c) Moodie, R. B.; Schofield, K. *Acc. Chem. Res.* **1976**, *9*, 287.
(2) Suzuki, H, *Synthesis* **1977**, 217.

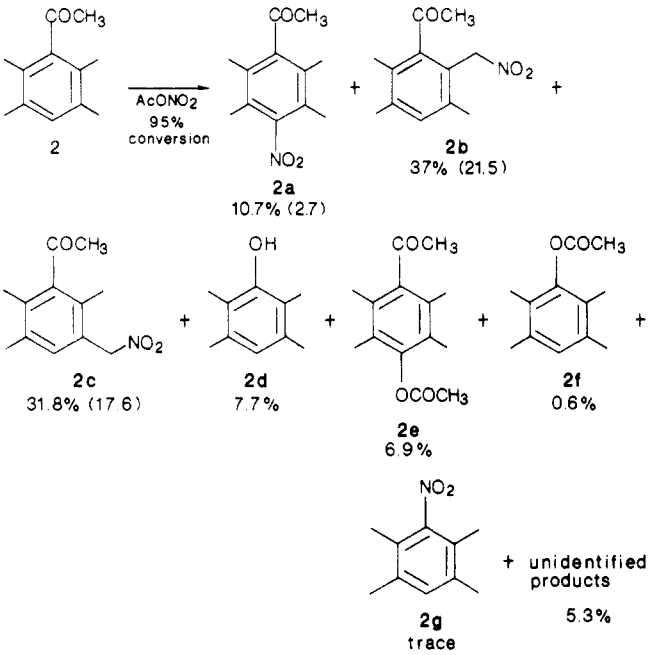
(3) A portion of this work has been reported in a short communication: Keumi, T.; Morita, T.; Mitzui, T.; Jōka, T.; Kitajima, H. *Synth. Commun.* **1985**, 223.

0022-3263/86/1951-3439$01.50/0

Scheme I



Scheme II



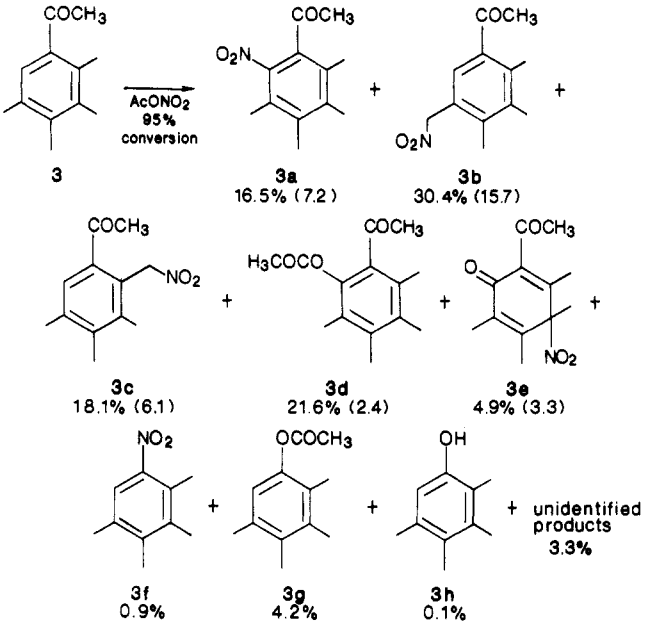
nitric acid in acetic anhydride was carried out at 0–5 °C for 2 h. The reaction mixture was poured into excess ice–water and stirred at room temperature overnight. The resulting solid products were analyzed by GLC and chromatographed on silica gel with benzene. Relative GLC percentages of the products are shown in Schemes I–IV. Isolated product yields are presented in parentheses. The product structures were ascertained by their spectroscopic data.

The nitration of **1** gave a mixture of three nitro compounds **1a–c** in yields of 27%, 72%, and 1%, respectively. From **2**, three predominant nitration products **2a–c** were obtained together with **2d–g**. The nitration of **3** also leads to the formation of a variety of products. The major products were three isomeric nitration products **3a–c** and one acetoxylation product **3d**. In addition, a small amount of the cyclohexadienone **3e** was also isolated. From **4**, **4a** was obtained in 91% yield along with small amounts of **4b–g**.[4]

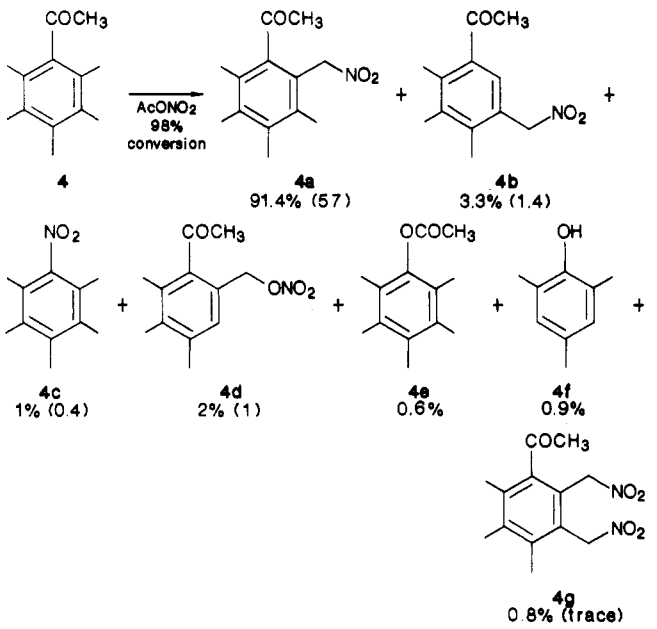
Nitration of Acylpentamethylbenzenes 5. The nitration of a variety of **5a–i** involving alkanoyl and aroyl groups as acyl functions was carried out under the same

(4) Compound **4d** partially decomposes at the temperature of GLC measurement to a mixture of several compounds, which appear at the shorter retention times. The percentage for **4d** is calibrated by the peaks resulting in the decomposition. Further, the percentages of products were in good agreement with those obtained by HPLC analysis.

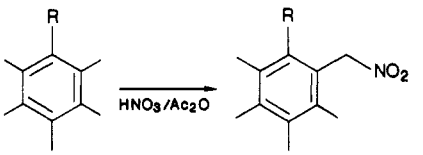
Scheme III



Scheme IV



Scheme V



4a: R = CH_3CO
6a: R = CH_3CH_2CO
6b: R = $CH_3CH_2CH_2CO$
6c: R = $(CH_3)_2CHCO$
6d: R = $ClCH_2CH_2CO$
6e: R = C_6H_5CO
6f: R = 4-FC_6H_4CO
6g: R = 4-ClC_6H_4CO
6h: R = 4-$CH_3C_6H_4CO$
6i: R = 4-$(CH_3)_3CC_6H_4CO$
8a: R = COOH

conditions as described above. The reactions proceeded smoothly to give the corresponding 2-(nitromethyl)-

Table I. Nitration of Acylpentamethylbenzenes 5 with Fuming Nitric Acid in Acetic Anhydride

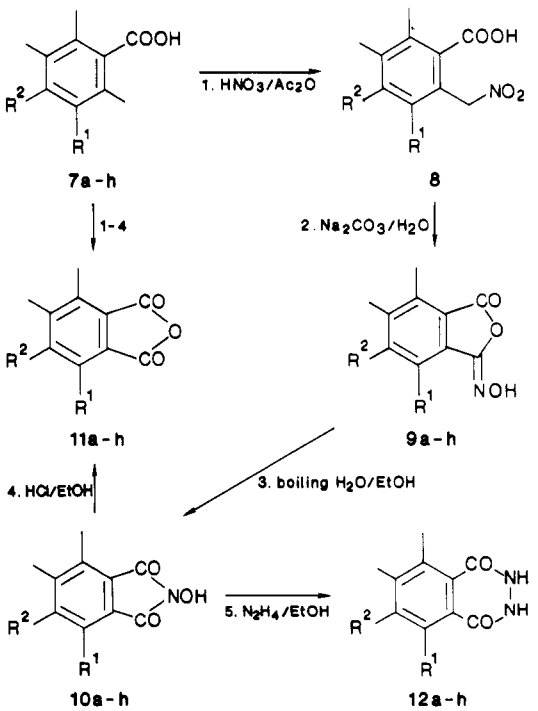
product	acyl group of 5	yield (%)	mp (°C)	formula[a]	IR (KBr) cm^{-1} ν(CO)	IR (KBr) cm^{-1} ν(NO_2)	^{1}H NMR ($CDCl_3$) δ ring CH_3	^{1}H NMR ($CDCl_3$) δ CH_2NO_2 (s, 2 H)	^{1}H NMR ($CDCl_3$) δ others
4a	CH_3CO	57	120–121	$C_{13}H_{17}NO_3$	1700	1560	2.22 (s, 3 H)	5.48	2.53 (s, 3 H)
						1380	2.26 (s, 9 H)		
6a	CH_3CH_2CO	53	111–112	$C_{14}H_{19}NO_3$	1700	1560	2.12 (s, 3 H)	5.30	1.15 (t, 3 H, J = 6 Hz)
						1380	2.23 (s, 9 H)		2.70 (q, 2 H, J = 6 Hz)
6b	$CH_3CH_2CH_2CO$	60	104–105	$C_{15}H_{21}NO_3$	1700	1560	2.12 (s, 3 H)	5.29	0.98 (t, 3 H, J = 6 Hz)
						1380	2.22 (s, 9 H)		1.68 (h, 2 H, J = 6 Hz)
									2.67 (t, 2 H, J = 6 Hz)
6c	$(CH_3)_2CHCO$	42	75–76	$C_{15}H_{21}NO_3$	1700	1560	2.07 (s, 3 H)	5.22	1.05 (d, 6 H, J = 6 Hz)
						1380	2.10 (s, 3 H)		2.83 (h, 1 H, J = 6 Hz)
							2.17 (s, 3 H)		
							2.20 (s, 3 H)		
6d	$ClCH_2CH_2CO$	64	124–125	$C_{14}H_{18}NO_3Cl$	1710	1560	2.21 (s, 3 H)	5.46	3.26 (t, 2 H, J = 3 Hz)
						1380	2.25 (s, 6 H)		3.89 (t, 2 H, J = 3 Hz)
							2.27 (s, 3 H)		
6e	C_6H_5CO	59	126–127	$C_{18}H_{19}NO_3$	1670	1565	2.20 (s, 3 H)	5.26	7.25–7.50 (m, 3 H)
						1382	2.23 (s, 3 H)		7.65 (m, 2 H)
							2.28 (s, 6 H)		
6f	4-FC_6H_4CO	63	139–140	$C_{18}H_{18}NO_3F$	1675	1550	2.02 (s, 3 H)	5.40	7.01–7.19 (m, 2 H)
						1376	2.27 (s, 6 H)		7.77–7.92 (m, 2 H)
							2.32 (s, 3 H)		
6g	4-ClC_6H_4CO	64	148–149	$C_{18}H_{18}NO_3Cl$	1670	1560	2.01 (s, 3 H)	5.40	7.40 (d, 2 H, J = 8 Hz)
						1375	2.27 (s, 6 H)		7.76 (d, 2 H, J = 8 Hz)
							2.33 (s, 3 H)		
6h	4-$CH_3C_6H_4CO$	86	169–170	$C_{19}H_{21}NO_3$	1660	1560	2.03 (s, 3 H)	5.39	7.23 (d, 2 H, J = 8 Hz)
						1380	2.22 (s, 3 H)		7.72 (d, 2 H, J = 8 Hz)
							2.27 (s, 3 H)		
							2.32 (s, 3 H)		
							2.41 (s, 3 H)		
6i	4-$(CH_3)_3CC_6H_4CO$	58	149–150	$C_{22}H_{27}NO_3$	1660	1560	2.03 (s, 3 H)	5.38	1.31 (s, 9 H)
						1370	2.23 (s, 3 H)		7.43 (d, 2 H, J = 8 Hz)
							2.26 (s, 3 H)		7.74 (d, 2 H, J = 8 Hz)
							2.30 (s, 3 H)		
8a	COOH	70	164 dec	$C_{12}H_{15}NO_4$	1700	1560	2.27 (s, 6 H)	5.65	5.50 (br, s, 1 H)
						1375	2.35 (s, 6 H)		

[a] The microanalyses were in satisfactory agreement with the calculated values (±0.4% for C, H, and N).

3,4,5,6-tetramethylacylbenzenes (**6a–i**) in good isolated yields after only one recrystallization of the resulting crude products from aqueous ethanol (Scheme V). The results are shown in Table I. The sites of side-chain nitration were easily determined by the change in intensity of methyl protons (at the 2- and 6-positions) in their ^{1}H NMR spectra which appear at higher fields compared to the other methyl protons due to the anisotropic effect by the sterically twisted carbonyl function. Singlets due to the nitromethyl group are observed at the region of 5.22–5.50 ppm. The IR spectra displayed characteristic absorption bands due to nitro and carbonyl functions (Table I).

Nitration of Polymethylbenzoic Acids 7. The nitration of the benzoic acid derivatives **7a–h** was carried out. For example, pentamethylbenzoic acid (**7a**) reacted with fuming nitric acid in acetic anhydride at 0 °C for 2 h which upon hydrolysis with excess ice–water provided 2-(nitromethyl)-3,4,5,6-tetramethylbenzoic acid (**8a**) in 70% yield. On the other hand, when the reaction mixture in ice–water was neutralized with sodium carbonate, *N*-hydroxytetramethylisophthalimide (**9a**) was obtained in 77% yield, which was converted to *N*-hydroxytetramethylphthalimide (**10a**) by recrystallization from 80% aqueous ethanol. Treatment of **10a** with concentrated hydrochloric acid in ethanol under reflux afforded tetramethylphthalic anhydride (**11a**) in 95% yield.[5] The crude product obtained in the nitration of **7a** could be directly converted to **11a** in 65% yield in an one-pot procedure

Scheme VI[a]



[a] **a**, R^1 = CH_3; R^2 = CH_3; **b**, R^1 = H, R^2 = CH_3; **c**, R^1 = H, R^2 = OCH_3; **d**, R^1 = CH_3, R^2 = H; **e**, R^1 = Cl, R^2 = CH_3; **f**, R^1 = CH_3, R^2 = Cl; **g**, R^1 = CH_3, R^2 = Br; **h**, R^1 = CH_3, R^2 = OCH_3.

(5) (a) Criegee, R.; Zaker, F. *Chem. Ber.* **1965**, *98*, 3838. (b) Chiba and Endo (Chiba, K.; Endo, E. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2614) have reported that alkaline hydrolysis of bis(nitromethyl)prehnitene, which was obtained by nitration of hexamethylbenzene with fuming nitric acid in acetic anhydride, gave **11a** (mp 238–239 °C). However, their physical data do not match ours.

Table II. Nitration of Polymethylbenzoic Acids 7 with Fuming Nitric Acid in Acetic Anhydride

product	reactn conditn temp/time (°C)/(h)	yield (%)	mp (°C)	formula[a]	IR (KBr) cm^{-1} ν(OH)	ν(C=O)	ν(C=N)	^{1}H NMR ($CDCl_3$) δ ring CH_3	OH	others
9a	0–5/2	77	234–235	$C_{12}H_{13}NO_3$	3340	1786	1660 946	2.31 (s, 3 H) 2.34 (s, 3 H) 2.55 (s, 3 H) 2.64 (s, 3 H)	7.04 (s, 1 H)	
10a	0–5/2	67	248–249	$C_{12}H_{13}NO_3$	3210	1771 1700		2.26 (s, 6 H) 2.64 (s, 6 H)	7.15 (s, 1 H)	
9b[b]	0–5/2	62	179–180	$C_{11}H_{11}NO_3$	3300	1800	1680 960	2.29 (s, 3 H) 2.42 (s, 3 H) 2.65 (s, 3 H)	7.15 (s, 1 H)	7.45 (s, 1 H, Ar H)
10b	0–5/2	54	181–182	$C_{11}H_{11}NO_3$	3150	1700 1710		2.27 (s, 3 H) 2.39 (s, 3 H) 2.62 (s, 3 H)	7.36 (s, 1 H)	7.45 (s, 1 H, Ar H)
9c	0–5/2	91	212–214	$C_{11}H_{11}NO_4$	3500	1768	1672 970	2.21 (s, 3 H) 2.61 (s, 3 H)	obsd	3.95 (s, 3 H, OCH_3) 7.26 (s, 1 H, Ar H)
10c	0–5/2	64	188	$C_{11}H_{11}NO_4$	3140	1773 1710		2.21 (s, 3 H) 2.60 (s, 3 H)		3.94 (s, 3 H, OCH_3) 7.18 (s, 1 H, Ar H)
9d[c]	0–5/2	20	179–180	$C_{11}H_{11}NO_3$	3350	1805	1680 950	2.36 (s, 3 H) 2.50 (s, 3 H) 2.59 (s, 3 H)	7.31 (s, 1 H)	7.17 (s, 1 H, Ar H)
10d	0–5/2	8	210–211	$C_{11}H_{11}NO_3$	3300	1770 1710		2.33 (s, 3 H) 2.57 (s, 3 H) 2.58 (s, 3 H)	7.30 (s, 1 H)	7.26 (s, 1 H, Ar H)
9e	25/30	62	239–240	$C_{11}H_{10}ClNO_3$	3300	1798	1675 973	2.37 (s, 3 H) 2.67 (s, 3 H) 2.52 (s, 3 H)	7.29 (s, 1 H)	
10e	25/30	63	247–248	$C_{11}H_{10}ClNO_3$	3420	1770 1704		2.35 (s, 3 H) 2.47 (s, 3 H)	7.38 (s, 1 H)	
9f	25/30	75	204–205	$C_{11}H_{10}ClNO_3$	3340	1762	1660 969	2.65 (s, 3 H) 2.46 (s, 3 H) 2.68 (s, 3 H)	7.20 (s, 1 H)	
10f	25/30	68	217–218	$C_{11}H_{10}ClNO_3$	3100	1765 1703		2.33 (s, 3 H) 2.64 (s, 3 H) 2.67 (s, 3 H)	7.36 (s, 1 H)	
10g[d]	25/30	82	258–259	$C_{11}H_{10}BrNO_3$	3260	1765 1710		2.53 (s, 3 H) 2.71 (s, 3 H) 2.77 (s, 3 H)	7.53 (s, 1 H)	
9h	0–5/2	82	192–193	$C_{12}H_{13}NO_4$	3303	1799	1678 947	2.30 (s, 3 H) 2.47 (s, 3 H) 2.61 (s, 3 H)	7.18 (s, 1 H)	3.76 (s, 3 H, OCH_3)
10h	0–5/2	63	197–198	$C_{12}H_{13}NO_4$	3150	1769 1713		2.54 (s, 6 H) 2.26 (s, 3 H)	7.27 (s, 1 H)	3.73 (s, 3 H, OCH_3)

[a] The microanalyses were in satisfactory agreement with the calculated values (±0.4% for C, H, and N). [b] Small amount of 3-nitro-2,4,5,6-tetramethylbenzoic acid was isolated. [c] 4-Nitro-2,3,5,6-tetramethylbenzoic acid, 2,3,5,6-tetramethyl-1,4-benzoquinone, and 2,3,5,6-tetramethylphenol were isolated along with **9d** in 1%, 7%, and 9% yields, respectively. [d] Isolation of **9g** failed.

without the isolation of intermediates **8a**, **9a**, or **10a**, by the successive treatments as described above (Scheme VI).

In a similar manner, benzoic acids **7b–h** were nitrated and the resulting crude products were directly converted to compounds **9** and **10**. Isolation of intermediate products **8b–h** was not undertaken because of their instability in alkali solution. The yields of **9** and **10** from **7** are shown in Table II together with the IR and ^{1}H NMR data. The nitration of **7** smoothly proceeded to give **9** and **10** in high isolated yields except for **9d** and **10d**. The reaction of **7e**, **7f**, and **7g** involving halogen groups needed higher reaction temperatures and longer reaction times. In the nitration of **7d**, 4-nitro-2,3,5,6-tetramethylbenzoic acid, 2,3,5,6-tetramethyl-1,4-benzoquinone, and 2,3,5,6-tetramethylphenol were obtained along with **9d**. IR spectra of **9** show the characteristic absorption peaks at 1660–1680 cm^{-1} and 946–990 cm^{-1} of the isoimide form.[6] In IR spectra of **10**, the two strong absorption peaks are observed at the expected region for phthalimides.[6] The *N*-hydroxyl functions of these compounds were also observed in the IR spectra.

The *N*-hydroxyphthalimides **10** could be easily converted to the phthalic anhydrides **11** in good yields by refluxing in ethanolic hydrochloric acid. The phthalic anhydrides **11b** and **11c** were obtained from their respective phthalimides under the acidic conditions only after heating at 200 °C. The *N*-hydroxy compounds **10** when reacted with hydrazine hydrate in boiling ethanol gave the phthalazines **12** in good yields. Their yields and spectroscopic data are collected in Table III. The spectral data are in good agreement with their assigned structures.

Discussion

Nitration of Acylpolymethylbenzenes. A mixture of fuming nitric acid and acetic anhydride is recognized to exist in the following equilibrium (eq 1). In the presence of excess acetic anhydride, the solution consists of acetyl nitrate, acetic acid, and excess anhydride. Therefore, the nitrating agent in this system should be acetyl nitrate.[7] The acetyl group, being an electron-withdrawing group, directs attack by the acetyl nitrate on poly-

$$Ac_2O + 2HNO_3 \rightleftarrows N_2O_5 + 2AcOH \qquad (1)$$

$$N_2O_5 + Ac_2O \rightleftarrows 2AcONO_2$$

(6) Carpino, L. A. *J. Am. Chem. Soc.* **1957**, *79*, 98.

(7) Vandoni, A.; Viala, P. M. *Services chim Etat* **1945**, *32*, 80.

Table III. Preparation of the Phthalic Anhydrides 11 and the Phthalazines 12 from the *N*-Hydroxyphthalimides 10

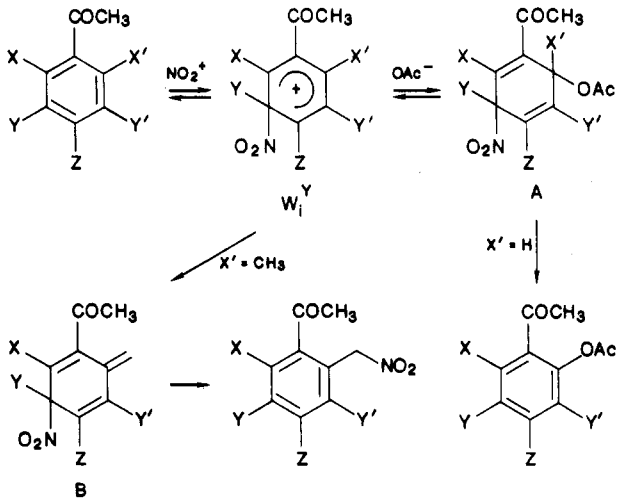
product	yield (%)	mp (°C)	formula[a]	IR (KBr) cm^{-1} ν(C=O)	^{1}H NMR ($CDCl_3$) δ ring CH_3	others
11a	95	262–263	260–261[5]	1845	2.65 (s, 6 H)	
				1775	2.35 (s, 6 H)	
11b[b]	47	180	$C_{11}H_{10}O_3$	1840	2.34 (s, 3 H), 2.68 (s, 3 H)	7.63 (s, 1 H, Ar H)
				1770	2.47 (s, 3 H)	
11c[b]	52	174–177	$C_{11}H_{10}O_4$	1858	2.27 (s, 3 H)	3.98 (s, 3 H, OCH_3)
				1758	2.64 (s, 3 H)	7.25 (s, 1 H, Ar H)
11d	81	219–220	$C_{11}H_{10}O_3$	1840	2.41 (s, 3 H), 2.63 (s, 3 H)	7.39 (s, 1 H, Ar H)
				1770	2.61 (s, 3 H)	
11e	79	211–213	$C_{11}H_9ClO_3$	1843	2.41 (s, 3 H), 2.68 (s, 3 H)	
				1772	2.52 (s, 3 H)	
11f	66	197–200	$C_{11}H_9ClO_3$	1841	2.51 (s, 3 H), 2.74 (s, 3 H)	
				1772	2.70 (s, 3 H)	
11g	72	206–207	$C_{11}H_9BrO_3$	1838	2.58 (s, 3 H), 2.79 (s, 3 H)	
				1768	2.73 (s, 3 H)	
11h	77	184–185	$C_{12}H_{12}O_4$	1831	2.61 (s, 6 H)	3.79 (s, 3 H, OCH_3)
				1771	2.23 (s, 3 H)	
12a	89	225–227	$C_{12}H_{14}N_2O_2$	1765	2.28 (s, 6 H)	4.12 (s, 2 H, NH)
				1710	2.61 (s, 3 H)	
12b	50	185–188	$C_{11}H_{12}N_2O_2$	1770	2.28 (s, 3 H)	4.07 (s, 2 H, NH)
				1705	2.40 (s, 3 H)	7.49 (s, 1 H, Ar H)
					2.66 (s, 3 H)	
12c	67	203	$C_{11}H_{12}N_2O_3$	1765	2.22 (s, 3 H)	4.05 (s, 2 H, NH)
				1715	2.63 (s, 3 H)	3.94 (s, 3 H, OCH_3)
						7.21 (s, 1 H, Ar H)
12d	72	188–189	$C_{11}H_{12}N_2O_2$	1770	2.34 (s, 3 H)	4.07 (s, 2 H, NH)
				1710	2.59 (s, 3 H)	7.20 (s, 1 H, Ar H)
					2.60 (s, 3 H)	
12e	90	231–233	$C_{11}H_{11}ClN_2O_2$	1770	2.35 (s, 3 H)	4.11 (s, 2 H, NH)
				1720	2.46 (s, 3 H)	
					2.66 (s, 3 H)	
12f	67	211–213	$C_{11}H_{11}ClN_2O_2$	1767	2.45 (s, 3 H)	4.10 (s, 2 H, NH)
				1720	2.69 (s, 3 H)	
					2.73 (s, 3 H)	
12g	40	215–216	$C_{11}H_{11}BrN_2O_2$	1763	2.56 (s, 3 H)	4.10 (s, 2 H, NH)
				1715	2.71 (s, 3 H)	
					2.77 (s, 3 H)	
12h	60	162–163	$C_{12}H_{14}N_2O_3$	1765	2.28 (s, 3 H)	4.06 (s, 2 H, NH)
				1700	2.58 (s, 3 H)	3.70 (s, 3 H, OCH_3)
					2.60 (s, 3 H)	

[a] The microanalyses were in satisfactory agreement with the calculated values (±0.4% for C, H, and N). [b] After hydrolysis, the resulting product was heated at 200 °C.

methylacetophenones at the meta position to give the Wheland intermediate W_i^Y, or, followed by attack of acetate at the para position with respect to the nitro group, to yield the acetate adduct A as illustrated in Scheme VII.[8] The subsequent reactions lead to the formation of the final products, the distribution being influenced by the leaving group ability of the substituents. The sequence of leaving group abilities of the substituents seems to be $H^+ > Ac^+ > NO_2^+ > CH_3^+$ for electrofugal groups[9] and $AcO^- > NO_2^-$ for nucleofugal groups.[10]

Therefore, W_i^Y in which Y is H will give conventional nitro-substitution products (e.g., **1a**). When X′ of W_i^Y is CH_3, deprotonation from the intermediate would occur to give the methylenecyclohexadiene intermediate B, which in turn leads to the formation of a side-chain nitrated product (e.g., **1b** and **2b**).[11] The adduct A in which X′ is H, however, will generate nitrous acid to give arylacetate (e.g., **3d**).[12] Compound **3e** seems to result in the nitration

Scheme VII



of **3d** followed by the deacetylation as shown in Scheme VIII. The ipso nitration on the carbon-bearing acetyl group will give nitro-deacetylation products (e.g., **1c** and **2g**).

Based on these mechanistic interpretations, it is possible to identify the Wheland intermediates, W_i^X–W_i^Z, responsible for the final product (Table IV). Moreover, we have

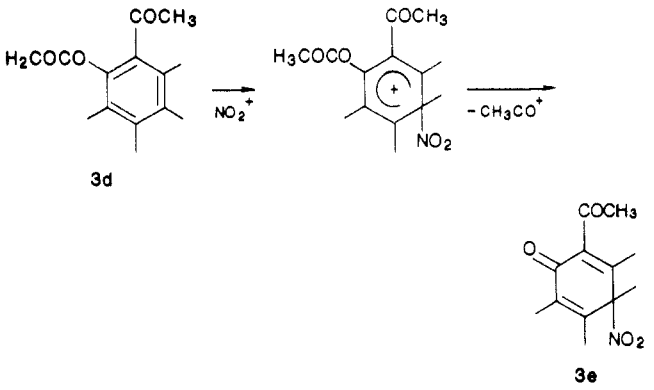
(8) Reference 1a, p 190.
(9) Perrin, C. L. *J. Org. Chem.* **1971**, *36*, 420.
(10) Lowry, T. H.; Richardson, K. S. In *Mechanism and Theory in Organic Chemistry*; Harper & Row Publisher: New York, 1976; p 187.
(11) (a) Nakamura, K. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 133. (b) Astolfi, R.; Baciocchi, E.; Illuminati, G. *Chim. Ind. (Milan)* **1971**, *53*, 1153.
(12) (a) Fisher, A.; Vaughan, J.; Wright, G. D. *J. Chem. Soc. B* **1967**, 368. (b) Banwell, T.; Morse, C. S.; Myhre, P. C.; Vollmar, A. J. *J. Am. Chem. Soc.* **1977**, *99*, 3042.

Table IV. Relative Distribution of the Ipso-Wheland Intermediates Initially Formed by the Nitration of Polymethylacetophenones with Fuming Nitric Acid in Acetic Anhydride

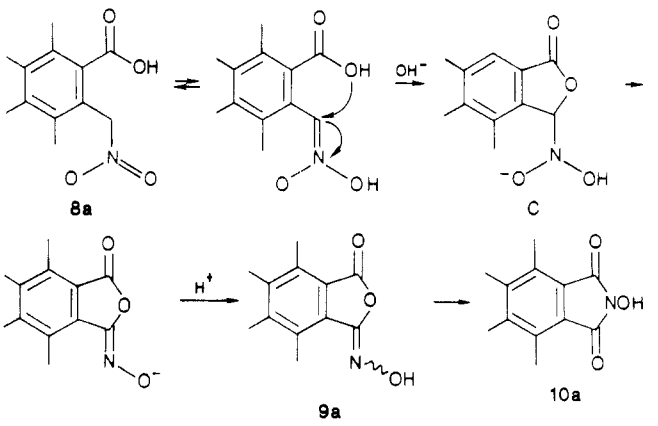
polymethyl-aceto-phenone	calculated,[a] %						observed,[b] %					
	W_i^{Ac}	W_i^{X}	$W_i^{X'}$	W_i^{Y}	$W_i^{Y'}$	W_i^{Z}	W_i^{Ac}	W_i^{X}	$W_i^{X'}$	W_i^{Y}	$W_i^{Y'}$	W_i^{Z}
1	0	0.1	0	24.4	75.5	0	1.0 (1c)	0	0	27.0 (1a)	72.0 (1b)	0
2	0	9.2	9.2	40.4	40.4	0.8	6.9 (2g + 2e)	15.9 (2c)	15.9 (2c)	18.5 (2b)	18.5 (2b)	19.0 (2a + 2d + 2f)
3	0	3.7	11.5	50.0	30.8	3.2	0.9 (3f)	16.5 (3a)	30.4 (3b)	18.1 (3c)	26.5 (3d + 3e)	4.3 (3g + 3h)
4	0	0.8	0.8	49.1	49.1	0.2	1.0 (4c)	1.7 (4b)	1.7 (4b)	47.1 (4a + 4d + 4g)	47.1 (4a + 4d + 4g)	1.5 (4e + 4f)

[a] Values calculated from the partial rate factors for the nitration of toluene and the isomer distribution on the nitration of acetophenone on the basis of additivity principle. [b] Values deduced from the products distributions obtained in the nitration of polymethylacetophenones.

Scheme VIII



Scheme IX



calculated the relative distributions of the Wheland intermediates produced from polymethylacetophenones 1–4 based on the additivity principle of substituents using the partial rate factors for the nitration of toluene and acetophenone with acetyl nitrate.[13] The results are again shown in Table IV. Comparing the calculated values with those of the actual product distributions, the following trends are noted. For 1 and 4, the calculated values are in good agreement with those estimated from the product distributions, suggesting that the distributions are determined mainly by the directing effects of the substituents. In the case of 2, however, the calculated distributions of the intermediate W_i^{Y} or $W_i^{Y'}$ are significantly larger than those estimated from the product composition. For 3 also the same discrepancy is observed. This would imply that some other factor should be taken into consideration to account for the observed product distributions. We prefer to consider that even for these ketones the distribution of the Wheland intermediates first produced by attack of acetyl nitrate is much the same as that expected from the directing effects of the substituents. However, the first resulting Wheland intermediates W_i^{Y} or $W_i^{Y'}$ from 2 and 3 are not as stable and, therefore, 1,2-migration of the nitro group prior to attack by the acetate moiety contributes considerably to give the intermediates W_i^{X}, $W_i^{X'}$, or W_i^{Z}, which in turn lead to the formation of products, **2a**, **2c**, particularly **3a** and **3b**. In contrast, the intermediates formed from 1 and 4 are stabilized by four methyl groups at the 2, 3, 4, and 6 positions of the ring, with the 1,2-migration of the nitro group prior to attack by acetate being significantly slowed down.

Thus, it can be seen that the acetophenones having methyl groups at least on the 2, 3, and 6 positions react with acetyl nitrate to give the side-chain nitrated products at the methyl ortho to the acetyl group as the major product. The regioselective side-chain nitration has been also observed in the nitration of a variety of acylpentamethylbenzenes.

Suzuki and co-workers have reported that nitration of 4 with excess fuming nitric acid in dichloromethane gives an oxynitrated product at the *o*-methyl group.[14] The authors attributed the product to collapse of the intermediate B to give the nitrite–benzylic ion pair, followed by substitution with nitrate ion. The nitration species in dichloromethane appears to be the nitronium–nitrate ion pair, which is responsible for the formation of the oxynitration product. In contrast, very little oxynitration takes place in our system because the nitrating entity is acetyl nitrate.

Nitration of Polymethylbenzoic Acids 7. The nitration of **7a** also selectively gives the side-chain nitrated product **8a** at the position ortho to the carboxyl group, which then is readily converted to **9a** by aqueous alkali solution treatment. Compound **8a** also seems to arise from the ipso intermediate formed by attack of nitronium ion at the meta position of carboxyl group of **7a**. The conversion of **8a** into **9a** would appear to proceed in such a way that an intramolecular Ad_N reaction of the nitronic acid form of **8a** with the carboxyl group occurs to afford C, which immediately loses water to give **9a** followed by rearrangement to **10a** as shown in Scheme IX.

The regioselective side-chain nitration of the benzoic acids having methyl group at the 2, 3, and 6 positions followed by the aqueous sodium carbonate treatment gives

(13) The ratios of partial rate factors including the ipso nitration of toluene with fuming nitric acid in acetic anhydride have been given: Fischer, A.; Wright, G. J. *Aust. J. Chem.* **1974**, *27*, 217. In the present work, we have determined the isomer distribution in nitration of acetophenone with fuming nitric acid acetic anhydride system as ortho: 17.8%; meta: 78.2%; para: 4.0% by HPLC analysis of the products.

(14) Suzuki, H.; Hashihama, M.; Mishina, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1186.

the corresponding compounds **9** and **10**. *N*-Hydroxyphthalimides **10**, especially fully substituted, ones can be easily converted to the phthalic anhydrides by treatment with boiling enthanolic hydrochloric acid. The reaction would proceed via hydrolysis of the *N*-hydroxy imide group followed by dehydration of the resulting phthalic acids. One reason why the dehydration reaction proceeds smoothly in the aqueous system is the release of steric strain of carboxylic acid groups (bumping into the ortho substituents) due to ring closure. Indeed, in the cases of **10b** and **10c** which are unsubstituted at the 3-position, the phthalic anhydrides **11b** and **11c** are formed only at 200 °C. Compounds **10** can be readily converted to the phthalazines by reaction with hydrazine hydrate in boiling ethanol.

Conclusion

Phthalic acid derivatives are potentially valuable synthetic intermediates. Among these, polysubstituted phthalic acids are difficult to prepare because of the inherent problems involved in the selective oxidation of polymethylbenzenes or in the introduction of new substituents into the ring of phthalic acids (or the anhydrides). The presently described method seems to offer a convenient procedure for the preparation of complex polysubstituted phthalic acid derivatives of **10**, **11**, and **12**, which are otherwise difficult to synthesize.

Experimental Section

All melting points are uncorrected. IR spectra were recorded on a Hitachi EPI-S2 Model spectrophotometer as KBr pellets. ^{1}H NMR spectra were recorded on a JEOL-FX 270 FT-NMR (270 MHz) spectrometer in chloroform-*d* solution with tetramethylsilane internal standard. GLC analysis was carried out on a Hitachi GC Model 163 gas chromatograph equipped with a hydrogen flame ionization detector and a stainless steel column (length 3 m, i.d. 3 mm) packed with 3% Dexil 300 GC on Chromosorb W. Product distributions were calculated from peak areas obtained by a Takeda TR 2220A Model integrator after calibration by each compound. HPLC analysis was carried out on a JASCO-TWINCLE high performance liquid chromatograph using Finepack SIL column (JASCO silica) as the column and *n*-hexane/dichloromethane solution (1/1 v/v) as the eluent. Acylpolymethylbenzenes and polymethylbenzoic acids were prepared from corresponding polymethylbenzenes and acid chlorides according to the literature procedures.[15,16]

(β-Chloropropionyl)pentamethylbenzene (5d): 75% yield; mp 99–100 °C; ^{1}H NMR δ 2.12 (s, 6 H), 2.18 (s, 6 H), 2.24 (s, 3 H), 3.14 (t, 2 H, J = 6 Hz), 3.89 (t, 2 H, J = 6 Hz); IR ν 2930, 1700, 1340 cm^{-1}. Anal. Calcd for $C_{14}H_{19}OCl$: C, 70.43; H, 8.02. Found: C, 70.32; H, 7.98.

(4-*tert*-Butylbenzoyl)pentamethylbenzene (5i): 94% yield; mp 138–139 °C; ^{1}H NMR δ 1.31 (s, 9 H), 2.02 (s, 6 H), 2.21 (s, 6 H), 2.27 (s, 3 H), 7.43 (d, 2 H, J = 8 Hz), 7.76 (d, 2 H, J = 8 Hz); IR ν 2970, 1676, 1610 cm^{-1}. Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.55; H, 9.22.

2,3,6-Trimethyl-4-methoxybenzoic acid (7c): 32% yield; mp 171–173 °C; ^{1}H NMR δ 2.13 (s, 3 H), 2.33 (s, 3 H), 2.42 (s, 3 H), 3.83 (s, 3 H), 6.57 (s, 1 H); IR ν 2900, 1680, 1592 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.30; H, 7.42.

General Procedure of Nitration of Acylpolymethylbenzenes. Nitration of Pentamethylacetophenone (4). To a solution of **4** (10.00 g, 52.55 mmol) in acetic anhydride (120 mL) was added a solution of 99% nitric acid (6.7 g, 106.3 mmol) in acetic anhydride (40 mL) with stirring at 0 °C over 20 min. After the reaction mixture was stirred for 2 h at the same temperature, it was poured into 1 L of ice–water, then stirred overnight. The resulting solid was filtered, washed with water, aqueous sodium carbonate, and water, and dried to give a white solid of mp 100–108 °C (12.11 g, 98% yield). After measurement of the GLC, the crude product was crystallyzed from ethanol of 15 mL to give **4a** (7.05 g, 57% yield, mp 118–119 °C). Repeated recrystallization gave purified **4a**. The residue obtained after evaporating the mother liquor of the first recrystallization was chromatographed on silica gel with benzene to isolate **4b** (0.173 g, 1.4%, mp 103–105 °C), **4c** (0.041 g, 0.4%, mp 150–154 °C), **4d** (0.132 g, 1.0%, mp 94–97 °C), and **4g** (trace, mp 171–173 °C). Recrystallization of the individual compounds from ethanol gave the purified compounds of **4a**, **4b**, **4c**, **4d**, and **4g**, respectively. The physical data of each compound are as follows.

2-(Nitromethyl)-3,4,5,6-tetramethylacetophenone (4a). The data are shown in Table I.

3-(Nitromethyl)-2,4,5,6-tetramethylacetophenone (4b): mp 108–109 °C; ^{1}H NMR δ 2.20 (s, 3 H), 2.23 (s, 3 H), 2.26 (s, 3 H), 2.35 (s, 3 H), 2.50 (s, 3 H), 5.66 (s, 2 H); IR ν 1700, 1560, 1380 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.21; H, 7.37; N, 6.00.

Pentamethylnitrobenzene (4c): mp 155–156 °C (lit.[17] mp 158–159 °C).

2-(Nitrooxymethyl)-3,4,5,6-tetramethylacetophenone (4d): mp 97–98 °C (lit.[14] mp 100–101 °C).

2,3-Bis(nitromethyl)-4,5,6-trimethylacetophenone (4g): mp 172–173 °C; ^{1}H NMR δ 2.28 (s, 3 H), 2.30 (s, 3 H), 2.40 (s, 3 H), 2.56 (s, 3 H), 5.65 (s, 2 H), 5.77 (s, 2 H); IR ν 1710, 1567, 1385 cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.75; N, 9.99. Found: C, 55.83; H, 5.62; N, 9.88.

Acetoxypentamethylbenzene (4e) was prepared from pentamethylphenol and acetic anhydride: 80% yield; mp 70–71 °C; ^{1}H NMR δ 2.07 (s, 6 H), 2.20 (s, 9 H), 2.35 (s, 3 H); IR ν 1755, 1390, 1220 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.55; H, 8.85.

Nitration of **1**, **2**, and **3** was also carried out under the same conditions described above. Yields of obtained products are given in Schemes I–III. The physical data of products are as follows.

3-Nitro-2,4,5,6-tetramethylacetophenone (1a): mp 111–112 °C (EtOH); ^{1}H NMR δ 2.08 (s, 3 H), 2.16 (s, 6 H), 2.19 (s, 3 H), 2.45 (s, 3 H); IR ν 1710, 1540, 1370 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.21; H, 6.73; N, 6.25.

2-(Nitromethyl)-4,5,6-trimethylacetophenone (1b): mp 155–156 °C (EtOH); ^{1}H NMR δ 2.23 (s, 3 H), 2.26 (s, 3 H), 2.34 (s, 3 H), 2.58 (s, 3 H), 5.39 (s, 2 H), 7.12 (s, 1 H); IR ν 1700, 1560, 1385 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.04; H, 6.67; N, 6.31.

4-Nitro-2,3,5,6-tetramethylacetophenone (2a): mp 158–160 °C (EtOH); ^{1}H NMR δ 2.16 (s, 12 H), 2.47 (s, 3 H); IR ν 1710, 1540, 1370 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.15; H, 6.94; N, 6.25.

2-(Nitromethyl)-3,5,6-trimethylacetophenone (2b): mp 106–107 °C (EtOH); ^{1}H NMR δ 2.10 (s, 3 H), 2.27 (s, 3 H), 2.32 (s, 3 H), 2.56 (s, 3 H), 5.45 (s, 2 H), 7.12 (s, 1 H); IR ν 1705, 1550, 1370 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.01; H, 6.68; N, 6.28.

3-(Nitromethyl)-2,5,6-trimethylacetophenone (2c): mp 102–103 °C (EtOH); ^{1}H NMR δ 2.10 (s, 3 H), 2.22 (s, 3 H), 2.26 (s, 3 H), 2.48 (s, 3 H), 5.45 (s, 2 H), 7.18 (s, 1 H); IR ν 1710, 1555, 1380 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.24; H, 6.76; N, 6.26.

4-Acetoxy-2,3,5,6-tetramethylacetophenone (2e) was prepared by acetylation of 4-acetoxydurene with acetyl chloride in the presence of aluminium chloride: 35% yield; mp 97–98 °C (EtOH); ^{1}H NMR δ 2.03 (s, 6 H), 2.12 (s, 6 H), 2.36 (s, 3 H), 2.46 (s, 3 H); IR ν 1770, 1720, 1235 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.65; H, 7.82.

2-Nitro-3,4,5,6-tetramethylacetophenone (3a): mp 90–92 °C (EtOH); ^{1}H NMR δ 2.22 (s, 3 H), 2.27 (s, 9 H), 2.52 (s, 3 H); IR ν 1715, 1530, 1370 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.18; H, 6.73; N, 6.31.

3-(Nitromethyl)-4,5,6-trimethylacetophenone (3b): mp 94–95 °C (EtOH); ^{1}H NMR δ 2.25 (s, 3 H), 2.32 (s, 3 H), 2.38 (s, 3 H), 2.56 (s, 3 H), 5.52 (s, 2 H), 7.38 (s, 1 H); IR ν 1690, 1550,

(15) Keumi, T.; Morita, T.; Korome, K.; Ikeda, M.; Kitajima, H. *Nippon Kagaku Kaishi* **1982**, 1785.
(16) Suzuki, H. *Nippon Kagaku Zasshi* **1970**, *91*, 484.
(17) Suzuki, H.; Nakamura, K. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 473.

1375 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.29; H, 6.86; N, 6.29.

2-(Nitromethyl)-3,4,5-trimethylacetophenone (3c): mp 115–116 °C (EtOH); ^1H NMR δ 2.25 (s, 3 H), 2.30 (s, 3 H), 2.39 (s, 3 H), 2.61 (s, 3 H), 5.88 (s, 2 H), 7.52 (s, 1 H); IR ν 1680, 1560, 1380 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.20; H, 6.94; N, 6.21.

2-Acetoxy-3,4,5,6-tetramethylacetophenone (3d): mp 79–81 °C; (MeOH); ^1H NMR δ 2.17 (s, 3 H), 2.20 (s, 6 H), 2.25 (s, 6 H), 2.42 (s, 3 H); IR ν 1755, 1710, 1220 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.68; H, 7.70.

2-Acetyl-4-nitro-3,4,5,6-tetramethyl-2,5-cyclohexadienone (3e): mp 118–119 °C; ^1H NMR δ 1.78 (s, 6 H), 1.87 (s, 3 H), 1.90 (s, 3 H), 2.43 (s, 3 H); IR ν 1760, 1745, 1350 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.63; H, 6.35; N, 5.82.

Nitration of **5a–i** and **7a** was carried out in a similar manner to give 2-(nitromethyl)-3,4,5,6-tetramethylacylbenzenes **6a-i** and **8a**. Yields and physical data are listed in Table I.

General Procedure for Nitration of Polymethylbenzoic Acids 7. *N*-Hydroxytetramethylisophthalimide (9a). To a solution of **7a** (1.00 g, 5.2 mmol) in acetic anhydride (10 mL) was added 99% nitric acid (0.66 g, 10.4 mmol) in acetic anhydride (5 mL) at 0 °C and the mixture was stirred for 2 h at the same temperature. The reaction mixture was poured into ice–water (ca 200 g), neutralized with sodium carbonate until weakly alkaline, and stirred overnight. The resulting solid was filtered and recrystallized from methanol to give **9a**: yield 0.71 g (77%); mp 234–235 °C; ^1H NMR and IR, shown in Table II.

***N*-Hydroxytetramethylphthalimide (10a).** Compound **9a** (0.5 g, 2.3 mmol) was heated in 80% aqueous ethanol (20 mL) under reflux for 3 h. After cooling, the resulting crystalline material was filtered to give **10a**: yield 0.48 g (96%); mp 248–249 °C; ^1H NMR and IR data are shown in Table II.

Nitration of **7b–h** was also carried out in a similar way to give **9b–h** and **10b–h**. The results are summarized in Table II with the spectral data. In the nitration of **7b**, 3-nitro-2,4,5,6-tetramethylbenzoic acid was obtained along with **9b**.

3-Nitro-2,4,5,6-tetramethylbenzoic acid: 7.2% yield; mp 205–206 °C; ^1H NMR δ 2.21 (s, 3 H), 2.25 (s, 3 H), 2.27 (s, 3 H), 2.35 (s, 3 H); IR ν 1700, 1525, 1345 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.11; H, 5.72; N, 6.16.

The nitration of **7d** gave following products in addition to **9d**.

4-Nitro-2,3,5,6-tetramethylbenzoic acid: 1% yield; mp 218–220 °C; ^1H NMR δ 2.16 (s, 6 H), 2.31 (s, 6 H); IR 1700, 1530, 1370 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.30; H, 5.90; N, 6.34.

2,3,5,6-Tetramethyl-1,4-benzoquinone: 7% yield; mp 110–111 °C (lit.[18] mp 111 °C). **2,3,5,6-Tetramethylphenol**: 9% yield; mp 116–117 °C (lit.[18] mp 118–119 °C).

Tetramethylphthalic Anhydride (11a). A solution of **10a** (0.5 g, 2.3 mmol) in ethanol (20 mL) containing concentrated hydrochloric acid (10 mL) was heated to reflux for 4 h and cooled. The precipitate formed with filtered and recrystallized from benzene to give **11a**: yield 0.45 g (95%); mp 262–263 °C (lit.[5] mp 260–261 °C).

Products **10b–h** were converted to the phthalic anhydrides **11b–h**. Obtained results and spectral data are summarized in Table III.

Typical Procedure for One-Pot Preparation of 11a. To a solution of **7a** (3.00 g, 15.6 mmol) in acetic anhydride (30 mL) was added a solution of 99% nitric acid (1.97 g, 31.2 mmol) in acetic anhydride (18 mL) over 30 min at 0 °C. The reaction mixture was stirred at the same temperature for 2 h, then poured into ice–water (500 mL), neutralized with solid sodium carbonate (55 g), and stirred overnight. The resulting solid were heated in ethanol (100 mL) containing concentrated hydrochloric acid (20 mL) under reflux for 4 h. After cooling, the resulting precipitate was filtered to give **11a**: yield 2.01 g (63%); mp 262–263 °C.

Preparation of Phthalazines 12. Tetramethylphthalazine (12a). A mixture of **10a** (0.5 g, 2.3 mmol) and hydrazine hydrate (1.14 g, 11.4 mmol) in ethanol (15 mL) was heated under reflux for 3 h. After cooling, the resulting yellow crystalline material was filtered to give the solid of mp 221–226 °C (0.418 g,, 89%). Recrystallization of the solid from 50% aqueous ethanol (40 mL) gave **12a**: yield 0.382 g (77%); mp 225–227 °C.

Similarly, other phthalazines **12b–h** were prepared. The results are summarized in Table III.

Acknowledgment. T.K. thanks Dr. G. K. Surya Prakash, University of Southern California, and Dr. M. Nojima, Osaka University, for help with this manuscript. This work was supported by a Grant-in-Aid for Scientific Research (No. 61550632) from the Ministry of Education, Science and Culture of Japan.

Registry No. **1**, 2142-78-1; **1a**, 78740-45-1; **1b**, 103224-55-1; **1c**, 42887-63-8; **2**, 2142-79-2; **2a**, 64853-55-0; **2b**, 103224-56-2; **2c**, 103224-57-3; **2d**, 527-35-5; **2e**, 103224-58-4; **2f**, 32134-69-3; **2g**, 3463-36-3; **3**, 34764-71-1; **3a**, 103224-59-5; **3b**, 103224-60-8; **3c**, 103224-61-9; **3d**, 103224-62-0; **3e**, 103224-63-1; **3f**, 42887-62-7; **3g**, 60368-01-6; **3h**, 488-70-0; **4**, 2040-01-9; **4a**, 103224-64-2; **4b**, 103224-65-3; **4c**, 13171-59-0; **4d**, 78740-44-0; **4e**, 73396-43-7; **4f**, 2819-86-5; **4g**, 103224-66-4; **5a**, 2040-17-7; **5b**, 84858-88-8; **5c**, 2040-24-6; **5d**, 22422-26-0; **5e**, 20386-33-8; **5f**, 84858-89-9; **5g**, 18780-05-7; **5h**, 103224-67-5; **5i**, 103224-68-6; **6a**, 103224-69-7; **6b**, 103224-70-0; **6c**, 103224-71-1; **6d**, 103224-72-2; **6e**, 103224-73-3; **6f**, 103224-74-4; **6g**, 103224-96-0; **6h**, 103224-75-5; **6i**, 103224-97-1; **7a**, 2243-32-5; **7b**, 2408-38-0; **7c**, 84244-56-4; **7d**, 2604-45-7; **7e**, 28195-34-8; **7f**, 28195-32-6; **7g**, 3360-64-3; **7h**, 86145-88-2; **8a**, 98055-25-5; **9a**, 98055-26-6; **9b**, 103224-76-6; **9c**, 103224-77-7; **9d**, 103224-78-8; **9e**, 103224-79-9; **9f**, 103224-80-2; **9h**, 103224-81-3; **10a**, 98055-17-5; **10b**, 98055-20-0; **10c**, 103224-82-4; **10d**, 98055-21-1; **10e**, 98055-18-6; **10f**, 98055-19-7; **10g**, 103224-83-5; **10h**, 103224-84-6; **11a**, 4540-48-1; **11b**, 98055-24-4; **11c**, 103224-85-7; **11d**, 91344-77-3; **11e**, 98055-22-2; **11f**, 98055-23-3; **11g**, 103224-86-8; **11h**, 103224-87-9; **12a**, 103224-88-0; **12b**, 103224-89-1; **12c**, 103224-90-4; **12d**, 103224-91-5; **12e**, 103224-92-6; **12f**, 103224-93-7; **12g**, 103224-94-8; **12h**, 103224-95-9.

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