During this time nitrogen evolved and the color of the reaction solution changed from deep red to light orange. The solvent was then removed *in vacuo* and the resulting solid was recrystallized from cyclohexane and then sublimed to give 2.8 g (75%) of **22** as a light orange solid, mp 91–92°.

Anal. Calcd for $C_{10}H_{10}BrNO_2$: C, 46.87; H, 3.90; N, 5.46. Found: C, 46.78; H, 3.99; N, 5.48.

α-*tert*-Butyl-γ-cyanobromomethylene-$\Delta^{\alpha,\beta}$-butenolide (23).—3-Azido-2-bromo-5-*tert*-butyl-1,4-benzoquinone (**21**), 2 g (0.007 mol), was slowly (20 min) added to 40 ml of vigorously stirred cold (0–5°) concentrated sulfuric acid. The reaction solution became a deep blue upon addition of the azide and nitrogen slowly evolved. Upon disappearance of the color the solution was poured into ice water, causing the butenolide to precipitate, yield 1.55 g (86%), mp 102–104. Recrystallization from ether–petroleum ether (bp 30–60°) gave an analytical sample.

Anal. Calcd for $C_{10}H_{10}BrNO_2$: C, 46.87; H, 3.90; N, 5.46; Br, 31.24. Found: C, 46.78; H, 3.87; N, 5.56; Br, 31.13.

Reaction of 3-Bromo-2,5-di-*tert*-butyl-1,4-benzoquinone (8) with HBr in the Presence of Cyclohexene.—3-Bromo-2,5-di-*tert*-butyl-1,4-benzoquinone (**8**) was dissolved in 20 ml of glacial acetic acid and 5 ml of cyclohexene. This solution was vigorously stirred at ambient temperature and saturated with anhydrous HBr. The solution immediately lightened in color and after 2 min it was quenched with water and extracted with diethyl ether. The ether extract was backwashed twice with water and then dried over anhydrous sodium sulfate. The solvent was then removed *in vacuo*, giving a light yellow oil. This oil was analyzed by gas chromatography using known standards of 1,2-dibromocyclohexane and 3-bromo-2,5-di-*tert*-butyl-1,4-benzoquinol, showing 0.337 g (92.5%) of the former and 0.404 g (90.5%) of the latter.

2-Chloro-5-*tert*-butyl-1,4-benzoquinonedibenzenesulfonamide (27).—Anhydrous HCl was bubbled through a solution of 180 mg (0.36 mmol) of 2,5-di-*tert*-butyl-1,4-benzoquinonedibenzenesulfonimide in 10 ml of glacial acetic acid for 4 min and the mixture was then allowed to stand at room temperature for 21 hr. The reaction solution was then poured into ice–H_2O and the resulting white precipitate (130 mg, 75%) was collected and washed with acetic acid, mp 162–166°. Recrystallization from acetone–ether gave the analytical sample.

Anal. Calcd for $C_{22}H_{23}ClN_2S_2O_4$: C, 55.17; H, 4.80; N, 5.85. Found: C, 55.22; H, 4.83; N, 5.98.

Reaction of 2,5-Di-*tert*-butyl-1,4-benzoquinonedibenzenesulfonimide with Anhydrous HBr in the Presence of Cyclohexene.—A suspension of 249 mg (0.52 mmol) of 2,5-di-*tert*-butyl-1,4-benzoquinonedibenzenesulfonimide (**26**) in 7 ml of glacial acetic acid and 4 ml of cyclohexene was treated with anhydrous HBr for 3 min. The reaction solution was then allowed to stand at ambient temperature for 7 hr. During this time the original yellow color disappeared and a white solid precipitated. The reaction solution was poured into water and basified with 1% NaOH. An ether extract of this mixture was analyzed by vpc, which showed 1,2-dibromocyclohexane. The basic solution was acidified with dilute HCl. The white solid (230 mg, 92%), mp 261–264°, was collected and recrystallized from acetone, giving pure 2,5-di-*tert*-butyl-1,4-benzoquinonedibenzenesulfonamide, mp and mmp 265–266°.

2-*tert*-Butyl-5,6-dibromo-1,4-cyclohexenedione (32).—A solution of 10 g (0.061 mol) of 2-*tert*-butyl-1,4-benzoquinone (**31**) was dissolved in 100 ml of glacial acetic acid. This solution was then treated with 9.7 g (0.061 mol) of bromine. The halogen was added over a period of 2 min. The bromine immediately reacted with the quinone, as evidenced by the disappearance of the bromine color. The reaction solution was then poured into water and the resulting precipitate was filtered to give 18.9 g (91%) of the dibromo derivative **32**, mp 103–106°. Recrystallization from diethyl ether gave 12.8 (61%), mp 104–106°.

Anal. Calcd for $C_{10}H_{12}Br_2O_2$: C, 33.63; H, 3.36; Br, 49.38. Found: C, 33.58; H, 3.42; Br, 49.27.

Reaction of 2,3-Dibromo-2,5-di-*tert*-butyl-1,4-cyclohexenedione (6) with HBr/CH_3CO_2H in the Presence of Cyclohexene.—2,3-Dibromo-2,5-di-*tert*-butyl-1,4-cyclohexenedione (**6**) (4.0 g, 0.0105 mol) was dissolved in 75 ml of glacial acetic acid and 10 ml of cyclohexene. Anhydrous HBr was slowly passed through the vigorously stirred solution for 45 min. The reaction was then quenched with water and extracted twice with ether. The combined ether extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated by removal of the solvent *in vacuo* to give 2.0 g (86%) of 2,5-di-*tert*-butyl-1,4-benzoquinol (**30**). This hydroquinone **30** was identified by comparison of its ir spectrum with that of an authentic sample as well as by a mixture melting point. The mother liquor contained 4.3 g (170%) of 1,2-dibromocyclohexane as determined by glc analysis.

Registry No.—**5**, 33611-72-2; **6**, 34403-11-7; **7**, 33611-70-0; **8**, 33611-71-1; **13**, 34403-14-0; **14**, 34403-15-1; **15**, 34403-16-2; **16**, 25762-86-1; **18**, 34403-18-4; **19**, 34403-19-5; **20**, 34403-20-8; **21**, 34403-21-9; **22**, 34403-22-0; **23**, 34403-23-1; **27**, 34403-24-2; **28**, 30221-31-9; **31**, 24197-48-6.

The Ortho Alkylation of Anisole

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Aluminum chloride catalyzed alkylation of anisole with a series of olefins and with γ-valerolactone is demonstrated to result primarily in the formation of ortho-substituted products. The extent of ortho alkylation is shown to be a function of solvent and of basic functionality in the alkylating agent.

The aluminum chloride catalyzed alkylation of aromatic compounds with olefins[2] and γ-lactones[3] is a well-documented reaction. Application of this reaction to anisole has generally been reported to result in a mixture of ortho and para isomers, with the para isomer predominating.[2] An unusual exception exists in the literature, however. This consists of a report that reaction of anisole with ethyl allylmalonate in the presence of $AlCl_3$ affords a product consisting of approximately 90% of the ortho isomer.[4] In view of this, we have carefully examined the isomer distribution produced on $AlCl_3$-catalyzed alkylation of anisole with a series of olefins and with γ-valerolactone (**7**). The results (Table I) demonstrate that, with all those alkylating agents studied, the ortho isomer is either the principal or nearly by exclusive alkylation product.

(1) National Science Foundation College Teacher Research Participant summer 1970.

(2) (a) S. H. Patinkin and B. S. Friedman in "Friedel–Crafts and Related Reactions," Vol. II, Part 1, G. A. Olah, Ed., Interscience, New York, N. Y., 1964, Chapter XIV; (b) R. Koncos and B. S. Friedman, Chapter XV.

(3) (a) J. F. Eijkman, *Chem. Zentr.*, **75**, I, 1416 (1904); (b) R. T. Arnold, J. S. Buckley, and J. Richter, *J. Amer. Chem. Soc.*, **69**, 2322 (1947); (c) R. V. Christian, *ibid.*, **74**, 1591 (1952); (d) W. L. Mosby, *ibid.*, **74**, 2564 (1952); (e) W. E. Truce and C. E. Olson, *ibid.*, **74**, 4721 (1952); (f) D. B. Bruce, A. J. S. Sorrie, and R. H. Thomson, *J. Chem. Soc.*, 2403 (1953); (g) J. I. Brauman and A. J. Pandell, *J. Amer. Chem. Soc.*, **89**, 5421 (1967); (h) D. W. Waples and J. I. Brauman, *Chem. Commun.*, 1075 (1971); (i) E. J. Eisenbraun, C. W. Hinman, J. M. Springer, J. W. Burnham, and T. S. Chou, *J. Org. Chem.*, **36**, 2480 (1971).

(4) A. S. Gupta, K. L. Murthy, and S. Dev, *Tetrahedron*, **23**, 2481 (1967).

TABLE I

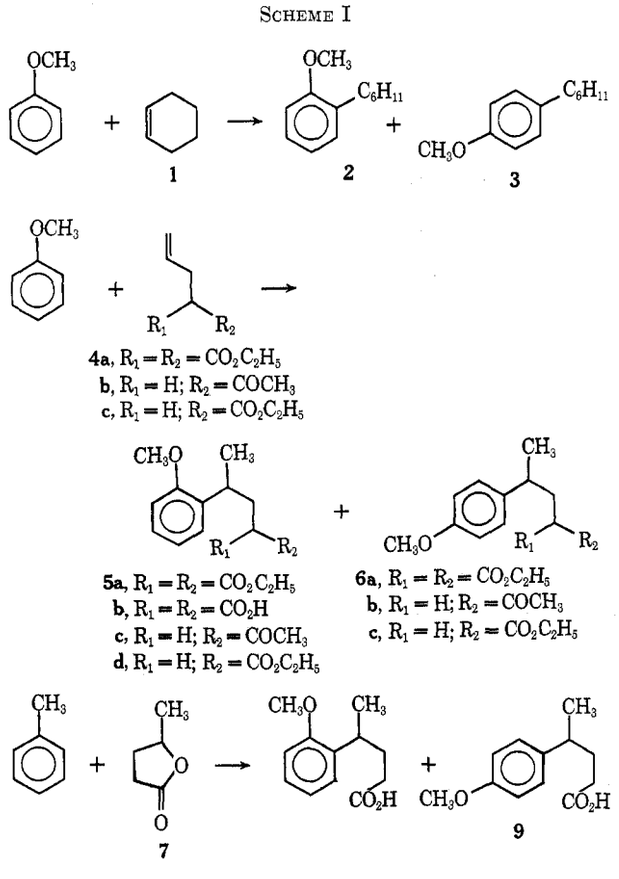
ALUMINUM CHLORIDE CATALYZED ALKYLATION OF ANISOLE

Alkylating agent	Product	Solvent	Time, hr[a]	Isolated yield, %	Isomer distribution, %[b] Ortho	Para
Cyclohexene (1)	$CH_3OC_6H_4(C_6H_{11})$	Hexane	3	63	66	34
		Anisole	3	78	64 (68[c])	36 (32[c])
Ethyl allylmalonate (4a)	$CH_3OC_6H_4CH(CH_3)CH_2CH(CO_2C_2H_5)_2$	Hexane	31	31	86	14
		Anisole	16	36	65[c]	35[c]
		1-Nitropropane	24	30	55[c]	45[c]
5-Hexen-2-one (4b)	$CH_3OC_6H_4CH(CH_3)CH_2CH_2COCH_3$	Hexane	25	33	97 (98[d])	3 (2[d])
		Anisole	2	10	94	6
		Anisole	6.3	20	93[e]	7[e]
Ethyl 4-pentenoate (4c)	$CH_3OC_6H_4CH(CH_3)CH_2CH_2CO_2C_2H_5$	Hexane	19	40	95	5
		Anisole	2.5[f]	2.4	86	14
		Anisole	18	23	87 (82[c])	13 (18[c])
γ-Valerolactone (7)	$CH_3OC_6H_4CH(CH_3)CH_2CH_2CO_2H$	Hexane	12[g]	24	81	19
		Anisole[h]	1.8[i]	41	67	33

[a] At room temperature unless otherwise incidcated. [b] Per cent of isolated product determined by nmr except where indicated. [c] Determined by gas chromatography on a 5 ft × 0.25 in. column packed with 15% silicone SF-96 on Chromosorb P. [d] Determined by gas chromatography on a 5 ft × 0.25 in. column packed with 15% Carbowax 20M on Chromosorb P. [e] Determined by gas chromatography on a 15 ft × 0.25 in. column packed with 10% silicone QF-1 on Chromosorb P. [f] At ice bath temperature. [g] At reflux. [h] A 1.00:0.50:0.52 mole ratio of anisole:γ-valerolactone:$AlCl_3$ was employed in this reaction. [i] At 90–100° bath temperature.

The alkylations were carried out using either hexane, excess anisole, or 1-nitropropane as a diluent. Reactions in hexane were conducted with a 1.28:1.00:0.20 mole ratio of $AlCl_3$:anisole:alkylating agent and were heterogeneous. Under these conditions, ethyl allylmalonate (**4a**), 5-hexen-2-one (**4b**), ethyl 4-pentenoate (**4c**), and γ-valerolactone (**7**) each afforded an alkylation product consisting of >80% of the ortho isomer. The essentially exclusive (98%) ortho alkylation obtained with 5-hexen-2-one (**4b**) appears to be without precedent. Cyclohexene (**1**), however, afforded only a modest 66% of the ortho isomer (Scheme I).

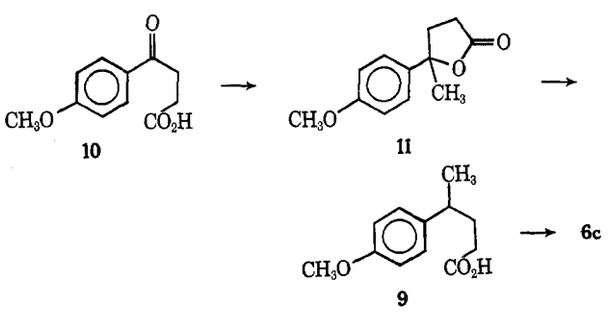
SCHEME I



When excess anisole was substituted for hexane as the solvent, a ratio of $AlCl_3$:anisole:alkylating agent of 0.20:1.00:0.10 was employed, and the reaction mixtures were homogeneous. The stereoselectivity of the reaction was reduced under these conditions with each alkylating agent except cyclohexene (**1**). This reduction in stereoselectivity is not large for 5-hexen-2-one (**4b**), which still affords 93–94% of the ortho isomer.[5] Alkylation with ethyl allylmalonate (**4a**) in excess anisole, however, demonstrates a somewhat more dramatic reduction in the stereoselectivity of alkylation. In the single experiment employing 1-nitropropane as solvent, the ratio of $AlCl_3$:anisole:ethyl allylmalonate (**4a**) was the same as that used for reactions carried out in hexane. This reaction demonstrates a further reduction in stereoselectivity to a point where the amounts of ortho and para isomers formed are essentially equal.

4-(*p*-Methoxyphenyl)valeric acid (**9**) and its ethyl ester **6c**, obtained as products in the reaction of anisole with γ-valerolactone (**7**) and ethyl 4-pentenoate (**4c**) respectively, were identified by comparison with authentic compounds prepared by independent synthesis (Scheme II). Conversion of keto acid **10** to γ-lactone

SCHEME II



11 was accomplished in 67% yield by reaction with 2.1 equiv of methylmagnesium iodide. Subsequent hydrogenolysis of **11** afforded 4-(*p*-methoxyphenyl)valeric

(5) The product of reaction of 5-hexen-2-one with anisole under similar conditions has been previously described in the literature[6] but was incorrectly regarded as consisting exclusively of the para isomer.

(6) S. M. Mukherji, O. P. Vig, and N. K. Maheshwary, *J. Indian Chem. Soc.*, **34**, 9 (1957).

acid (**9**). Fischer esterification with ethanol and sulfuric acid then gave the corresponding ethyl ester **6c**.

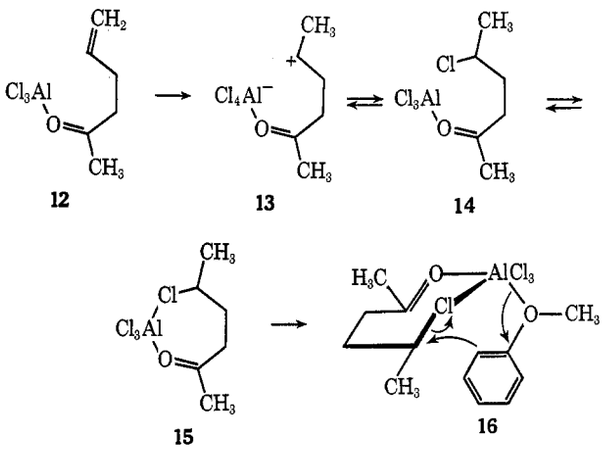
4-(*o*-Methoxyphenyl)valeric acid (**8**) and its ethyl ester **5d** were also identified by comparison with authentic compounds. Reaction products resulting from alkylation of anisole with cyclohexene (**1**), ethyl allylmalonate (**4a**), and 5-hexen-2-one (**4b**) were identified by isolation and characterization.

Discussion

The exclusive or nearly exclusive electrophilic ortho substitution of aromatic compounds is an uncommon reaction with interesting synthetic potential. Reactions of this type include the Kolbe–Schmitt reaction,[7] alkylation of phenol[8] and aromatic amines[9] with olefins, bromination of phenol,[10] and thallation of suitably substituted benzene derivatives.[11] A cyclic mechanism has been proposed for each of these examples.

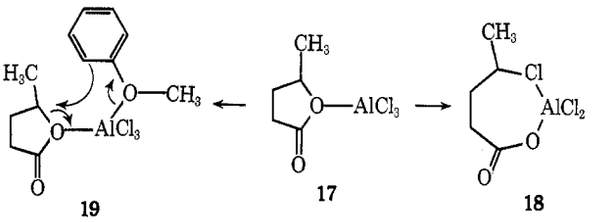
The results in Table I indicate that, with properly chosen alkylating agents, the $AlCl_3$-catalyzed alkylation of anisole represents still another example of near exclusive ortho substitution. The fact that extensive ortho alkylation is observed only with those alkylating agents which represent potential sources of reactive intermediates carrying a positive charge γ to a carbonyl, carbethoxy, or carboxyl group suggests that the oxygen-containing functional groups assume more than a passive role in the reaction. In hexane solution, the amount of $AlCl_3$ used was slightly greater, on a mole basis, than the combined amounts of anisole and alkylating agent. In view of the ability of $AlCl_3$ to form stable complexes with ethers, ketones, and esters,[12] it may be assumed that little free anisole or alkylating agent is present. The unusual amount of ortho alkylation further suggests that both reactants may be associated with the same aluminum atom and that the alkylating agent is delivered through a cyclic process. In the case of 5-hexen-2-one (**4b**) (Scheme III), the coordinated ketone **12** could react with adventitious HCl to give species such as **13**, **14**, or **15**.[13] Structure **15** may be the best representation, however, since the chelate structure would be anticipated to afford a modest amount of stability. Coordination of anisole with $AlCl_3$ should reduce its reactivity toward electrophilic reagents and, in addition, any increase in electrophile

SCHEME III



stability would be expected to further reduce the rate of reaction. Therefore, although attack by **15** on the $AlCl_3$·anisole complex should produce a mixture of ortho and para products, the rate of reaction should not be large. Alternatively, coordination of a molecule of anisole with the aluminum of **15** would afford **16** in which ortho alkylation of the aromatic ring could take place by way of a six-center cyclic mechanism. A similar sequence of events can also be postulated for esters **4a** and **4c**. γ-Valerolactone (**7**), however, requires a slight modification (Scheme IV). In this case, cleavage

SCHEME IV



of the lactone ring could provide the intermediate **18**,[3g] which is analogous to **15**. Coordination of one or two molecules of anisole with the aluminum atom of **18** would then permit ortho alkylation to proceed by way of a cyclic process as depicted for **16**. Alternatively, coordination of anisole with the aluminum atom of **17** would afford **19**, which could also permit an intramolecular delivery of the alkylating agent. The relatively low yield (81%) of ortho product **8** obtained in this reaction may be a consequence of the higher reaction temperature required.

Reduction of the stereoselectivity produced by use of excess anisole as solvent is presumably a result of the availability of substantial amounts of free anisole. The free anisole should be more reactive than the $AlCl_3$·anisole complex toward electrophilic reagents and result in an increase in the extent of intermolecular reaction, which would be anticipated to be less stereoselective than an intramolecular process. The independence of isomer ratio from reaction time in anisole solution for both **4b** and **4c** suggests that selective destruction of one isomer is not responsible for the still substantial amount of ortho product obtained.

Transition to 1-nitropropane as the solvent would be expected to result in a low ortho/para ratio as a result

(7) A. S. Lindsey and H. Jeskey, *Chem. Rev.*, **57**, 583 (1957).

(8) (a) A. J. Kolka, J. P. Napolitano, A. H. Filbey, and G. G. Ecke, *J. Org. Chem.*, **22**, 642 (1957); (b) R. Stroh, R. Seydel, and W. Hahn, *Angew. Chem.*, **69**, 699 (1957); (c) E. A. Goldsmith, M. J. Schlatter, and W. G. Toland, *J. Org. Chem.*, **23**, 1871 (1958).

(9) (a) G. G. Ecke, J. P. Napolitano, A. H. Filbey, and A. J. Kolka, *ibid.*, **22**, 639 (1957); (b) R. Stroh, J. Ebersberger, H. Haberland, and W. Hahn, *Angew. Chem.*, **69**, 124 (1957).

(10) D. E. Pearson, R. D. Wysong, and C. V. Breder, *J. Org. Chem.*, **32**, 2358 (1967).

(11) E. C. Taylor, F. Kienzle, R. L. Robey, A. McKillop, and J. D. Hunt, *J. Amer. Chem. Soc.*, **93**, 4845 (1971).

(12) N. N. Greenwood and K. Wade in "Friedel–Crafts and Related Reactions," Vol. I, G. A. Olah, Ed., Interscience, New York, N. Y., 1963, Chapter VII.

(13) Stable compounds containing four-coordinate and six-coordinate aluminum are well known.[14] Five-coordination of aluminum is less common, but examples have been documented.[15] Therefore, postulation of a five-coordinate aluminum compound as a reactive intermediate, such as **13** or **15**, does not appear unreasonable.

(14) P. J. Durrant and B. Durrant, "Introduction to Advanced Inorganic Chemistry," 2nd ed, Wiley, New York, N. Y., 1970, pp 564–579.

(15) (a) I. Pattison and K. Wade, *J. Chem. Soc. A*, 2618 (1968); (b) C. W. Heitsch and R. N. Kniseley, *Spectrochim. Acta*, **19**, 1385 (1963); (c) G. W. Fraser, N. N. Greenwood, and B. P. Straughan, *J. Chem. Soc.*, 3742 (1963).

of competition between solvent and anisole for coordination sites on aluminum. Under these conditions, intramolecular delivery of alkylating agent should be almost entirely suppressed in favor of an intermolecular reaction pathway. This appears to be substantiated by the reaction of ethyl allylmalonate (**4a**) with anisole in this solvent to provide only 55% of ortho product **5a**.

The relatively small amount of ortho product obtained with cyclopentene,[16] where it represents the minor product, and with cyclohexene (64–68%) argues strongly against the operation of a cyclic mechanism where participation by a neighboring oxygen-containing functional group is not possible. The apparent lack of solvent dependence of the isomer distribution in the case of cyclohexene provides additional evidence for the importance of such neighboring functionality. The composite of these results indicates that upon proper selection of an alkylating agent, manipulation of the reaction conditions can afford a substantial degree of control over the orientation of substitution.

Experimental Section[17]

Analyses.—Analyses were accomplished either by integration of the nmr singlets produced by methoxyl protons of the isomeric products or by gas chromatography.

4-(*p*-Methoxyphenyl)-4-hydroxyvaleric Acid Lactone (11).—A solution of methylmagnesium iodide was prepared under nitrogen by dropwise addition of 73.0 g (0.515 mol) of methyl iodide in 350 ml of anhydrous ether to a flask containing 13.11 g (0.540 g-atom) of magnesium turnings over a period of 2 hr with mechanical stirring at ice bath temperature. Stirring was continued at room temperature for an additional 45 min after addition was complete. After cooling again at ice bath temperature, a solution of 50.0 g (0.240 mol) of 3-(*p*-methoxybenzoyl)propionic acid (**10**),[18] mp 148.5–150.0°, in 1 l. of tetrahydrofuran (freshly distilled from $LiAlH_4$) was added dropwise over a period of 110 min with mechanical stirring. The mixture was then heated at reflux under nitrogen with mechanical stirring for 14 hr. After cooling, the mixture was decomposed with 800 ml of 3 *M* HCl. The aqueous layer was separated and extracted twice with 700-ml portions of ether. The combined ether layers were washed once with 300 ml of 5% sodium bisulfite solution, once with 500 ml of water, once with 300 ml of 10% aqueous K_2CO_3, once with 500 ml of water, and once with 300 ml of saturated sodium chloride solution, and dried over anhydrous $MgSO_4$. Removal of solvent *in vacuo* afforded 34.05 g of brown oil which was fractionated through a 9-cm Vigreux column to give 25.2 g (51%) of γ-lactone **11** as a pale yellow oil, bp 137.0–139.0° (0.30 mm) [lit.[4] bp 140–142° (1.5–2 mm)]. Acidification of the potassium carbonate wash afforded 12.1 g of recovered 3-(*p*-methoxybenzoyl)propionic acid (**10**), mp 145.0–148.0°, indicating a 67% yield of γ-lactone **11** based on recovered starting material.

4-(*p*-Methoxyphenyl)valeric Acid (9).—Hydrogenolysis of 25.18 g (0.122 mol) of γ-lactone **11** over 3.00 g of 5% palladium on carbon powder at 60 psi in 200 ml of absolute ethanol was complete after 2 hr. After filtration, concentration of the filtrate *in vacuo* followed by distillation of the residue afforded 22.64 g (89%) of 4-(*p*-methoxyphenyl)valeric acid (**9**) as a colorless oil which solidified on standing: bp 135.0–139.0° (0.2 mm); mp 38.0–40.5° (lit.[4] mp 39–40.5°); nmr (CCl_4) δ 1.22 (3 H, d J = 7 Hz, $CHCH_3$), 3.68 (3 H, s, OCH_3) and 6.57–7.15 (4 H, symmetrical A_2B_2 m, aromatic CH).

Ethyl 4-(*p*-Methoxyphenyl)valerate (6c).—To a solution of 3.040 g (14.6 mmol) of 4-(*p*-methoxyphenyl)valeric acid (**9**) in 25.0 ml of absolute ethanol was added 0.50 ml of concentrated sulfuric acid and the mixture was heated at reflux for 6.5 hr. After cooling, the resulting mixture was diluted with 75 ml of water and extracted with 75 ml of benzene. The benzene extract was washed once with 75 ml of saturated $NaHCO_3$ solution and once with 75 ml of water, and dried over anhydrous $MgSO_4$. Concentration of the resulting solution *in vacuo* followed by distillation afforded 3.019 g (88%) of ethyl 4-(*p*-methoxyphenyl)valerate (**6c**) as a colorless liquid: bp 112.0–116.0° (0.4 mm); ir (neat) 1734 (ester C=O) and 836 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.17 (3 H, t, J = 7 Hz, CH_2CH_3), 1.21 (3 H, d, J = 7 Hz, $CHCH_3$), 3.68 (3 H, s, OCH_3), 4.00 (2 H, q, J = 7 Hz, OCH_2CH_3), and 6.58–7.17 (4 H, symmetrical A_2B_2 m, aromatic CH).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.31; H, 8.76.

4-(*o*-Methoxyphenyl)valeric Acid (8).—Using the procedure of Fourneau and Baranger,[19] pure **8** was obtained as large white crystals: mp 66.0–67.0° (lit.[4,19] mp 63–65°); nmr (CCl_4) δ 1.22 (3 H, d, J = 7 Hz, $CHCH_3$), 3.74 (3 H, s, OCH_3), and 6.60–7.25 (4 H, complex, m, aromatic CH).

Ethyl 4-(*o*-Methoxyphenyl)valerate (5d).—Using the procedure employed for the para isomer, 4-(*o*-methoxyphenyl)-valeric acid (**8**) was converted to the ethyl ester **5d**, which was obtained in 90% yield as a colorless liquid: bp 98.0–99.0° (0.25 mm); ir (neat) 1735 (ester C=O) and 760 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.16 (3 H, t, J = 7 Hz, CH_2CH_3), 1.20 (3 H, d, J = 7 Hz, $CHCH_3$), 3.74 (3 H, s, OCH_3), 3.99 (2 H, q, J = 7 Hz, OCH_2CH_3), and 6.62–7.24 (4 H, complex m, aromatic CH).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.49; H, 8.45.

Oxidation of 0.493 g (2.09 mmol) of **5d** with 3.004 g (19.0 mmol) of $KMnO_4$ in 60 ml of 0.32% aqueous NaOH afforded 0.050 g of crude acidic product. Sublimation (85° bath temperature at 0.35 mm) followed by crystallization from benzene–hexane afforded 0.035 g (11%) of *o*-methoxybenzoic acid, mp 102.5–104.0°, undepressed on admixture with authentic material.

Alkylation of Anisole with 5-Hexen-2-one (4b) in Excess Anisole.—The following preparation is representative of the general procedure using excess anisole as the solvent. Under a $CaCl_2$ drying tube, 26.7 g (0.20 mol) of anhydrous aluminum chloride was added to 108.1 g (1.00 mol) of anisole with mechanical stirring over a period of 11 min. To this was added a solution of 9.815 g (0.10 mol) of 5-hexen-2-one (**4b**) in 10.0 g (0.093 mol) of anisole over a period of 28 min at room temperature with stirring. Stirring was then continued at room temperature for 6.3 hr. The resulting brown mixture was decomposed with 100 g of ice and extracted with 100 ml of hexane. The hexane extract was washed with four 100-ml portions of water and dried over anhydrous $MgSO_4$. Hexane was removed at aspirator pressure, and the residue was fractionated through a 10-cm Vigreux column to give 4.019 g (20%) of 5-anisylhexan-2-one, bp 95.0–102.0° (0.4 mm). Gas chromatography[20] indicated the presence of two isomers in a 93:7 ratio.

The principal component, 5-(*o*-methoxyphenyl)hexan-2-one (**5c**), was obtained as a colorless liquid after preparative gas chromatography[20] followed by short path distillation (0.2 mm and 92° bath): ir (neat), 1717 (C=O) and 760 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.18 (3 H, d, J = 7 Hz, $CHCH_3$), 1.90 (3 H, s, $COCH_3$), 3.73 (3 H, s, OCH_3), and 6.62–7.24 (4 H, complex m, aromatic CH).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.87; H, 8.69.

The minor component, 5-(*p*-methoxyphenyl)hexan-2-one (**6b**), was obtained as a pale yellow liquid after preparative gas chromatography[20] followed by short path distillation (0.2 mm and 95° bath): ir (neat) 1715 (C=O) and 836 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.18 (3 H, d, J = 7 Hz, $CHCH_3$), 1.90 (3 H, s, $COCH_3$), 3.68 (3 H, s, OCH_3), and 6.62–7.17 (4 H, symmetrical A_2B_2 m, aromatic CH).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.65; H, 8.53.

Alkylation of Anisole with Cyclohexene (1) in Hexane.—The following preparation is representative of the general procedure

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(17) Melting points are uncorrected. The infrared spectra were recorded with either a Beckman IR-8 or a Perkin-Elmer 257 infrared spectrophotometer. Nmr spectra were determined with a Varian A-60 spectrometer using tetramethylsilane as internal standard. Microanalyses were performed by M-H-W Laboratories, Garden City, Mich.

(18) Y. S. Rao and R. A. Kretchmer, *Org. Prep. Proced. Int.*, **3**, 177 (1971).

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(20) A 15 ft × 0.25 in. column packed with 10% silicone QF-1 on Chromosorb P was employed.

using hexane as the solvent. Under a $CaCl_2$ drying tube, 85.0 g (0.64 mol) of anhydrous aluminum chloride was added to a solution of 54.0 g (0.50 mol) of anisole in 140 ml of hexane over a period of 12 min with mechanical stirring. To this was added a solution of 8.22 g (0.10 mol) of cyclohexene (1) in 10.0 ml of hexane over a period of 67 min with stirring. The resulting mixture was stirred at room temperature for 3 hr, then decomposed with 100 g of ice. The organic layer was separated, washed five times with 100-ml portions of water, and dried over anhydrous $MgSO_4$. The solution was concentrated *in vacuo* and the residue was fractionated through a 10-cm Vigreux column to give 11.98 g (63%) of cyclohexylanisole, bp 108.5–117.0° (2.5 mm). Integration of the nmr singlets at δ 3.68 and 3.63 indicated a 66:34 mixture of ortho and para isomers.

The major isomer, *o*-cyclohexylanisole (**2**), was isolated from the product of an analogous reaction by preparative gas chromatography[21] as a colorless liquid, ir (neat) 760 cm^{-1} (aromatic CH). The minor isomer, *p*-cyclohexylanisole (**3**), was obtained in similar fashion as a white solid, mp 55–56° (lit.[22] mp 57–58°), ir (KBr) 824 cm^{-1} (aromatic CH).

Ethyl [2-(Methoxyphenyl)propyl]malonate.—The minor (35%) isomer, ethyl [2-(*p*-methoxyphenyl)propyl]malonate (**6a**), produced on monoalkylation of anisole with ethyl allylmalonate (**4a**) in excess anisole, was isolated after preparative gas chromatography[21] and short path distillation (0.5 mm and 160° bath) as a colorless liquid: ir (neat) 1748, 1732 (ester C=O), and 836 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.18 (3 H, t, J = 7 Hz, CH_2CH_3), 1.24 (3 H, t, J = 7 Hz, CH_2CH_3), 1.24 (3 H, d, J = 7 Hz, $CHCH_3$), 3.71 (3 H, s, OCH_3), 4.04 (2 H, q, J = 7 Hz, OCH_2CH_2), 4.12 (2 H, q, J = 7 Hz, OCH_2CH_3), and 6.60–7.15 (4 H, symmetrical A_2B_2 m, aromatic CH).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.57; H, 7.86.

The major (65%) isomer, ethyl [2-(*o*-methoxyphenyl)propyl]malonate (**5a**), was also isolated by preparative gas chromatography[21] as a colorless liquid: ir (neat) 1750, 1734 (ester C=O), and 760 cm^{-1} (aromatic CH); nmr (CCl_4) δ 1.14 (3 H, t, J = 7 Hz, CH_2CH_3), 1.18 (3 H, t, J = 7 Hz, CH_2CH_3), 1.22 (3 H, d, J = 7 Hz, $CHCH_3$), 3.73 (3 H, s, OCH_3), 4.02 (2 H, q, J = 7 Hz, OCH_2CH_2), 4.11 (2 H, q, J = 7 Hz, OCH_2CH_3), and 6.67–7.30 (4 H, complex m, aromatic CH). Characterization was accomplished by saponification to [2-(*o*-methoxyphenyl)propyl]malonic acid (**5b**), mp 148.0–149.5° dec (lit.[4] mp 143–144°).

Registry No.—**1**, 110-83-8; **4a**, 2049-80-1; **4b**, 109-49-9; **4c**, 1968-40-7; **5a**, 34399-51-4; **5c**, 34399-52-5; **5d**, 34399-53-6; **6a**, 34399-54-7; **6b**, 34399-55-8; **6c**, 34399-56-9; **7**, 108-29-2; **10**, 3153-44-4; $AlCl_3$, 7446-70-0; anisole, 100-66-3.

(21) A 5 ft × 0.25 in. column packed with 15% silicone SF-96 on Chromosorb P was employed.

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General Acid Catalysis of Ortho Ester Hydrolysis

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The rates of hydrolysis of diethylphenyl orthoformate, diphenylethyl orthoformate, and diphenylethyl orthoacetate have been determined in 50% dioxane–H_2O (v/v) at 25 and 45°. A pronounced general acid catalysis is observed in the hydrolysis of these compounds. The value of the Brønsted coefficient α is 0.47, 0.68, and 0.49, respectively. Thus, general acid catalysis is more favorable with very weak acids in the case of diethylphenyl orthoformate in comparison with diphenylethyl orthoformate even though the latter compound is of lower basicity. This is due to the more stable oxocarbonium ion produced from diethylphenyl orthoformate which causes the bond-breaking process to be more facile.

It has long been known that certain types of ortho esters are subject to general acid catalyzed hydrolysis in aqueous solution.[2] The pseudo-first-order rate constants for hydrolysis of ethyl orthocarbonate, ethyl orthoacetate, and ethyl orthopropionate are dependent on buffer acid concentration at constant pH.[2] The hydrolysis of methyl orthobenzoate was reported to be catalyzed by general acids in aqueous methanol,[3] and general acid catalysis was claimed for hydrolysis of triethyl orthoformate in 70% dioxane–H_2O but not in H_2O.[4] However, it has recently been shown that this result was possibly due to specific salt effects in aqueous dioxane.[5] Bunton and DeWolfe[6] stressed relatively low basicity of ortho esters as a feature responsible for general acid catalysis. The Brønsted coefficient α for general acid catalyzed hydrolysis of ethyl orthocarbonate[2,7] and also methyl orthobenzoate[3] is approximately 0.7. It has been considered that ortho ester hydrolysis will generally be characterized by high α values.[8]

General acid catalysis has also been observed in acetal and ketal hydrolysis with 2-(substituted phenoxy)-tetrahydropyrans,[9] tropone diethyl ketal,[10] and benzaldehyde di-*tert*-butyl acetals.[11] Electron withdrawal in the leaving group of a phenoxytetrahydropyran will both lower basicity and increase the ease of C–O bond breaking. With tropone diethyl ketal[10] the leaving group is poor, but the great stability of the intermediate carbonium ion makes C–O bond breaking relatively easy. In the case of the benzaldehyde di-*tert*-butyl acetals[11] the bond breaking process is facilitated by relief of ground state strain during the hydrolytic reaction. With all of these compounds, ease of bond breaking is most likely the predominant feature giving rise to general acid catalysis.[9-12]

Triphenyl orthoformate, an ortho ester with which basicity would be very low and with which the leaving group would be reasonably good, has been studied.[13]

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