The *ortho/para* Ratio in Electrophilic Aromatic Substitution. Mercuration and Alkylation of Chlorobenzene and Anisole. Evidence for a Coordination Effect[1]

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The *ortho/para* ratios were obtained for nitration, chlorination, mercuration, alkylation, and benzenesulfonylation of toluene, chlorobenzene, and anisole. Mercuration and alkylation gave ratios of $\geqq 1.0$ for $(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$ and $(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$ in contrast with values of $\leqq 0.4$ for nitration, chlorination, and benzenesulfonylation. We conclude from the data that the relatively high ratios for mercuration and alkylation result from coordination of the attacking electrophiles with the Lewis base substituent groups. Transfer of the complexed moiety to the nucleus may involve migration *via* the delocalized electron cloud or by a bridging mechanism. The relatively high *ortho/para* ratios for mercuration and alkylation of chlorobenzene and anisole are all the more remarkable since they arise in spite of a large number of opposing influences: steric factors of the attacking groups, inductive effects, and resonance interactions in both the ground state and σ-complex intermediate.

Beginning with the early days of organic chemical research, much attention has been devoted to factors governing orientation in electrophilic aromatic substitution. Nevertheless, although impressive advances have been made, certain aspects are regretably still not well understood. Since many effects are operating and interacting, difficulties abound in connection with attempts to treat the individual influences.

Our objective was to advance the knowledge of factors controlling the *ortho/para* ratio, particularly in relation to coordination phenomena. There are several reviews which adequately deal with the previous work on orientation.[3-8] Those aspects which are most pertinent to our approach are listed, together with leading references: ground, transition, and intermediate states[9-12]; steric effect[3,5-7]; resonance effect[3-6,10,12a,b]; inductive effect[4,5]; coordination (cyclic or quasi-ring) effect[12-15]; solvent effect[14a,16,17]; temperature effect[5,18]; activity of the attacking species.[19,20]

Results and Discussion

In order to provide a favorable opportunity for correlating structure with orientation, we selected for study a variety of electrophilic substitution reactions, including nitration, chlorination, mercuration, alkylation, and benzenesulfonylation. Although the aromatic reactants (toluene, chlorobenzene, and anisole) which were chosen differ widely in reactivity, all are *ortho–para* directors. Since the isomer distribution data are useful only in the absence of product rearrangement, a careful investigation was made relative to the validity of our results. Whenever necessary, the question of subsequent isomerization was resolved by determining the effect on orientation of variation in temperature or time. Gas chromatography and infrared spectroscopy were used to obtain the isomer distributions.

Nitration.—Of the various aromatic substitution reactions, nitration is one of the most thoroughly studied,[4] both qualitatively and quantitatively. The requisite data are available in the literature[21,22] (see Table I following).

TABLE I

NITRATION WITH NITRIC ACID–SULFURIC ACID

C_6H_5Z, Z =	Temp., °C.	$NO_2C_6H_4Z$, % o	m	p	o/p	Ref.
CH_3	25–30	58.5	4.4	37.1	1.58	*a*
Cl	30	31.3	0.4	68.3	0.46	*b*
OCH_3	45	31.3	1.7	67.0	0.47	*c*

[a] See ref. 21. [b] See ref. 22*a*. [c] See ref. 22*b*.

Chlorination.—Chlorination of the three substrates was accomplished (Table II) with molecular chlorine and aluminum chloride in nitromethane, conditions similar to those used in some of our alkylation studies. Although toluene and anisole underwent halogenation with chlorine in acetic acid, chlorobenzene did not give a detectable amount of product under these conditions.

(1) From the Ph.D. Thesis (1965) of J. J. H., presented at the 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964.

(2) Case Institute of Technology Honors Fellow, 1961–1962; National Science Foundation Fellow, summer 1963.

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TABLE II

CHLORINATION WITH CHLORINE AND ALUMINUM CHLORIDE IN NITROMETHANE

C_6H_5Z, Z =	Temp., °C.	Time, min.	ClC_6H_4Z, % o	m	p	o/p	Method of analysis[a]
CH_3	16–17	15	62	3	35	1.77	B1
Cl	18–20	25	42	3	55	0.76	A1
Cl	17–19	15	43	3	54	0.80	A1
Cl[b]	18–19	20	44	2	54	0.81	A1
OCH_3	18–20	11	21	0	79	0.27	A11
OCH_3	17–19	8	21	0	79	0.27	A11
OCH_3[b]	17–18	12	20	0	80	0.25	A11

[a] See Analytical Procedures, Experimental. [b] Ferric chloride catalyst.

Our results are in good agreement with orientation values reported in the literature.[5,15a,23-27]

Benzenesulfonylation.—The kinetic studies of Brown and Jensen[20] have aided in elucidating the mechanistic aspects of benzenesulfonylation. Since orientation data for the toluene reaction are available in the literature,[20] our investigations were limited to chlorobenzene and anisole (Table III).

TABLE III

BENZENESULFONYLATION WITH BENZENESULFONYL CHLORIDE AND ALUMINUM CHLORIDE AT 24 ± 1°

C_6H_5Z, Z =	Time, hr.	$ZC_6H_4SO_2C_6H_5$, % o	m	p	Crude product, m.p., °C.[a]
CH_3[b]		28.4	8.7	62.9	
Cl	5	<1	<1	100	91.5–93.5
Cl	3	<1	<1	100	91–94
OCH_3	0.5	<1	<1	100	
OCH_3	1	<1	<1	100	86.5–88[c]

[a] Mixture melting point with authentic material showed no depression. [b] See ref. 20. [c] M.p. 88–89° after crystallization from 85% ethanol.

Mercuration.—Previous reports indicate that mercuration may proceed by either an electrophilic or free-radical mechanism.[3,28,29]

Our experiments were carried out in perchloric acid solution with mercuric perchlorate so as to favor the polar pathway (Tables IV–VI). Conditions were selected such that less than 7% of dimercuration occurred. In the case of anisole, very precise regulation of reaction variables was necessary in order to meet the requirement set for dimercuration.

When toluene and chlorobenzene served as the aromatic substrates, orientation data obtained with mercuric perchlorate corresponded closely to that reported for the mercuric acetate reactions.[30a,b] In contrast, anisole gave a much higher *ortho/para* ratio with mercuric perchlorate (1.25) compared with mercuric acetate (0.14).[30c] The difference in the case of anisole conceivably results from the greater ionic character of the electrophile derived from the perchlorate system.

TABLE IV

MERCURATION WITH MERCURIC OXIDE AND PERCHLORIC ACID AT 25°

C_6H_5Z, Z =	Time, min.	BrC_6H_4Z, % o	m	p	o/p	Dimercuration, %	Method of analysis[a]
CH_3	5	19	8	73	0.26	5	B1, B2
CH_3	1	17	9	74	0.23	5	B1
CH_3[b]	1	17	9	74	0.23	3	B1
Cl	5	28	15	57	0.49	4	A1, B1
Cl[c]	15	26	12	62	0.42	4	A1, B1
Br	5	31	12	57	0.54	2	A1, B1
Br	25	32	11	57	0.56	3	A1, B1
OCH_3	0.17	55	<1	44	1.25	7	B1
OCH_3	0.33	51	<1	47	1.09	10	B1
OCH_3[d]	5	53	<1	46	1.15	6	B1, B2
OCH_3[d]	1	55	<1	44	1.25	5	B1

[a] See Analytical Procedures, Experimental. [b] $C_6H_5CH_2$/HgO = 4:1 (molar ratio). [c] C_6H_5Cl/HgO = 4:1 (molar ratio). [d] $C_6H_5OCH_3$/HgO = 4:1 (molar ratio).

TABLE V

MERCURATION WITH MERCURIC PERCHLORATE AND PERCHLORIC ACID AT 25°[a,b]

C_6H_5Z, Z =	Time, min.	BrC_6H_4Z, % o	m	p	o/p	Dimercuration, %[c]
CH_3	5	17	9	74	0.23	6
CH_3	1	19	7	74	0.26	5
Cl	8	30	16	54	0.56	6
OCH_3[d]	1	55[e]	<1	44	1.25	5
OCH_3	0.17	53	<1	46	1.15	6

[a] Results given are the average of at least two runs. [b] Method of analysis: B1 (see Experimental). [c] Predominantly the 2,4 isomer. [d] $C_6H_5OCH_3/Hg(ClO_4)_2$ = 4:1 (molar ratio). [e] Also analyzed by method B2 (see Experimental).

TABLE VI

MERCURATION WITH MERCURIC ACETATE AND ACETIC ACID AT 25°[a]

C_6H_5Z, Z =	Time, min.	BrC_6H_4Z, % o	m	p	o/p
CH_3	25	21[b]	10	70	0.30
CH_3	15	20	9	72	0.28
OCH_3	7	12	<1	88	0.14
OCH_3	12	14	<1	88	0.16

[a] Method of analysis: B1 (see Experimental). [b] Also analyzed by method B2 (see Experimental).

Isomer distributions were determined with the bromo derivatives obtained by treatment of the organomercurial product with bromine. It has been demonstrated that the bromination reaction proceeds without rearrangement.[31] We have verified the previous observation that reaction of bromine with the mercurated derivative from anisole proceeds as desired with a negligible amount of extraneous bromination.[30c]

Mercuration gave a higher *ortho/para* ratio with bromobenzene than with chlorobenzene (Table IV), in keeping with the results from other electrophilic substitutions in the halobenzene series.[3]

Alkylation.—It is difficult to standardize experimental conditions for all of the desired alkylations,

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(30) (a) H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2300 (1955); (b) H. C. Brown and G. Goldman, *ibid.*, **84**, 1650 (1962); (c) H. C. Brown and M. Dubeck, *ibid.*, **82**, 1939 (1960).
(31) M. S. Kharasch and L. Chalkley, *ibid.*, **43**, 607 (1921).

since the rates vary widely and the problem of rearrangement is particularly serious in this series. In general, low temperatures and short reaction times were used.

Methylation, isopropylation, and tertiary butylation of the substrates were carried out with the corresponding alkyl chlorides and aluminum chloride in nitromethane[32] (Tables VII–IX). Limited studies were also made with the catalysts, stannic chloride, ferric chloride, titanium tetrachloride, and antimony pentachloride (Table X), as well as with methyl bromide–aluminum bromide (Table XI). Our results agree quite well with literature data for alkylations performed under somewhat different conditions.[32-39]

TABLE VII

METHYLATION WITH METHYL CHLORIDE AND CATALYST IN NITROMETHANE[a]

C_6H_5Z, Z =	Catalyst	Temp., °C.	Time, hr.	$CH_3C_6H_4Z$ % o	m	p	o/p
CH_3	$AlCl_3$	12–14	1.3	52[b]	16	32	1.62
CH_3[c]	$AlCl_3$	13–14	0.67	53[b]	15	32	1.65
CH_3	$SnCl_4$	16–18	1.7	55	14	31	1.77
CH_3	$FeCl_3$	16–17	1.3	55	16	29	1.89
CH_3	$TiCl_4$	16–17	1.8	54	14	32	1.69
Cl	$AlCl_3$	18–21	12.2	57	10	33	1.73
Cl	$AlCl_3$	18–20	9.8	58	9	33	1.76
OCH_3[d]	$AlCl_3$	19–21	6[e]	56	12	32	1.75
OCH_3[c]	$AlCl_3$	18–21	3[f]	61	7	32	1.91
OCH_3[g]	$AlCl_3$	19–21	2[h]	60	8	32	1.87

[a] Method of analysis: B1 (see Experimental). [b] Also analyzed by method B2 (see Experimental). [c] Double scale. [d] With methyl bromide. [e] Phenol plus cresol (25% total). [f] Phenol plus cresol (10% total). [g] Triple scale. [h] Phenol plus cresol (8% total).

TABLE VIII

ISOPROPYLATION WITH ISOPROPYL CHLORIDE AND ALUMINUM CHLORIDE IN NITROMETHANE

C_6H_5Z, Z =	Temp., °C.	Time, min.	i-PrC_6H_4Z % o	m	p	o/p	Method of analysis[a]
CH_3	16–19	42	43	19	38	1.13	A3
CH_3	16–17	18	46	15	39	1.18	A3
CH_3	16–18	12	47	15	38	1.24	A3
Cl	17–18	60	51	8	41	1.24	A4
Cl	17–19	120	53	9	38	1.39	A4
OCH_3	14–17	140	60	<2	38	1.58	A5[b]
OCH_3	11–13	11	61	<2	38	1.60	A5[c]

[a] See Table XVII. [b] Isopropylphenol (6%). [c] Isopropylphenol (3%).

We found a small amount of *ortho* isomer in the chloro-*t*-butylbenzene product, in contrast with a previous report that only *meta* and *para* orientation is obtained.[33] The absence of any *ortho* isomer in the *t*-butylation of anisole can be rationalized on the basis of a solvent effect.[16] By analogy, chlorination of anisole in 2-nitropropane yielded less than 1% of the *ortho* isomer[16] compared with 21% in acetic acid.[27]

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TABLE IX

TERTIARY BUTYLATION WITH *t*-BUTYL CHLORIDE AND ALUMINUM CHLORIDE IN NITROMETHANE

C_6H_5Z, Z =	Temp., °C.	Time, min.	t-BuC_6H_4Z % o	m	p	o/p	Method of analysis[a]
CH_3	14–17	12	...	17	83	...	A6
CH_3	15–17	6	...	9	91	...	A6
CH_3	14–16	1.5	...	9	91	...	A6
Cl	16–17	132	3	3	94	0.03	B2
Cl	15–16	63	4	3	93	0.04	B2
OCH_3	12–14	14	...	7	93	...	A7
OCH_3	11–14	3	...	6	94	...	A7
Br	15–18	164	...	<1	100	...	A8

[a] See Analytical Procedures, Experimental.

TABLE X

ALKYLATION WITH ALKYL HALIDES AND ANTIMONY PENTACHLORIDE

C_6H_5Z, Z =	RCl, R =	Temp., °C.	Time, hr.	RC_6H_4Z % o	m	p	o/p	Method of analysis[a]
CH_3	Me	11–13	1.0	52	18	30	1.73	B2
CH_3	Me	12–14	0.58	53	17	30	1.77	B1
Cl	Me	16–19	11.0	53	9	36	1.47	B2
Cl	Me	16–17	7.3	55	10	35	1.57	B1
CH_3	*i*-Pr	14–16	2.2	43	21	36	1.19	A3
CH_3	*i*-Pr	14–16	0.22	42	19	39	1.08	A3
CH_3	*t*-Bu	13–14	0.27	..	15	85	...	A6
CH_3	*t*-Bu	13–14	0.033	..	10	90	...	A6
Cl	*t*-Bu	15–17	1.3	..	13	87	...	B2
Cl	*t*-Bu	13–16	0.58	..	11	89	...	B1

[a] See Analytical Procedures, Experimental.

TABLE XI

METHYLATION WITH METHYL BROMIDE AND ALUMINUM BROMIDE[a,b]

C_6H_5Z, Z =	Temp., °C.	$CH_3C_6H_4Z$ % o	m	p	o/p
CH_3	−7 to −1	54	17	29	1.86
Cl	−3 to 4	57	8	33	1.73

[a] Time, 20 min. [b] Method of analysis: B2 (see Experimental).

Alkylations were also performed with alcohols in 60% perchloric acid. Our results for isopropylation and tertiary butylation of anisole confirm the findings of Gold and Riley.[40] The reaction was also extended to toluene (Table XII). In this way, we were able to obtain orientation data for the tertiary butylation of toluene and anisole under similar conditions. However, chlorobenzene did not undergo attack, nor did methanol function as a substituting agent.

By use of *t*-butyl chloride in perchloric acid, alkylation of all three aromatic substrates was effected (Table XIII).

The over-all orientation data are compiled in Tables XIV and XV in the form $(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$ and $(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$.

A plausible interpretation of the data is that the unusually high values for $(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$ and for $(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$ in mercuration and

(40) V. Gold and T. Riley, *J. Chem. Soc.*, 4183 (1962).

TABLE XII

ALKYLATION OF AROMATICS WITH ALCOHOLS AND PERCHLORIC ACID AT 25°

C_6H_5Z, Z =	ROH, R =	Time, hr.	ZC_6H_4R % o	m	p	o/p	Method of analysis[a]
CH_3	*t*-Bu	0.5	..	7	93	...	A10
CH_3		4	..	7	93	...	A10
CH_3		21	..	7	93	...	A10
CH_3	*i*-Pr	4	43	21	36	1.19	A9, A10
CH_3		21	43	19	38	1.13	A9, A10
OCH_3	*t*-Bu	4	20	<1	80	0.25	A8, A9, A10
OCH_3		26	17	<1	83	0.20	A8, A9, A10
OCH_3	*i*-Pr	4	50	<1	50	1.00	A9, A10
OCH_3		12	51	<1	49	1.04	A9, A10

[a] See Table XVII.

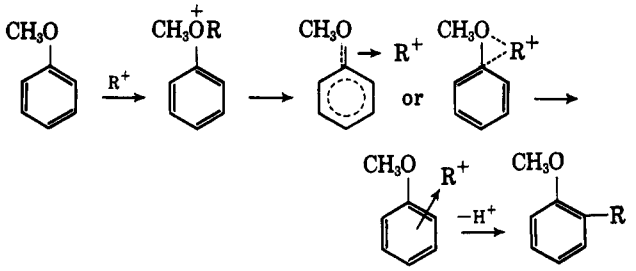
TABLE XIII

ALKYLATION WITH ALKYL CHLORIDE AND PERCHLORIC ACID AT 25°

C_6H_5Z, Z =	RCl, R =	Time, hr.	*t*-BuC_6H_4Z % o	m	p	o/p	Method of analysis[a]
CH_3	*t*-Bu	1.5	..	10	90	...	A10
CH_3	*t*-Bu	2.5	..	10	90	...	A10
CH_3	*i*-Pr	8	47	16	37	1.27	A10
CH_3	*i*-Pr	25	45	16	39	1.15	A10
Cl	*t*-Bu	12[b]	..	6	94	...	B1
Cl	*t*-Bu	8[b]	..	5	95	...	B1
OCH_3	*t*-Bu	5	23	...	77	0.30	A2
OCH_3	*t*-Bu	2.5	22	...	78	0.28	A2
OCH_3	*i*-Pr	12	54	<1	46	1.17	A10
OCH_3	*i*-Pr	24	51	<1	49	1.04	A10

[a] See Analytical Procedures, Experimental. [b] Days.

alkylation result from linear coordination[41] of the attacking electrophiles with the Lewis base substituent groups. Presumably, the postulated complexes then rearrange to nuclear-substituted products with the *ortho* isomer favored. The reaction pathway can be visualized as shown (with anisole and an attacking carbonium ion). Transfer of the complexed group to



the nucleus may involve migration *via* the delocalized electron cloud or by a bridging mechanism. It is reasonable to expect the rearrangement route to yield a small amount of *para* isomer also.[42] In addition, reaction would be proceeding by direct attack on the aromatic nucleus.

As evidenced by the summations in Tables XIV and XV, there is an element of specificity in the coordination phenomena displayed in mercuration and alkylation. Appropriate conditions must be selected in order to provide the electrophile best suited for side-chain association. It should be emphasized that the nature of both the donor and acceptor plays an important role in determining whether or not complexing at the side chain, followed by intramolecular rearrangement, will occur.

An uncertain point in the theoretical treatment is the relative size of chlorine and methoxyl. As deduced from the conformational free-energy differences for substituents in cyclohexane,[43] methoxyl possesses a steric factor equal to, or greater than, that of chlorine. If similar spatial effects apply in the case of electrophilic aromatic substitution, then the generally higher *ortho/para* ratios for anisole *vs.* chlorobenzene in mercuration and alkylation cannot be rationalized on steric grounds. On the other hand, an interpretation based on coordination possesses merit since oxygen would be expected to function as a better nucleophile than chlorine in complex formation.

Lewis acid complexes analogous to those discussed herein are reported for anisole–boron trifluoride[44a] and chlorobenzene–aluminum chloride (n-complexes).[44b] Anisole forms mainly the n-complex with phenol, along with some of the π-complex.[45] With this background, we would like now to call attention to similarities between certain literature material and some of our results relating to coordination, as well as the interpretation. An interesting resemblance may be found to several reactions involving migration of a group from the side chain to the aromatic nucleus. The acid-catalyzed rearrangement of aralkyl ethers is regarded as intramolecular, at least in part.[42] Our mechanistic scheme for *ortho* alkylation and *ortho* mercuration of chlorobenzene and anisole *via* coordination is essentially identical with that advanced[42] for

TABLE XIV

THE *ortho/para* RATIO IN ELECTROPHILIC AROMATIC SUBSTITUTION

Reaction	Table no.	$(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$	$(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$
Mercuration	V	2.2	4.8
Methylation	VII	1.1	1.2
Isopropylation	VIII	1.1	1.3
Tertiary butylation	XIII	...	>30
Nitration	I	0.3	0.3
Chlorination	II	0.4	0.2
Benzenesulfonylation	III	<0.02	<0.02

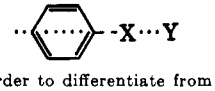
TABLE XV

THE *ortho/para* RATIO IN MERCURATION AND ALKYLATION

Reaction	Table no.	$(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$	$(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$
Mercuration	VI[a]	1.5	0.5
Tertiary butylation	XII	...	>20
Tertiary butylation	IX	>3	...
Isopropylation	XII	...	0.9
Isopropylation	XIII	...	0.9

[a] Also see ref. 30a and b.

(41) We suggest the more specific term "linear coordination," since the electrophile (Y) coordinates with a donor atom which is in line with the



aromatic nucleus and in order to differentiate from nonlinear coordination involving quasi 5- and 6-membered rings.

(42) M. J. S. Dewar in "Molecular Rearrangements," part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 5.

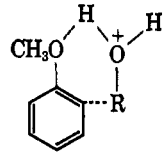
(43) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 236.

(44) (a) H. Bowlus and J. A. Nieuwland, *J. Am. Chem. Soc.*, **53**, 3835 (1931); H. Meerwein and H. Maier-Hüser, *J. prakt. Chem.*, **134**, 51 (1932). (b) G. A. Olah, W. S. Tolgyesi, and R. E. A. Dear, *J. Org. Chem.*, **27**, 3441 (1962).

(45) B. B. Wayland and R. S. Drago, *J. Am. Chem. Soc.*, **86**, 5240 (1964).

the aralkyl ether rearrangement. A similar interpretation applies to the nitramine rearrangement.[42,46] Although the situation apparently does not prevail with aryl esters generally,[42] phenyl isobutyrate seems to undergo the Fries rearrangement by an intramolecular mechanism.[47]

On the other hand, the alternative hypothesis involving nonlinear coordination cannot be conclusively discounted in all cases. For example, alkylation of anisole with alcohols might entail formation of the complex A. However, this possibility is given lesser status partly because of the resulting decrease in the



A

positive nature of the electrophile and the sacrifice in resonance contribution by the substituent group.[48] These objections would not apply to the route involving linear coordination.

Our general hypothesis is further strengthened by the insufficiency of the other operative factors in completely rationalizing the results. Alternative possibilities will now be considered.

Data from various studies,[7,43,49-52] point to the following steric relationship: *t*-Bu > *i*-Pr > Me > Cl, OCH_3. Furthermore, based on the *ortho/para* ratios for the toluene reactions, the following order of bulkiness is indicated for the attacking species: tertiary butylation > mercuration > benzenesulfonylation[53] > isopropylation > methylation > nitration = chlorination.

The items listed subsequently cannot be adequately interpreted on steric grounds: (1) the increased *ortho/para* ratio from anisole in mercuration, compared with nitration and chlorination; and (2) the increased *ortho/para* ratio for isopropylation of chlorobenzene and anisole, compared with nitration and chlorination.

Ingold[6] has suggested that the high *ortho/para* ratios obtained with *meta* directors, such as nitrobenzene, result from specific *para* deactivation through resonance. The selectivity presumably arises from preferance for the *para* quinoid *vs.* the *ortho* form. From an extension of the argument to *ortho/para* directors, one would logically expect specific *para* activation. Similar reasoning would apply both to the ground state and the σ-complex intermediate. Rate data for the solvolysis of *para*-substituted phenyldimethylcarbinyl chlorides indicates that methoxyl participates in resonance interaction much better than chloro or methyl.[54] Therefore, *para* activation in this manner should be of greatest significance in the case of anisole, favoring a low *ortho/para* ratio. Indeed, the interpretation is generally consistent with the *ortho/para* ratios from nitration, chlorination, and benzenesulfonylation of the three substrates. Furthermore, the inductive effects of the chloro and methoxyl substituents, in comparison with methyl, are in harmony with the experimental results. The increase in the ratios, $(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$ and $(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$, for mercuration and alkylation suggests the important involvement of another factor, presumably a coordination phenomenon.

It has been proposed[19] that for reactants of high activity the *ortho/para* ratio is determined by the electron distribution in the ground state, whereas with low-activity electrophiles the charge distribution in the σ-complex intermediate becomes important. In pursuit of this thesis, Norman and Radda[19] pointed out that *ortho* deactivation should be quite pronounced in the reaction of anisole with highly active reagents.[55] Our data indicate that this is certainly not a predominant factor in the alkylation of anisole. We would like to direct particular attention to the high value (1.9), essentially statistical, for methylation of anisole. This is quite striking since Friedel–Crafts alkylation exhibits marked sensitivity to steric factors.[56] Since anisole and chlorobenzene resemble one another quite closely in many of the *ortho/para* changes which are observed in this series, the orientation interpretation of Paul[57] based on electrostatic, dipolar interactions does not appear highly relevant.

It is clear that the observed changes in the *ortho/para* ratios cannot result from a solvent effect. Environments of high polarity have been used for those reactions such as chlorination (acetic acid)[26,27] and nitration (mixed acid), which are characterized by low values for $(o/p)_{C_6H_5Cl}/(o/p)_{C_6H_5CH_3}$ and $(o/p)_{C_6H_5OCH_3}/(o/p)_{C_6H_5CH_3}$, as well as for the substitutions such as alkylation and mercuration (aqueous perchloric acid) which display relatively high values. Since all of the experiments were carried out within a 20° range, the temperature effect can be discounted as an important factor. Furthermore, no assistance is provided by the substituent inductive effect in illuminating the relatively high *ortho/para* ratios for chlorobenzene and anisole *vs.* toluene.

Thus, the ratios observed in mercuration and alkylation of chlorobenzene and anisole are all the more remarkable since they arise in spite of a number of opposing influences: steric factors of the attacking groups, inductive effects, and resonance interactions in both the ground state and σ-complex intermediate.

Another interpretation of the main body of our data arises from a combined consideration of reagent activity and steric influence. For this approach, use is made of the steric order, Cl > OCH_3, as indicated by studies of the racemization of optically active biphen-

(46) For an alternative viewpoint, see W. N. White, J. R. Klink, D. Lazdins, C. Hathaway, J. T. Golden, and H. S. White, *ibid.*, **83**, 2024 (1961).

(47) T. I. Briggs, G. G. S. Dutton, and E. Merler, *Can. J. Chem.*, **34**, 851 (1956).

(48) K. Halvarson and L. Melander, *Arkiv Kemi*, **11**, 77 (1957).

(49) G. S. Hammond and M. F. Hawthorne, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 171.

(50) R. W. Taft in ref. 49, p. 598.

(51) R. L. Shriner, R. Adams, and C. S. Marvel in "Organic Chemistry—An Advanced Treatise," H. Gilman, Ed., Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, Chapter 4.

(52) R. Adams and J. B. Hale, *J. Am. Chem. Soc.*, **61**, 2825 (1939).

(53) We recognize that there may possibly be some involvement of a coordination effect [see H. Cerfontain, F. L. J. Sixma, and L. Vollbracht, *Rec. trav. chim.*, **82**, 659 (1963)].

(54) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **79**, 1913 (1957).

(55) Consideration should be given to the possible decrease in activity through coordination with excess anisole.

(56) M. J. S. Dewar and W. H. Poesche, *J. Am. Chem. Soc.*, **85**, 2253 (1963).

(57) M. A. Paul, *ibid.*, **80**, 5332 (1958).

TABLE XVI
RELATIVE RATES

Reaction	$k_{toluene}/k_{benzene}$ Calcd.[a] (conditions)	$k_{toluene}/k_{benzene}$ Experimental (conditions)
Mercuration	9.0 (HgO–aq. $HClO_4$)	7.9 ($Hg(OAc)_2$–$HClO_4$–HOAc)[b]
Methylation	3.2 (MeCl–$AlCl_3$–CH_3NO_2)	3.8 (MeBr–$AlBr_3$)[c]
Isopropylation	4.0 (*i*-PrCl–$AlCl_3$–CH_3NO_2)	2.0 (*i*-PrBr–$AlCl_3$–CH_3NO_2)[d]
Isopropylation	2.7 (*i*-PrOH–$HClO_4$)	2.7 (propylene–$HClO_4$–CH_3NO_2)[d]
Tertiary butylation	8.3 (*t*-BuCl–$HClO_4$)	16.3 (isobutene–H_2SO_4–CH_3NO_2)[e]
Tertiary butylation	9.5 (*t*-BuCl–$AlCl_3$–CH_3NO_2)	1.9 (*t*-BuBr–$AlCl_3$–CH_3NO_2)[e,f]
Tertiary butylation	13.4 (*t*-BuOH–$HClO_4$)	16.6 (*t*-BuBr–$SnCl_4$–CH_3NO_2)
Nitration	21 (HNO_3–H_2SO_4)[g]	21 (HNO_3–CH_3NO_2)[h]
Nitration	...	23 ($AcONO_2$–Ac_2O)[h]
Chlorination	29 (Cl_2–$AlCl_3$–CH_3NO_2)	18 (Cl_2–$AlCl_3$–CH_3NO_2)[d]
Benzenesulfonylation	8.7 ($C_6H_5SO_2Cl$–$AlCl_3$)[i]	8 ($C_6H_5SO_2Cl$–$AlCl_3$)[i]

[a] From the isomer distributions; see ref. 35. [b] See ref. 30a. [c] See ref. 34, 0–5°. [d] See ref. 37. [e] See ref. 38. [f] Undoubtedly isomerized (46.4% *meta*). [g] See ref. 8. [h] L. M. Stock, *J. Org. Chem.*, **26**, 4120 (1961). [i] See ref. 20.

yls,[51,52] and steric substituent constants derived from hydrolysis of *ortho*-substituted benzoates.[50] As a consequence, the generally higher *ortho/para* ratios obtained with anisole in comparison with chlorobenzene would simply reflect a steric difference. Also, reagent activity (Table XVI) and the increasing *ortho/para* ratios for chlorobenzene and anisole correlate in this manner: alkylation and mercuration > nitration and chlorination.

This alternative postulate is less favored, since, in contrast to the coordination view, it cannot satisfactorily cope with the indicated items. (1) In the toluene reactions, mercuration and alkylation yield lower *ortho/para* ratios than do nitration and chlorination. Therefore, the increased activity certainly does not outweigh the increase in steric factor. (2) Although the substituting entity in benzenesulfonylation is as active as that in mercuration and of similar steric requirement, no *ortho* isomer was formed from chlorobenzene or anisole. (3) In size, bromine is equal to[50] or greater than[51,52] methyl. However, mercuration affords a greater amount of *ortho* isomer with bromobenzene than with toluene. The opposite result would be predicted from the standpoint of inductive effects. In this case, the most satisfying rationalization entails coordination or resonance.

In addition, theoretical considerations[19] suggest that *ortho* deactivation should be quite marked in the reaction of anisole with reagents of high activity.

Linear coordination constitutes a novel addition to the repertory of factors which influence the isomer distribution in aromatic substitution. Since the problem is so exceedingly complex, final judgment on the validity of this approach must await additional experimentation.

Experimental[58]

Materials.—Toluene (Fisher Certified Reagent) was distilled over sodium. Chlorobenzene and bromobenzene (Fisher Certified Reagent) were distilled over molecular sieves. 2-Methyl-2-chloropropane, 2-methyl-2-bromopropane, 2-chloropropane, and 2-bromopropane (Eastman, White Label) were fractionated through a 2-ft. helices-packed column. Nitromethane was purified by washing with a solution containing sodium bicarbonate and sodium bisulfite, then with water, dilute sulfuric acid, and again with water. After treatment with Drierite, the solvent was distilled over molecular sieves.

(58) Melting points and boiling points are uncorrected. Elemental analyses were performed by Dr. Weiler and Dr. Strauss, Oxford, England.

The standards for infrared and gas chromatographic analyses were purified when necessary. We are grateful to Dr. George Olah for samples of *m*-*t*-butyltoluene, *o*-cymene, and *o*- and *p*-chlorocumene; to Dr. Lester Friedman for *m*-cymene; and to the Dow Chemical Co. for *o*- and *p*-butyl- and isopropylphenols. Other reagents were high purity commercial materials which were used as obtained.

General Procedures. A. Mercuration. 1. With Mercuric Perchlorate–Perchloric Acid.—A solution of mercuric perchlorate (0.50 mole) and perchloric acid (350 ml., 40% solution by weight) was vigorously stirred and kept at 25 ± 1° for 20 min. under nitrogen. After the aromatic compound (0.47 mole) was added at 25° during 5 sec. to 2 min., the reaction mixture was stirred for the requisite time, and then a cold solution of sodium bromide (210 g.) and sodium acetate (200 g.) in water (400 ml.) was added. The white precipitate was filtered on a medium-porosity glass frit, washed successively with a 10% sodium bromide solution (75 ml.) and water (150 ml.), and then dried to constant weight under vacuum. For the very short-term runs the flask was immersed in Dry Ice–acetone at the end of the designated time.

The organomercurial (3.00 g.) was slurried at room temperature with distilled chloroform (200 ml.), and then a 40% solution (by weight) of bromine in chloroform was added dropwise until the red color persisted. After 2 hr. the excess bromine was destroyed by washing with a 5% sodium bisulfite solution. The filtered mercuric bromide was washed with 10% sodium bromide solution. After the chloroform solution was washed with water and dried over sodium sulfate, most of the chloroform was removed through a 2-ft. helices-packed distillation column at atmospheric pressure. The distilled chloroform was checked for codistillate by gas chromatography. The chloroform wash (two 5-ml. portions) of the column was combined with the residue, and the analysis was performed.

In certain cases, after bromination of a larger quantity of the organomercurial, the yields of main product and nonvolatile residue were determined by distillation. For very short reaction times, a large beaker was used since addition of the aromatic compound and reaction termination could be accomplished very quickly. Carbon disulfide also served satisfactorily as the bromination solvent. Lower bromination temperatures (5–12°) did not alter the results.

2. With Mercuric Oxide–Perchloric Acid.—Mercuric oxide (0.50 mole) and perchloric acid (500 ml., 40% by weight) were stirred together until the mixture became homogeneous. Then the aromatic compound (0.47 mole) was added rapidly at 25 ± 1° during 5–20 sec., and the reaction was allowed to proceed for an additional 10 sec. to 25 min. The reaction flask was then immersed in a Dry Ice–acetone bath and a cold (0°) solution of sodium bromide (210 g.) and sodium acetate (200 g.) in 400 ml. of water was added. The work-up procedure described in A1 was followed. The data are summarized in Table IV.

3. With Mercuric Acetate–Acetic Acid.—The aromatic compound (0.60 mole) in glacial acetic acid (200 ml.) was added at 25 ± 1° during 1 min. under nitrogen to a solution of mercuric acetate (0.06 mole) in glacial acetic acid (400 ml.). After 7–25 min., the reaction was terminated by the introduction of cold water (600 ml.). Most of the unchanged aromatic component was removed by aspiration at room temperature, and then a solution of potassium bromide (0.18 mole, 46.8 g.) in 100 ml.

of water was added. The remaining procedure was similar to that described in A1. Carbon disulfide served as the bromination solvent. Table VI contains the pertinent data.

B. Alkylation. 1. With Alkyl Halide and Catalyst in Nitromethane.—The catalyst (0.20 mole) in nitromethane (80 g.) was added with good stirring to a solution of the aromatic compound (2.0 moles) in nitromethane (120 g.) under nitrogen. This solution was brought to the desired temperature before the addition of the alkyl halide (0.20 mole) in nitromethane (80 g.). Hydrogen chloride evolution was followed by titration with standard base (phenolphthalein indicator).

Termination of reaction was effected by addition of the mixture to ice–water. The organic layer was then washed with water, 10% sodium hydroxide, water, dilute hydrochloric acid, and water. Drying was accomplished with calcium carbonate and then with magnesium sulfate. Conditions were selected so that 10–15 g. of product resulted, which was fractionated in order to obtain information on identity and by-products. In addition the amount of phenolic by-product from anisole was determined.

Caution should be exercised since nitromethane may decompose violently in the presence of alkali.

2. Alkylation with Alkyl Halides and Antimony Pentachloride.—Gaseous methyl chloride (2.83 moles) was slowly bubbled into a stirred mixture of the aromatic compound (6.00 moles) and antimony pentachloride (0.30 mole) at 17°. A Dry Ice–acetone condenser was used to minimize the loss of methyl chloride. After 11 hr. at 17–19°, the reaction mixture was worked up as described in B1.

3. Alkylation with Methyl Bromide and Aluminum Bromide.—Methyl bromide (24.6 g., 0.259 mole) at −40° was quickly added in a drybox under nitrogen to a stirred mixture of the aromatic compound (1.533 moles) and anhydrous aluminum bromide (136.5 g., 0.273 mole) at −7° (Dry Ice–acetone condenser). The temperature rose to −1°. After 20 min. of vigorous stirring, the dark red mixture was essentially homogeneous. Then the reaction mixture was poured into ice–water and the organic layer was separated and washed in succession with water, 10% sodium carbonate, and water. Following removal of the unchanged aromatic component from the dried solution by distillation through a 2-ft. helices-packed column, the residual product was fractionated with a 50-plate, spinning-band column. The data are summarized in Table XI.

4. Alkylation with Isopropyl Alcohol or *t*-Butyl Alcohol (or Chlorides) and Perchloric Acid.—The alcohol or alkyl chloride (0.135 mole) was added to a stirred mixture of the aromatic (0.278 mole) and perchloric acid (100 ml., 60% by weight) at 25 ± 1°. After vigorous stirring for the specified period, 750 ml. of cold water was added. The water layer was extracted with four portions of ether which were combined with the organic layer. Washing was accomplished with water, 10% sodium bicarbonate, and water. Following the evaporation of ether from the dried solution, the residue was subjected to analysis.

In several experiments, the products were distilled. Reactions carried out with each of the alcohols or alkyl chlorides on a 2× scale were followed by analysis at intervals (4, 8, and 12 hr., 15 ml. of solution). The data are summarized in Tables XII and XIII.

The *t*-butyl alcohol and *t*-butyl chloride reactions yielded olefinic by-products. The major component displayed the same infrared spectrum and retention time in gas chromatography as did authentic diisobutylene. The yields increased with time. The same products were formed in corresponding amounts from perchloric acid and *t*-butyl alcohol or *t*-butyl chloride.

C. Chlorination. 1. Chlorination with Chlorine–Catalyst–Nitromethane.—A solution of the catalyst (aluminum chloride or ferric chloride, 0.02 mole) in nitromethane (90 g.) was slowly added with stirring to a solution of the aromatic compound (2.00 moles) in nitromethane (200 g.) at 15 ± 1°. Liquid chlorine (0.21 mole, 14.2 g.) was then vaporized into the mixture during 8 min. After termination of the reaction with ice–water, the organic layer was washed with water, 5% hydrochloric acid, and water, and then dried over anhydrous magnesium sulfate. In one reaction the amount of nonvolatile by-product was determined by distillation. The results are summarized in Table II.

D. Benzenesulfonylation.—After chlorobenzene (0.07 mole) was added dropwise to a solution of aluminum chloride (0.04 mole) in benzenesulfonyl chloride (0.80 mole) at 24 ± 1°, the mixture was vigorously stirred for the appropriate reaction time. Following dilution with ice–water, the organic layer was separated and washed with water, and then washed with dilute caustic. Removal of unchanged starting material by distillation at 3 mm. left a brown oil which crystallized on cooling. The crude product, 3.24 g., was dissolved in hot, 85% ethanol, filtered from traces of insoluble material, and diluted in the cold to effect recovery of the sulfone, 3.21 g.

In the case of anisole, the caustic wash was omitted. The crude product, 1.28 g., was heated with hot, aqueous ethanol containing potassium hydroxide, filtered from a small amount of insoluble material, and then diluted in the cold with water. The recovered, white solid weighed 1.14 g. The basic filtrate yielded 0.06 g. of solid on acidification.

The crude sulfones were subjected to infrared analysis. No isomerization of *o*-chlorophenyl phenyl sulfone was detected in a control experiment. Of the isomeric methoxyphenyl phenyl sulfones, only the *para* compound was synthesized for purposes of comparison. The data are recorded in Table III.

***o*-Chloro-*t*-butylbenzene.**—A solution of chlorine (71 g.) in carbon tetrachloride (2.9 l.) was added below 27° during 3 hr. with stirring to a mixture of purified 4-*t*-butylbenzoic acid (180 g.), concentrated sulfuric acid (1.5 l.), silver sulfate (156 g.), and water (150 ml.). The reaction mixture was then stirred for 3 hr. at 25°, added to water (5 l.), and filtered. After being washed with water, the carbon tetrachloride solution was evaporated on a steam bath under reduced pressure. The 3-chloro-4-*t*-butylbenzoic acid was crystallized repeatedly from ethanol–water to yield 98.3 g. (46%), m.p. 185–186°.

Anal. Calcd. for $C_{11}H_{13}ClO_2$: C, 62.2; H, 6.13; Cl, 16.7; neut. equiv., 212. Found: C, 62.3; H, 6.10; Cl, 17.2; neut. equiv., 211.

An intimate mixture of the acid (40 g.) and calcium oxide (80 g.) was heated to redness. The distillate was washed with dilute hydrochloric acid, dilute caustic, and water. Fractionation of the dried mixture gave a white liquid, 4.23 g. (13%), b.p. 97–98° (25 mm.), $n^{20}D$ 1.5200 (lit.[59] $n^{20}D$ 1.5203).

Anal. Calcd. for $C_{10}H_{13}Cl$: C, 71.21; H, 7.71; Cl, 21.08. Found: C, 71.09; H, 7.83; Cl, 21.00.

The infrared spectrum was identical with that reported[59] for *o*-chloro-*t*-butylbenzene prepared by another method. Gas chromatography (12 ft., 14% Apiezon L on Chromosorb P, 170°, helium flow rate at 90 ml./min.) gave the following retention times (min.) for the isomeric chloro-*t*-butylbenzenes: *ortho* (19.9), *meta* (19.7), and *para* (22.1).

Isopropyl- and *t*-Butylanisoles.—The purified phenol was methylated according to the procedure of Hiers and Hager.[60] The distilled product was shown to be pure by infrared and gas chromatographic analyses.

Chlorophenyl Phenyl Sulfones.—*o*-Chlorophenyl phenyl sulfone was prepared by the method of Kobrich,[61] m.p. 104.5–105.5° (lit.[61] m.p. 103.5–105°), and the corresponding *meta* isomer by an adaptation of the procedure of Truce and Amos,[62] m.p. 111.5–112° (lit.[63] m.p. 112.5°).

p-Chlorophenyl phenyl sulfone was synthesized as follows. A mixture of benzene (120 ml.), *p*-chlorobenzenesulfonyl chloride (0.20 mole), and aluminum chloride (0.20 mole) was stirred on a steam bath for 2 hr. After the addition of water, extraction was carried out with chloroform. Evaporation of the volatile material under reduced pressure gave a brown oil which was crystallized first from ethanol–water (1:1) and then several times from 95% ethanol, m.p. 93.5–94.5° (lit.[64] m.p. 94.5°).

Analytical Procedures. A. Gas Chromatography.—F & M 500 and Aerograph A-90-P2 gas chromatographs were used. The isomer distributions, calculated from the peak areas, represent the mean of at least three analyses. See Table XVII for conditions.

B. Infrared Spectroscopy.—Infrared analyses, used for those cases in which gas chromatography did not provide reliable results, were carried out in cyclohexane with a Beckman IR-7 or IR-8 spectrophotometer. The characteristic regions (μ)

(59) M. Lerer and C. Fabre, *Bull. soc. chim. France*, 198 (1956).

(60) G. S. Hiers and F. D. Hager, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 58.

(61) G. Kobrich, *Ber.*, **92**, 2981 (1959).

(62) W. E. Truce and M. F. Amos, *J. Am. Chem. Soc.*, **73**, 3013 (1951).

(63) R. Passerini, *Boll. Sci. fac. chim. ind. Bologna*, **9**, 1 (1951); *Chem. Abstr.*, **45**, 10210 (1951).

(64) R. Joly, R. Bucourt, and J. Mathlieu, *Rec. trav. chim.*, **78**, 527 (1959).

TABLE XVII
GAS CHROMATOGRAPHY CONDITIONS

Method	Column	Temp., °C.	He flow rate (ml./min.)
A1	Tritolyl phosphate (15%), 8 ft.	95	85
A2	Apiezon L (14%), 12 ft.	180	75
A3	Apiezon L (14%), 12 ft.	120	60
A4	Apiezon L (14%), 12 ft.	130	55
A5	Apiezon L (14%), 12 ft.	150	100
A6	Apiezon L (14%), 12 ft.	125	120
A7	Apiezon L (14%), 12 ft.	135	90
A8	DEGS (15%), 15 ft.	130	120
A9	*m*-Phenyl ether, 5-ring (15%), 12 ft.	140	120
A10	Apiezon L (14%), 12 ft.	110	120
A11	*m*-Phenyl ether, 5-ring (5%), 4 ft., and terephthalic acid–Carbowax (5% reacted), 4 ft.	150	80

used were *ortho*, 13.3–13.8; *meta*, 12.8–13.1; and *para*, 12.1–12.5. The determinations were made with products which were isolated by one of several methods: B1, gas chromatography (20% Apiezon L grease) (known mixtures of authentic materials were subjected to infrared analysis before and after collection in order to ascertain that the collection was essentially quantitative; the isomer distributions represent the mean of at least two collections and a minimum of three determinations for each sample); and B2, distillation (the isomer distributions represent the mean of at least three determinations on each of two distillations).

C. **Distillation.**—A large-scale run was carried out for each set of reaction conditions in order to determine the amount of distillation residue. After fractionation of the volatile products, the residue comprised <4% of the total product.

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A Quantitative Study of the Perkin Synthesis of α-Phenyl-*trans*-cinnamic Acid

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Quantitative product isolations were carried out on the triethylamine-catalyzed Perkin condensation of phenylacetic anhydride with benzaldehyde. A 96% recovery of purified major product, α-phenyl-*trans*-cinnamic acid (**1**), was possible. Variations of the yield of this product with reaction conditions led to an optimum procedure (96% yield) involving phenylacetic acid, acetic anhydride, and triethylamine in a 2:3:4 molar ratio reacting at 65° in benzaldehyde as a solvent. The amine was best added slowly as the reaction progressed. The results were consistent with a slow aldol-type condensation of phenylacetic anhydride with benzaldehyde followed by an irreversible, stereoselective dehydration promoted by anhydrides and catalyzed by the amine. The main competing reactions were Claisen condensations of the anhydrides. Self-condensation of phenylacetic anhydride gave varying yields of phenylacetic acid, 1,3-diphenyl-2-propanone (**2**), and the enol phenylacetate of **2**.

In an earlier investigation[1] it was suggested on the basis of kinetic results that the apparent condensation of phenylacetic acid with benzaldehyde in acetic anhydride was an aldol-type condensation of the mixed anhydride of acetic acid and phenylacetic acid with benzaldehyde. It was further implied that the benzylmethylene group of this mixed anhydride was more reactive to the base than was the methyl group so that the major product isolated from such a reaction is always α-phenylcinnamic acid (α,β-diphenylacrylic acid) rather than cinnamic acid. Because of the leveling effect of the acetic acid in the medium it appeared that the only effective basic catalyst was acetate ion whether a tertiary amine or an acetate salt was added initially as the catalyst.

A similar conclusion concerning the nature of the Perkin condensation can be drawn from the kinetic study reported[2] for the amine-catalyzed condensation of benzaldehydes with acetic anhydride in kerosine. Of course no comparison of the relative reactivity of benzyl groups and methyl groups could be made in this case. Also no test was made of the possibility that the catalytic activity of the amine could be lessened by the acid formed during the reaction. Essentially only initial rates were studied.

Admittedly the reaction is more complex than was assumed originally.[1] Product-isolation experiments[1,3] led to only about 60% yield of pure α-phenyl-*trans*-cinnamic acid (*cis*-α,β-diphenylacrylic acid, **1**), m.p. 172–173°. Other investigators,[4–6] using amine-catalyzed condensations under conditions vigorous enough to cause some isomerization[5,6] to α-phenyl-*cis*-cinnamic acid (*trans*-α,β-diphenylacrylic acid), m.p. 138–139°, isolated this acid as a by-product. Also from these condensations *trans*-stilbene has often been isolated.[4] The possibility of Claisen-type self-condensations of the anhydride to give 1,3-diphenyl-2-propanone (**2**) as a side reaction to the Perkin condensation has also been demonstrated[7] with a carboxylate ion as a catalyst.

The best isolated yields (92–95%) of α-phenyl-*trans*-cinnamic acid (**1**) were reported[6] for the stereoselective dehydration of either *erythro*- or *threo*-2,3-diphenylhydracrylic acid in a mixture of boiling acetic anhydride and triethylamine for 35 min. Under the same conditions the apparent Perkin condensation of phenylacetic acid with benzaldehyde gave an 83% yield of essentially pure **1**. It was also shown[6] that the hydroxy acids did not undergo any appreciable reversal of the aldol condensation. It was proposed[6] that the dehydration

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