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Electrophilic Aromatic Substitution. 12.[1] Kinetic Studies of the $TiCl_4$-Catalyzed Reactions of Benzyl Chloride, *p*-Xylyl Chloride, and *p*-Nitrobenzyl Chloride with Benzene and Anisole in Nitromethane and Dichloromethane

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Abstract: Through the use of vacuum line techniques, noncompetitive and competitive kinetic data have been obtained for the $TiCl_4$-catalyzed reactions of benzyl chloride and *p*-methyl- and *p*-nitrobenzyl chloride with anisole and with benzene in solvents nitromethane and dichloromethane. In solvent nitromethane, the rate law for both *p*-xylylation and benzylation is $R = k_3[\mathrm{TiCl_4}]_0{}^2[\mathrm{RCl}]$ and for *p*-nitrobenzylation $R = k_4[\mathrm{TiCl_4}]_0{}^2[\mathrm{RCl}][\mathrm{Arom}]$. Consistent with our earlier toluene results, *p*-xylylation and *p*-nitrobenzylation fit Brown's selectivity relationship (BSR) while benzylation with benzyl chloride does not. Arrhenius/Eyring values for the benzylation of anisole, $\Delta H^* = 52\ (\pm 8)$ kJ/mol and $\Delta S^* = -74\ (\pm 29)$ J/(deg mol), equal those for toluene, as required for zero-order arene dependence. In solvent dichloromethane the rate law for benzyl chloride benzylation of anisole is $R = k_3[\mathrm{TiCl_4}]_0[\mathrm{RCl}][\mathrm{anisole}]$ and for benzene $R = k_4[\mathrm{TiCl_4}]_0{}^2[\mathrm{RCl}][\mathrm{benzene}]$. The mechanism for the benzylation of benzene is different than that for anisole as evidenced by differing rate laws. Attempts to "force" a common mechanism by adding 2,4-dichloro-3,5,6-trimethylanisole were unsuccessful. It is likely that benzene and anisole are also benzylated through different mechanisms in a 50/50 anisole/benzene medium. Thus k_A/k_B ratios determined competitively in either medium may not be valid, i.e., may not be used to test the applicability of Brown's relationship. In dichloromethane the reactions of *p*-xylyl chloride with benzene and anisole follow the same rate law, $R = k_3[\mathrm{TiCl_4}]_0[\mathrm{RCl}][\mathrm{Arom}]$. Competitive *p*-xylylation runs yielded k_A/k_B ratios and anisole product isomer distributions that fit BSR, whereas noncompetitively determined k_A/k_B ratios do not. Noncompetitive k_A's were shown to be anomalously low due to $TiCl_4$–anisole complexation. All reactions fit BSR except benzylation with benzyl chloride in nitromethane; its mechanism is explained through Jencks' model of carbocation activity.

One of the unresolved fundamental questions of electrophilic aromatic substitution (EAS) reactions concerns the source of meta products. Is the increase in meta product percentage with increasing reactivity of the electrophile a kinetic condition as Brown has claimed or primarily a thermodynamic (isomerization) condition as Olah has argued? For example, our absolute rate data for the benzylation of benzene and toluene in nitromethane with various substituted benzyl halides[2] appear to fit Jencks' model of carbocation reactivity[3] better than Olah's π-complex model. Olah has responded[4] by suggesting that our and his meta isomer percentages for the *p*-nitrobenzyl chloride (PNBZ) reaction with toluene were increased by isomerization of the intermediate arenium ion. Since all our product isomer percentages were constant with time through the entire reaction,[5] Olah cannot prove his assertion. On the other hand, since some arenium ion intermediates of toluene do isomerize, it is also difficult to disprove.

A solution to this problem has been suggested. EAS reactions of anisole, in contrast to toluene, have received relatively little attention, although isomerization of anisole intermediates is *much* less pronounced than with toluene.[4]

The following kinetic studies of anisole alkylation have been reported. In 1960 Stock and Brown,[6] on the basis of six reactions, concluded that the substitution of anisole followed a linear free energy relationship. When data were plotted in the form of Brown's selectivity relationship (BSR) (log $p_f^{\mathrm{OMe}} = b^{\mathrm{OMe}}\log(p_f^{\mathrm{OMe}}/m_f^{\mathrm{OMe}})$), the slope of the resulting straight line, b^{OMe}, was found to be 0.89 ± 0.03. Kovacic and Hiller[7] found anomalously high ortho/para ≥ 1.0 for $AlCl_3$-catalyzed methylation, isopropylation, and *tert*-butylation of anisole in nitromethane. These results were attributed to initial O-alkylation followed by intramolecular isomerization primarily to the ortho position. Stang and Anderson[8] postulated separate steps for substrate and positional selectivity to account for vinyl triflate alkylation results with anisole. Their work finds support from Olah[4] who, while calling into question Kovacic's "linear coordination effect", reports that the $TiCl_4$-catalyzed benzylation of anisole and benzene with substituted benzyl chlorides does not fit a linear free energy relationship. In fact, Olah's competitively determined k_A/k_B values and product isomer percentages are all *very* different from those predicted by BSR. Olah's conclusion was that "No simple selectivity-reactivity relationship is apparent in the studied alkylations as was the case in previously studied nitrations and other substitutions as substrate and positional selectivities are determined in separate steps."[4] But is his study conclusive? Competitive data are valid only if both aromatic species, benzene and anisole, follow the same mechanism. This was not determined, nor could it be by the competitive method. Thus, it seemed appropriate to attempt to obtain absolute (noncompetitive) kinetic data on these reactions through the use of vacuum line techniques developed earlier.[2]

Experimental Section

Materials. Purification, drying, apportionment procedures, and purity analyses have been published for $TiCl_4$,[9] benzene,[9] benzyl chloride,[9]

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(1) Electrophilic Aromatic Substitution. 11. DeHaan, F. P.; Chan, W. H.; Chen, D. W.; Ferrara, D. M.; Giggy, C. L.; Pinkerton, M. J. *J. Org. Chem.* **1989**, *54*, 1206–1209.

(2) DeHaan, F. P.; Delker, G. L.; Covey, W. D.; Ahn, J.; Anisman, M. S.; Brehm, E. C.; Chang, J.; Chicz, R. M.; Cowan, R. L.; Ferrara, D. M.; Fong, C. H.; Harper, J. D.; Irani, C. D.; Kim, J. Y.; Meinhold, R. W.; Miller, K. D.; Roberts, M. P.; Stoler, E. M.; Suh, Y. J.; Tang, M.; Williams, E. L. *J. Am. Chem. Soc.* **1984**, *106*, 7038–7046.

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(5) For further discussion of the likelihood of *p*-nitrobenzyl group migration, the reader is referred to ref 2.

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Table I. Initial Rates and Rate Constants for the $TiCl_4$-Catalyzed Reaction of Benzyl Chloride and Anisole in Nitromethane

temp, °C	[anisole], M	$[PhCH_2Cl]$, M	$[TiCl_4]$, M	init rate × 10^5, M s^{-1}	init rate/ $[cat]_0^2[hal]_0$	10^4k_1, s^{-1}	$k_1/[TiCl_4]_0^2$, M^{-2} s^{-1}	$k_1/$ $[TiCl_4]_0^2[arom]_0$, M^{-3} s^{-1}
25	0.2040	0.0161	0.0341	1.36 ± 0.14[a]	0.73 ± 0.07[a]	7.73 ± 0.31[a]	0.66 ± 0.03[a]	3.3 ± 0.1[a]
	0.1875	0.0114	0.0313	1.13 ± 0.10	1.0 ± 0.1	9.38 ± 0.18	0.957 ± 0.018	5.1 ± 0.9
	0.1850	0.0139	0.0594	4.1 ± 1.3	0.84 ± 0.23	27 ± 2	0.77 ± 0.06	4.1 ± 0.3
	0.3302	0.0146	0.0374	1.6 ± 0.2	0.78 ± 0.09	12.4 ± 0.6	0.89 ± 0.04	2.7 ± 0.1
	0.4636	0.0143	0.0379	1.20 ± 0.07	0.58 ± 0.03	8.3 ± 0.1	0.58 ± 0.01	1.24 ± 0.01
				av ± SD[b]	0.78 ± 0.15 19.2%		0.77 ± 0.16[c] 20.8%	3.3 ± 1.5 45.5%
0	0.4076	0.0169	0.0579				0.094 ± 0.001	
10	0.4039	0.0154	0.0374				0.175 ± 0.004	
40	0.3789	0.0159	0.0343				1.74 ± 0.01	

[a] ±95% confidence limits. [b] Standard deviation. [c] Rate constant for corresponding benzylation of benzene at 25 °C, $k_1/[cat]_0^2 = 0.24$ M^{-2} s^{-1}, determined using linear regression analysis of benzylation data at 20, 30, 40, and 55 °C.

Table II. Competitively Determined Rate Constant Ratios and Product Isomer Percentages for the $TiCl_4$-Catalyzed Benzylation of Anisole and Benzene in Nitromethane

$XC_6H_4CH_2Cl$	k_A/k_B	% ortho	% meta	% para	b[a]
H	3.2 ± 0.3[b]	54.2 ± 0.6[b]	0.3 ± 0.1[b]	45.5 ± 0.6[b]	0.38
p-CH_3	72 ± 6	42.1 ± 0.9	0.11 ± 0.02	57.8 ± 0.9	0.80
p-NO_2	7.4 ± 0.2	39.5 ± 1.3	2.8 ± 0.8	57.7 ± 1.2	0.87

[a] Calculated slope for the Brown selectivity relationship. [b] Standard deviation.

Table III. Competitively Determined Rate Constant Ratios and Product Isomer Percentages for the Benzylation of Toluene and Benzene in Nitromethane[a]

$XC_6H_4CH_2Cl$	catalyst	k_T/k_B	% ortho	% meta	% para	b
H	$TiCl_4$	2.3 ± 0.4	46.2 ± 0.5	6.0 ± 0.6	47.7 ± 0.8	0.68
p-CH_3	$TiCl_4$	40.2 ± 1.6	27.2 ± 0.2	1.9 ± 0.3	70.9 ± 0.4	1.2
p-NO_2	$AlCl_3$	2.5 ± 0.1	43.6 ± 0.7	21.5 ± 1.2	34.9 ± 0.8	1.4

[a] Reference 2.

$AlCl_3$,[10] nitromethane,[10] and p-xylyl chloride.[2] p-Nitrobenzyl chloride (PNBZ) was recrystallized from petroleum ether and then found to be 99.7% pure via capillary GC analysis. Internal standard o-dichlorobenzene (99.75% purity, GC) was vacuum distilled after a 24-h drying time with CaH_2. Solvent dichloromethane was dried 48 h with CaH_2, then vacuum distilled, and poured under vacuum into the usual solvent tubes. Its purity was 99.85% (GC), and its water content was <0.001 M (Poropak Q column–thermal conductivity detector). Aldrich anhydrous anisole (99.96% purity, GC) was used without further purification.

GC product peak retention times were matched with those of authentic samples or were matched by the process of elimination. For example, the retention time of the meta product in p-xylylation of anisole was determined from the products of the 3-methoxybenzyl chloride reaction with toluene. GC response curves were calculated from data obtained with known mixtures of internal standard and benzylation product.

Eight grams of 2,4-dichloro-3,5,6-trimethylanisole was synthesized by stirring and refluxing 11 g of the parent phenol (Aldrich) with 8 g of dry K_2CO_3 and 5 mL of CH_3I in 270 mL of acetone for 24 h.[11] After refluxing, a TLC plate was developed with 12/1 hexane/ethyl acetate. The solute was filtered and the solvent rotoevaporated. The yellow-white crystals were dissolved in hexane and then extracted with 5% NaOH solution to remove unreacted phenol. The solute was dried with $MgSO_4$ and run through a silica gel plug to remove the yellow color. Hexane served as eluent. The solvent was rotoevaporated, leaving white crystals of product, mp 75–76 °C. Purity was established by capillary GC and ^1H NMR (200 MHz): δ 2.25 (s, 3 H, CH_3Ar), 2.31 (s, 3 H, CH_3Ar), 2.46 (s, 3 H, CH_3Ar), 3.74 (s, 3 H, OCH_3). Solutions of this compound in CH_2Cl_2 were prepared in the same manner as those for PNBZ (vide infra).

Kinetic Procedures. Published procedures[2,9] were followed in all cases. PNBZ solution preparation procedures have been given earlier.[2] Reaction mixture aliquots were removed with syringes preequilibrated to reaction temperature. Reactions in nitromethane and in dichloromethane were quenched with saturated NaCl solution and distilled water, respectively.

Gas Chromatographic Analysis. GC conditions: column, 25-m methyl silicone; oven temperature program, 150 °C for 5 min, 30 °C/min to final 190 °C; injection port temperature, 300 °C; detector temperature, 250 °C; He carrier gas flow, 22 cm/s. Typical retention times (min) are as follows. Benzyl chloride reactions: o-dichlorobenzene, 4.6; diphenylmethane, 8.8; anisole products, ortho 12.6, meta 13.5, para 14.1. p-Xylyl chloride reactions: 4-methyldiphenylmethane, 10.6; anisole products, ortho 15.4, meta 16.9, para 17.6. PNBZ reactions were analyzed with a 10-m cross-linked methyl silicone column: oven temperature program, 100 °C for 1.75 min, 30 °C/min to final value of 200 °C; injection port temperature, 375 °C (Supelco Pyrosep S-1 Septa); detector temperature, 350 °C; He carrier gas flow, 22 cm/s. Retention times (min) for PNBZ reactions: o-dichlorobenzene, 2.5; p-nitrodiphenylmethane, 8.9; anisole products, ortho 12.5, meta 13.6, para 14.5.

Kinetic Results in Solvent Nitromethane

Benzylation with Benzyl Chloride. A logical place to begin our study was the $TiCl_4$-catalyzed reaction of benzyl chloride with anisole in solvent nitromethane. We have already reported both noncompetitive and competitive results for the $TiCl_4$-catalyzed benzylation of benzene and toluene in this solvent.[2]

The addition of anisole to a yellow solution of $TiCl_4$ in nitromethane produced an amber color. When a small amount of benzyl chloride was then added, the homogeneous solution slowly darkened. The anticipated faster reaction with the more reactive arene did not occur; the reaction proceeded at a speed comparable to that of benzene and toluene.[2] This is consistent with the rate law (Table I)

$$\text{rate} = k_3[TiCl_4]_0^2[PhCH_2Cl] \qquad (1)$$

which shows no arene dependence.

Product isomer percentages [ortho, 52.8 ± 0.3; meta, 0.3 ± 0.1; para, 46.9 ± 0.3 (±SD)] remained constant throughout each run and from run to run.

From anisole benzylation absolute rate data at 0, 10, 25, and 40 °C (Table I) Arrhenius/Eyring parameters were calculated from regression analysis of a plot of $k_1/[TiCl_4]_0^2$ vs $^1/T$ (r(coef)

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Table IV. Rate Constants for the $TiCl_4$-Catalyzed Reaction of *p*-Xylyl Chloride with Benzene and Anisole in Nitromethane at 0 °C

$[C_6H_6]$, M	[anisole], M	[*p*-XyCl], M	$[TiCl_4]$, M	10^3k_1, s^{-1}	$k_1/[TiCl_4]_0 \times 10$, $M^{-1}\ s^{-1}$	$k_1/[TiCl_4]_0^2$, $M^{-2}\ s^{-1}$	$k_1/[TiCl_4]_0[arom]_0$, $M^{-2}\ s^{-1}$	$k_1[TiCl_4]_0^2[arom]_0$, $M^{-3}\ s^{-1}$
0.3872		0.0321	0.0336	3.9 ± 1.3	1.2 ± 0.4	3.5 ± 1.2	0.30 ± 0.10	8.9 ± 3.0
0.2127		0.0155	0.0295	3.7 ± 0.4	1.3 ± 0.1	4.3 ± 0.5	0.59 ± 0.06	20 ± 2
0.6034		0.0200	0.0230	2.7 ± 0.2	1.2 ± 0.1	5.1 ± 0.4	0.19 ± 0.01	8.5 ± 0.6
0.5868		0.0226	0.0458	12 ± 3	2.6 ± 0.6	5.7 ± 1.4	0.45 ± 0.11	9.7 ± 2.4
				av ± SD	1.6 ± 0.7	4.6 ± 1.0	0.38 ± 0.17	11.8 ± 5.5
	0.2944	0.0137	0.0488	26.4 ± 2.0	5.4 ± 0.4	11.1 ± 0.8	1.84 ± 0.14	37.7 ± 2.85
	0.5221	0.0133	0.0238	5.8 ± 0.5	2.4 ± 0.2	10.2 ± 0.9	0.47 ± 0.04	19.6 ± 1.7
	0.1061	0.0148	0.0329	11.4 ± 0.4	3.4 ± 0.1	10.5 ± 0.4	3.3 ± 0.1	92.3 ± 3.5
				av ± SD	3.7 ± 1.5	10.6 ± 0.5	1.9 ± 1.4	49.9 ± 38.8
					40.5%	4.72%	73.7%	77.8%

Table V. Initial Rates and Rate Constants for the $TiCl_4$-Catalyzed Reaction of *p*-Nitrobenzyl Chloride with Anisole and Benzene in Nitromethane

temp, °C	$[C_6H_6]$, M	[anisole], M	[PNBZ], M	$[TiCl_4]$, M	init rates × 10^8, M s^{-1}	init rates/ $[cat]_0^2[hal]_0[arom]_0 \times 10^5$, $M^{-3}\ s^{-1}$	$k_1 \times 10^7$, s^{-1}	$k_1/[cat]_0^2 \times 10^5$, $M^{-1}\ s^{-1}$	$k_1/[cat]_0^2[arom]_0 \times 10^5$, $M^{-3}\ s^{-1}$
45		0.5494	0.0570	0.1103	1.1 ± 0.1	2.9 ± 0.3	1.9 ± 0.2	1.6 ± 0.2	2.8 ± 0.3
		0.9044	0.0598	0.2392	7.55 ± 0.03	2.45 ± 0.01	12.7 ± 0.5	2.22 ± 0.02	2.45 ± 0.01
		0.4676	0.0485	0.1749	1.97 ± 0.10	2.84 ± 0.14	4.08 ± 0.21	1.33 ± 0.01	2.85 ± 0.01
					av ± SD	2.73 ± 0.24		1.72 ± 0.46	2.70 ± 0.22
								26.7%	8.15%
30		0.4756	0.0684	0.1527			0.80 ± 0.16		0.73 ± 0.14
60		0.4524	0.0651	0.1538			8.1 ± 0.6		7.6 ± 0.6
45	0.6953		0.0901	0.2890	7.0 ± 0.5	1.3 ± 0.1	7.8 ± 0.5	0.93 ± 0.06	1.34 ± 0.09
	0.5984		0.0841	0.3065	8.9 ± 0.9	1.9 ± 0.2	10.1 ± 0.1	1.1 ± 0.1	1.8 ± 0.1
	0.4516		0.0637	0.3162	5.8 ± 0.2	2.0 ± 0.1	9.1 ± 0.3	0.9 ± 0.1	2.0 ± 0.1
	0.2703		0.0949	0.1759	2.9 ± 0.2	3.7 ± 0.3	3.1 ± 0.2	1.0 ± 0.1	3.7 ± 0.2
	0.2698[a]		0.0871	0.1642	1.4 ± 0.1	2.2 ± 0.2	1.6 ± 0.1	0.58 ± 0.04	2.1 ± 0.1
	0.4291[b]		0.0939	0.0953	0.83 ± 0.02	2.28 ± 0.06	0.89 ± 0.02	0.98 ± 0.02	2.28 ± 0.05
30	0.4681		0.0710	0.2309			1.11 ± 0.03		0.44 ± 0.01
60	0.4683		0.0609	0.1233			5.0 ± 0.1		7.0 ± 0.1

[a] Solution was also 0.2819 M in cyclohexane to maintain concentration of nonpolar species. [b] Solution was also 0.2155 M in cyclohexane.

= −0.994): $E_a = 54 \pm 9$ kJ/mol, $\Delta H^\ddagger = 52 \pm 8$ kJ/mol, $\Delta G^\ddagger = 73.6 \pm 0.4$ kJ/mol, $\Delta S^\ddagger = -74 \pm 29$ J/(mol deg) (±SD).

Since both the $TiCl_4$-catalyzed benzylation of anisole and of benzene[2] in nitromethane are zero order in arene, the competitive method was used to determine a meaningful anisole/benzene (k_A/k_B) rate constant ratio. This is reported in Table II. Competitively determined product isomer percentages are also given; these remained constant throughout the run and agree with the noncompetitive values.

Benzylation with *p*-Methylbenzyl Chloride (*p*-Xylyl Chloride). One of the substituted benzyl halides examined by Olah is *p*-xylyl chloride.[4] Since we already had absolute kinetic data for the $TiCl_4$-catalyzed reaction of *p*-xylyl chloride with benzene in nitromethane,[2] it seemed appropriate to make a kinetic study of the same system with anisole.

Although the $TiCl_4$-catalyzed reaction of *p*-xylyl chloride with anisole in nitromethane at 0 °C is too fast for an initial rates study, i.e., approximately 70% completion in 100 s, pseudo-first-order plots with respect to *p*-xylyl chloride were linear (≥0.997 linear correlation coefficient). These data (Table IV) fit the rate law

$$\text{rate} = k_3[TiCl_4]_0^2[p\text{-xylyl chloride}] \qquad (2)$$

Unlike the analogous reaction with toluene,[2] no secondary products were seen. Meta product peaks were very small even at the end of a reaction. After it was established that product isomer percentages were independent of GC syringe injections in the 1–10-μL range, product percentages were determined via 8-μL injections of quenched aliquots taken at long reaction times. The percentages are as follows: ortho, 42.6 ± 0.9; meta, 0.10 ± 0.02; para, 57.3 ± 0.9. On the basis of the constancy of the ortho and para peak ratio with time, as well as the low meta percentage at long times, it is safe to say isomerization is not complicating the data.

Competitive data were also obtained and are reported in Table II. Again ortho and para product GC peak areas maintained a constant relationship, with the meta percentage determined through 8-μL GC injections of longer reaction time samples.

Benzylation with *p*-Nitrobenzyl Chloride. Since *p*-nitrobenzyl chloride is a weak benzylating agent and since results with $AlCl_3$ and benzene in nitromethane had already been obtained,[2] we chose to study the analogous reaction with anisole. The results suggested the reaction with anisole was first order in *p*-nitrobenzyl chloride and in $AlCl_3$ as catalyst but zero order in anisole. This seemed odd since our earlier study[2] involving PNBZ, $AlCl_3$, and toluene had shown a definite first-order arene dependence. Anisole, being more reactive than toluene, should also be involved in the rate law. The unusual zero-order anisole dependence appears to be due to offsetting factors: the reaction is first order in anisole as reagent, as expected, but inversely first order in anisole through methoxy oxygen complexation of $AlCl_3$. Small amounts of phenol and phenol benzylation products were seen on chromatograms. Apparently even in the presence of solvent nitromethane, some $AlCl_3$ complexes with anisole's methoxy oxygen and to some degree converts anisole to phenol.[12] When a nitromethane solution containing anisole and $AlCl_3$ of comparable concentration to our reaction mixtures was analyzed over typical time intervals, approximately 3–4% of the anisole was converted to phenol. Although only a small amount of phenol was produced, it is likely that a considerable percentage of the catalyst was being deactivated.

To avoid such complications, an anisole solution in nitromethane containing the milder catalyst $TiCl_4$ was tested. Some cleavage did occur at late reaction times, but the amount of phenol produced was insignificant. However, the possibility still existed that $TiCl_4$ would be deactivated, to a certain extent, by complexation with anisole's methoxy oxygen.

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(12) The literature supports this hypothesis. For example see: Johnson, F. *Friedel–Crafts and Related Reactions*; Olah, G. A., Ed.; Interscience: New York, 1963; Vol. IV, p 5ff.

Table VI. Absolute Rate Data for Friedel–Crafts Benzylation Reactions in Nitromethane

$XC_6H_4CH_2Cl$	arene	catalyst	$\Delta H^{\ddagger}$, kJ/mol	$\Delta S^{\ddagger}$, J/(deg mol)
p-NO_2	benzene	$AlCl_3$[a]	71 ± 15[b]	−85 ± 46[b]
	benzene	$TiCl_4$	70 ± 20	−100 ± 70
	anisole	$TiCl_4$	60 ± 20	−140 ± 50
p-CH_3	benzene	$TiCl_4$[a]	52 ± 8	−41 ± 32
H	benzene	$TiCl_4$[a]	53 ± 11	−78 ± 35
	anisole	$TiCl_4$	52 ± 8	−74 ± 29

[a] Reference 2. [b] Standard deviation.

As can be seen from Table V, our results with anisole and $TiCl_4$ are excellent. Both, initial rates and pseudo-first-order plots (first order with respect to PNBZ) indicate the following rate law:

$$\text{rate} = k_4[TiCl_4]_0{}^2[\text{PNBZ}][\text{anisole}] \tag{3}$$

Instinctively, we would expect benzene to react through the same mechanism. However, our benzene data (Table V) seem to be very inconsistent. Apparently we are observing a dielectric effect. The intermediate electrophile in this reaction is probably a polar catalyst–PNBZ complex. The aromatic molecule displaces chlorine in an S_N2 manner, and substitution occurs. However, with increased concentrations of nonpolar benzene in the polar solvent mixture, the dielectric constant or polarity of the solution is changed. This occurred in the $AlCl_3$-catalyzed reaction of PNBZ with benzene and toluene in nitromethane[2] but was less pronounced due to the speed of those reactions. With *p*-nitrobenzyl chloride and benzene, the reaction is slow enough that the slight dielectric change is significant. As can be seen from Table V, reactions in which the benzene concentrations were high went slower than reactions in which the benzene concentrations were low.

The best illustration of this effect is shown by the fourth and fifth benzene reactions at 45 °C (Table V). The reagent amounts are almost identical except that the last reaction mixture was 0.2819 M in cyclohexane along with being 0.2698 M in benzene. Cyclohexane, while not directly involved in the reaction, does serve to decrease the dielectric constant of the reaction mixture. As expected, the reaction containing cyclohexane was much slower. Thus only reactions having comparable total concentrations of nonpolar species should be compared; when they are, it is evident that both benzene and anisole follow the same rate law (3).

Competitive rate data from the $TiCl_4$-catalyzed *p*-nitrobenzylation of benzene and anisole in nitromethane are given in Table II. Product isomer percentages remained constant throughout the run and are in good agreement with those obtained from absolute rate data: ortho, 37.2 ± 0.6%; meta, 3.1 ± 0.5%; para, 59.8 ± 0.3%. These also remained constant during runs and from run to run.

Arrhenius/Eyring values were calculated for both benzene and anisole *p*-nitrobenzylation reactions. For the benzene reaction the slope and intercept of a ln $(k_1/[TiCl_4]_0{}^2[\text{benzene}]_0)$ vs $^1/T$ plot (r(coef) = −0.999) produced $E_a = 80 \pm 20$ kJ/mol, $\Delta H^{\ddagger} = 70 \pm 20$ kJ/mol, $\Delta G^{\ddagger} = 106.8 \pm 0.1$ kJ/mol, and $\Delta S^{\ddagger} = -100 \pm 70$ J/(mol deg) (±SD). For anisole a similar plot (r(coef) = −0.999) yielded $E_a = 60 \pm 16$ kJ/mol, $\Delta H^{\ddagger} = 60 \pm 20$ kJ/mol, $\Delta G^{\ddagger} = 106.1 \pm 0.3$ kJ/mol, and $\Delta S^{\ddagger} = -140 \pm 50$ J/(mol deg) (±SD). These data are summarized in Table VI.

Kinetic Results in Solvent Dichloromethane

In nitromethane, electrophile formation is rate-determining for the $TiCl_4$-catalyzed benzylation and *p*-xylylation of anisole and benzene. It seemed appropriate to examine these reactions kinetically in a less polar solvent with a smaller donor number[13] for two reasons: First, this would more closely approximate Olah's solvent, a 50/50 mixture of anisole and benzene.[4] Second, carbocation intermediates would be more weakly solvated in such a solvent. If the rates of such reactions were to be dependent upon the arene, we would test Brown's selectivity relationship (BSR) under very different mechanistic conditions. Dichloromethane seemed a reasonable choice. However, since the literature contains reports of it undergoing alkylation reactions under Friedel–Crafts conditions, $TiCl_4$–anisole and $TiCl_4$–benzene mixtures in CH_2Cl_2 were tested for reaction at typical reaction temperatures and times. None were observed.

Benzylation with Benzyl Chloride. The $TiCl_4$-catalyzed reactions of benzyl chloride with either benzene or anisole proceeded homogeneously in dichloromethane. However, the data, Table VII, for benzene benzylation were complicated by two factors: when the benzene concentration was doubled to a value above 0.7 M while the $TiCl_4$ and benzyl chloride concentrations were kept essentially constant, the reaction slowed down. This was unexpected, since a reaction first or zero order in benzene should have either sped up or remained the same. Substitution of cyclohexane for the added benzene (last benzene run, Table VII) produced the same effect—apparently solvent dielectric or polarity effects are involved at higher benzene concentrations.[14]

We obtained other inexplicable results when the $TiCl_4$ concentration was quadrupled (next to the last benzene run, Table VII). We speculated that water in the reaction mixture was responsible for this behavior, since the addition of small amounts of water can markedly affect reaction rates.[15] However, similar results were obtained when the reaction was repeated. It is expected that dichloromethane would complex $TiCl_4$ to a much smaller extent than nitromethane. It follows that large amounts of $TiCl_4$ (well above benzyl chloride concentrations) not effectively complexed by the solvent might cause products to disproportionate to secondary products and benzene. Thus, the seemingly lower rate of reaction. All runs to date were reexamined; only those with quadruple $TiCl_4$ concentrations showed appreciable secondary products at longer retention times. These runs were not included in rate law and rate constant determinations.

When reagent concentrations were varied within the limits defined by these two factors, the $TiCl_4$-catalyzed reaction of benzyl chloride with benzene in dichloromethane, the rate data, Table VII, and initial rates data, Table VIII, support the rate law

$$\text{rate} = k_4[TiCl_4]_0{}^2[PhCH_2Cl][C_6H_6] \tag{4}$$

When anisole was added to a colorless solution of $TiCl_4$ in CH_2Cl_2 the solution turned orange–brown (rather than the yellow to yellow-orange color produced by benzene). Again all reactions were homogeneous and readily followable at 25 °C. Both regular and initial rates data, Tables VII and VIII, support a *different* rate law for $TiCl_4$-catalyzed anisole benzylation:

$$\text{rate} = k_3[TiCl_4]_0[PhCH_2Cl][\text{anisole}] \tag{5}$$

Ortho and para product isomer percentages showed no upward or downward trend during or between runs. The meta GC peak was integrable only for 10-μL injections of "infinity" (next day) samples. The overall averages with standard deviations are as follows: ortho, 51.4 ± 0.9%; meta, 0.12 ± 0.02%; para, 48.5 ± 0.9%.

Because the $TiCl_4$-catalyzed reactions of benzyl chloride with anisole and benzene follow different rate laws, and therefore mechanisms, in dichloromethane, neither absolute nor competitive rate data may be used to test Brown's relationship. Our FT-NMR spectra clearly show complexation between $TiCl_4$ and anisole's methoxy oxygen in dichloromethane (with no $TiCl_4$–CH_2Cl_2 interaction seen when anisole is present). Since this O-complexation cannot be present in benzene benzylation, we undertook a kinetic study of the $TiCl_4$-catalyzed reaction of benzyl chloride with benzene in CH_2Cl_2 in the presence of 2,4-dichloro-3,5,6-tri-

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(13) Although the donor number of dichloromethane is low and probably comparable to that of 1,2-dichloroethane, weak Lewis base behavior is often observed: Gutmann, V. *Coordination Chemistry in Non-aqueous Solvents*; Springer-Verlag: New York, 1968; p 127. For example see: Fernandez, J. M.; Gladys, J. A. *Organometallics* **1989**, *8*, 207–219.

(14) For similar effects on Friedel–Crafts isopropylations, see: DeHaan, F. P.; Delker, G. L.; Covey, W. D.; Ahn, J.; Cowan, R. L.; Fong, C. H.; Kim, G. Y.; Kumar, A.; Roberts, M. P.; Schubert, D. M.; Stoler, E. M.; Suh, Y. J.; Tang, M. *J. Org. Chem.* **1986**, *51*, 1587–1590.

(15) See ref 2, particularly footnote 24.

Table VII. Rate Constants for the $TiCl_4$-Catalyzed Reaction of Benzyl Chloride with Benzene and Anisole in Dichloromethane at 25 °C

$[C_6H_6]$, M	$[CH_3OC_6H_5]$, M	$[PhCH_2Cl]$, M	$[TiCl_4]$, M	$k_1 \times 10^5$, s^{-1}	$k_1/[cat]_0[arom]_0 \times 10^3$, $M^{-2}\,s^{-1}$	$k_1/[cat]_0^2[arom]_0 \times 10^3$, $M^{-3}\,s^{-1}$
0.4640		0.0442	0.0490	0.84 ± 0.07[a]	0.37 ± 0.03[a]	7.6 ± 0.6[a]
0.4231		0.0420	0.1038	2.96 ± 0.09	0.67 ± 0.02	6.5 ± 0.2
0.2801		0.0204	0.0656	0.933 ± 0.008	0.508 ± 0.004	7.74 ± 0.07
0.6121		0.0391	0.0550	1.85 ± 0.06	0.55 ± 0.02	10.0 ± 0.3
0.1851		0.0143	0.0473	0.37 ± 0.01	0.42 ± 0.01	8.9 ± 0.2
0.3460		0.0316	0.0317	0.36 ± 0.01	0.32 ± 0.01	10.2 ± 0.3
0.2406		0.0148	0.0438	0.38 ± 0.01	0.36 ± 0.01	8.2 ± 0.2
0.5156		0.0565	0.0262	0.220 ± 0.007	1.63 ± 0.05	6.2 ± 0.2
0.4717		0.0439	0.2084	(7.75 ± 0.01)	(0.789 ± 0.001)[b]	(3.783 ± 0.004)[b]
0.4156[c]		0.0397	0.0510	(0.50 ± 0.01)	(0.216 ± 0.004)[b]	(4.08 ± 0.08)[b]
				av ± SD	0.6 ± 0.4 (67%)	8.2 ± 1.5 (18%)
	0.3782	0.0365	0.0623	5.2 ± 0.6	2.2 ± 0.2	35 ± 4
	0.3457	0.0387	0.1266	1.6 ± 0.9	2.2 ± 1.2	17 ± 10
	0.7345	0.0396	0.0538	10.8 ± 0.4	2.7 ± 0.1	50 ± 2
	0.2157	0.0197	0.0653	2.4 ± 0.3	1.9 ± 0.2	29 ± 4
				av ± SD	2.3 ± 0.3 (13%)	33 ± 14 (42%)

[a] ±95% confidence limit. [b] Not included in average. [c] Solution was also 0.3785 M in cyclohexane.

Table VIII. Initial Rate Data for the $TiCl_4$-Catalyzed Reaction of Benzyl Chloride with Benzene and Anisole in Dichloromethane at 25 °C

$[C_6H_6]$, M	$[CH_3OC_6H_5]$, M	$[PhCH_2Cl]$, M	$[TiCl_4]$, M	init rate × 10^6, M s^{-1}	init rates/ $[cat]_0[hal]_0[arom]_0 \times 10^3$, $M^{-2}\,s^{-1}$	init rates/ $[cat]_0^2[hal]_0[arom]_0 \times 10^3$, $M^{-3}\,s^{-1}$
0.4640		0.0442	0.0490	0.38 ± 0.04[a]	0.36 ± 0.04[a]	7.7 ± 0.8[a]
0.4231		0.0420	0.1038	1.22 ± 0.04	0.66 ± 0.02	6.4 ± 0.2
0.2801		0.0204	0.0656	1.19 ± 0.05	0.64 ± 0.03	6.2 ± 0.3
0.6121		0.0391	0.0550	0.75 ± 0.02	0.56 ± 0.01	10.0 ± 0.3
0.1851		0.0143	0.0473	0.041 ± 0.004	0.33 ± 0.03	6.9 ± 0.7
0.3460		0.0316	0.0317	0.109 ± 0.004	0.30 ± 0.01	9.9 ± 0.4
0.2406		0.0148	0.0438	0.054 ± 0.002	0.35 ± 0.01	7.9 ± 0.3
0.5156		0.0565	0.0262	0.122 ± 0.004	0.160 ± 0.005	6.1 ± 0.2
0.4717		0.0439	0.2084	(3.2 ± 0.3)	(0.74 ± 0.06)[b]	(3.6 ± 0.3)[b]
0.4156[c]		0.0397	0.0510	(0.20 ± 0.01)	(0.24 ± 0.01)[b]	(4.7 ± 0.2)[b]
				av ± SD	0.42 ± 0.18	7.6 ± 1.6
	0.3782	0.0365	0.0623	1.8 ± 0.2	2.1 ± 0.2	33 ± 4
	0.3457	0.0387	0.1266	3.5 ± 0.3	2.1 ± 0.2	16 ± 2
	0.7345	0.0396	0.0538	3.4 ± 0.3	2.5 ± 0.2	46 ± 4
	0.2157	0.0197	0.0653	0.51 ± 0.6	1.8 ± 2.1	28 ± 33
				av ± SD	2.1 ± 0.3	31 ± 12

[a] ±95% confidence limit. [b] Not included in average. [c] Solution was also 0.3785 M in cyclohexane.

Table IX. Rate Constants for the $TiCl_4$-Catalyzed Reaction between Benzyl Chloride and Benzene in the Presence of 2,4-Dichloro-3,5,6-trimethylanisole in Dichloromethane at 25 °C

$[C_6H_6]$, M	$[PhCH_2Cl]$, M	$[TiCl_4]$, M	[subst anisole], M	$k_1 \times 10^5$, s^{-1}	$k_1/[cat]_0[arom]_0 \times 10^3$, $M^{-2}\,s^{-1}$	$k_1/[cat]_0^2[arom]_0 \times 10^3$, $M^{-3}\,s^{-1}$
0.4421	0.0387	0.0639	0.2256	0.71 ± 0.02[a]	0.251 ± 0.007[a]	3.9 ± 0.1[a]
0.8078	0.0386	0.0568	0.2330	1.08 ± 0.03	0.235 ± 0.006	4.1 ± 0.1
0.4285	0.0349	0.1003	0.2125	2.01 ± 0.06	0.47 ± 0.01	4.7 ± 0.1
0.1866	0.0460	0.0659	0.1177	0.33 ± 0.02	0.27 ± 0.02	4.1 ± 0.2
					av ± SD[b]	4.2 ± 0.3

[a] ±95% confidence limit. [b] Standard deviation.

methylanisole, after verifying via FT-NMR that the latter compound had comparable O-complexing ability to that of anisole.[16] As the data in Table IX show, the reaction slowed down as expected due to $TiCl_4$ complexation, but the rate law did not change.

Benzylation with *p*-Methylbenzyl Chloride (*p*-Xylyl Chloride). Absolute rate data for the $TiCl_4$-catalyzed reaction of *p*-xylyl chloride with benzene or anisole in solvent dichloromethane have been determined. Both reactions follow the same rate law.

$$\text{rate} = k_3[\text{TiCl}_4]_0[p\text{-xylyl chloride}][\text{arene}] \qquad (6)$$

The rate law for the anisole reaction was particularly difficult to determine. As was mentioned, in CH_2Cl_2 $TiCl_4$ complexes with the methoxy oxygen of anisole. As a consequence we found it necessary to vary the concentrations of $TiCl_4$ and of anisole within the context of an overall high [anisole]/[$TiCl_4$] ratio of 10–35/1. In this range the reaction is clearly first order in each component, Table X. In the ratio range 3–10/1 the reactions were faster because of the higher availability of the catalyst (for example see data for the last anisole reaction listed in Table X). One cannot simply compare runs with small and high ratios.

Product isomer percentages for anisole *p*-xylylation were constant during each run and from run to run. The overall averages [46.6 ± 0.3%, ortho; 0.18 ± 0.01%, meta; 53.2 ± 0.3%, para] were the same for noncompetitive and competitive runs. Table XI also lists noncompetitive and competitively determined k_A/k_B ratios.

Benzylation with *p*-Nitrobenzyl Chloride. The $TiCl_4$-catalyzed reaction between *p*-nitrobenzyl chloride and anisole is so slow in CH_2Cl_2 that after 10 d at 40 °C only 0.3% reaction was observed. When the reaction was repeated in *o*-dichlorobenzene at 55 °C

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[16] When anisole and 2,4-dichloro-3,5,6-trimethylanisole were present in CD_2Cl_2 with a much smaller amount of $TiCl_4$, the magnitudes of the methoxy methyl proton NMR peak shifts were directly proportional to the relative amounts of substituted and unsubstituted anisole.

Table X. Rate Constants for the $TiCl_4$-Catalyzed Reactions between *p*-Xylyl Chloride and Benzene or Anisole in Dichloromethane at 0 °C

$[C_6H_6]$, M	$[C_6H_5OCH_3]$, M	[*p*-XyCl], M	$[TiCl_4]$, M	$k_1 \times 10^4$, s^{-1}	$k_1/[cat]_0[arom]_0 \times 10^2$, $M^{-2}\,s^{-1}$
0.4236		0.0331	0.0592	4.1 ± 0.5[a]	1.6 ± 0.2[a]
0.8197		0.0348	0.0577	6.6 ± 0.1	1.39 ± 0.02
0.4440		0.0435	0.1278	7.6 ± 0.4	1.34 ± 0.07
0.2407		0.0440	0.0681	1.87 ± 0.06	1.14 ± 0.04
0.4595		0.0132	0.0386	2.0 ± 0.1	1.13 ± 0.06
				av ± SD[b]	1.3 ± 0.2
	0.2205	0.0171	0.0172	5.5 ± 0.2	14.5 ± 0.5
	0.4416	0.0165	0.0219	13.7 ± 0.3	14.2 ± 0.3
	0.2094	0.0135	0.0196	4.9 ± 0.2	12.0 ± 0.5
	0.7169	0.0369	0.0249	18.5 ± 0.7	10.4 ± 0.4
	0.4653	0.0441	0.0240	12.3 ± 0.1	11.01 ± 0.09
	0.4627	0.0544	0.0172	10.7 ± 0.3	13.4 ± 0.4
	1.2683	0.0500	0.0405	53 ± 3	10.3 ± 0.6
	0.2301	0.0178	0.0729	(47 ± 1)	(28.0 ± 0.6)[c]
				av ± SD	12.3 ± 1.8

[a] ±95% confidence limit. [b] Standard deviation. [c] Not included in average.

Table XI. Competitive and Noncompetitive Rate Constant Ratios and Product Isomer Distributions for the $TiCl_4$-Catalyzed Reaction of *p*-Xylyl Chloride and Anisole and Benzene in Dichloromethane at 0 °C

$XC_6H_4CH_2Cl$	X = CH_3
k_A/k_B	
noncomp	9.5 ± 2.8[b]
comp	89 ± 8[b]
% ortho	46.6 ± 0.3[b]
% meta	0.18 ± 0.01[b]
% para	53.2 ± 0.3[b]
b[a]	
noncomp	0.53
comp	0.89

[a] Calculated slope for the Brown selectivity relationship. [b] Standard deviation.

for 10 d, 1.1% reaction occurred. In addition phenol was produced in both instances as well as other "side" reaction products, the latter in amounts 4 times greater than normal products. Due to the extremely slow reaction time and the fact that larger amounts of undesirable side products were formed, this study was abandoned.

Discussion

Because of the strong correlation between rate constants and σ-complex stability of the arene being attacked in electrophilic substitution, it is commonly accepted that reactions whose data fit Brown's selectivity relationship involve a rate-determining transition state resembling a σ-complex that determines both the substrate and positional selectivity.[17] When substrate and positional selectivity do not correlate, it is equally plausible to assume a two-step mechanism that involves both π- and σ-complexes.[18] Although Brown and co-workers found some 60 reactions to fit a BSR plot,[17] many recent studies have suggested exceptions to BSR. However, when these reactions were reexamined via vacuum line methods, which minimize water effects, many were found to fit BSR. For example, ethylation in hexane,[19] benzylation in excess arene,[9] sulfonylation,[20] acylation,[10,20] formylation,[21] isopropylation,[14] and *tert*-butylation[22] all fit BSR although all were previously suggested to involve a π-complex-like highest energy transition state. However, there are valid exceptions to BSR: benzylation with benzyl chloride,[2,9] benzyl sulfonyl chlorides,[23] and *p*-chloro- and 3,4-dichlorobenzyl chlorides[2] in polar solvents. In an earlier paper[2] Jencks' explanation[3] of changes in selectivity with carbocation reactivity changes was suggested as an alternative to Olah's π-complex mechanism. Jencks' approach best explains the data and places electrophilic aromatic substitution in a more explicable, predictable, and broader context.

Kinetic Results in Solvent Nitromethane. Although Olah found no evidence for a selectivity–reactivity relationship in his study of the benzylation of anisole with various substituted benzyl chlorides,[4] our results strongly support a different conclusion. The fit or lack of fit to BSR is predictable and consistent with our toluene benzylation data and Jencks' model.

Just as in the case of toluene the rate law for both the benzylation and *p*-xylylation of anisole is

$$\text{rate} = k_3[TiCl_4]_0^2[RCl] \tag{7}$$

and for *p*-nitrobenzylation

$$\text{rate} = k_4[TiCl_4]_0^2[RCl][Arom] \tag{8}$$

In the case of benzylation with benzyl chloride, the formation of the electrophile is rate determining for toluene.[2] Zero-order arene dependence for more reactive anisole is expected and observed. The Arrhenius/Eyring values are also consistent. The calculated values of $\Delta H^{\ddagger} = 52 \pm 8$ kJ/mol and $\Delta S^{\ddagger} = -74 \pm 29$ J/(deg mol) for anisole are equal to those for toluene, Table VI, as they must be, since neither reaction shows arene rate dependence.

Neither competitive reaction of benzyl chloride with toluene/benzene or anisole/benzene fits BSR, Tables II and III. These results could be explained by Olah's model[4] of an "early" transition state resembling a π-complex. Alternatively, Jenck's model[2,3] suggests the loss in substrate selectivity (relative to the more stable *p*-xylylcarbenium ion, see below) could be due to the increased reactivity (decreased stability) of the benzyl cation, which may react at a rate approaching diffusion control[24] and thus would show

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(17) Stock, L. M.; Brown, H. C. *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic Press: New York, 1963; Vol. 1, pp 35–154. See also: Brown, H. C.; Wirkkala, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 1447–1452.

(18) For review, see: Olah, G. A. *Acc. Chem. Res.* **1971**, *4*, 240–248.

(19) Carter, B. J.; Covey, W. D.; DeHaan, F. P. *J. Am. Chem. Soc.* **1975**, *97*, 4783–4784.

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(23) Covey, W. D.; DeHaan, F. P.; Delker, G. L.; Dawson, S. F.; Kilpatrick, P. K.; Rattinger, G. B.; Read, W. G. *J. Org. Chem.* **1984**, *49*, 3967–3970.

(24) Dorfman et al. have used pulsed radiolysis to measure absolute rate constants for the reaction of the benzyl cation with halides, amines, and alcohols: Sujdak, R. J.; Jones, R. L.; Dorfman, L. M. *J. Am. Chem. Soc.* **1976**, *98*, 4875–4879. Rate constants range from 10^7 to 10^{11} $M^{-1}\,s^{-1}$, i.e., in or near the diffusion-controlled range, with values decreasing with increased size of the nucleophile. The benzyl cation–benzene reaction was not studied, but the data do suggest this reaction of two large species would occur at or near the diffusion-controlled limit. See also: Jaarinen, S.; Niiranen, J.; Koskikallio, J. *Int. J. Chem. Kinet.* **1985**, *17*, 925–930.

little selectivity. Since the presence of more reactive anisole would not affect the stability of the benzyl cation, a similar deviation from Brown's relationship is expected and observed.

As in the case of the $TiCl_4$-catalyzed *p*-xylylation of toluene,[2] the analogous reaction with anisole follows a rate law, eq 6, that shows no dependence on the aromatic reagent. Again, electrophile formation is rate determining in both instances. However, this electrophile, presumably the *p*-xylyl carbocation, is more stable, i.e., diffusionally equilibrated in Jencks' terminology, and shows considerably higher substrate selectivity than the benzyl moiety. As expected, competitively determined k_A/k_B and product isomer percentages yield a Brown slope *b* value of 0.80 (Table II), reasonably close to Brown's value of 0.89 for anisole substitution.[6] Since the same "diffusionally equilibrated" carbocation is involved, both toluene and anisole data should fit Brown's relationship, Tables II and III, and they do.

The results for $TiCl_4$-catalyzed reaction between *p*-nitrobenzyl chloride and anisole are consistent with those for *p*-nitrobenzylation of toluene.[2] Although different catalysts were used and different rate laws determined (eq 8 and 7[2]), both reactions are first order in arene and appear to follow a S_N2 displacement mechanism as evidenced by the arene rate order dependence and by $\Delta S^{\ddagger}$ values, Table VI. The calculated Brown slope values of 0.87 and 1.4 for anisole and toluene *p*-nitrobenzylation both fit Brown's relationship. Of particular relevance is the increased selectivity found in the *p*-nitrobenzylation of anisole. The increase in k_A/k_B from 2.5 for benzylation to 7.4 for *p*-nitrobenzylation is predicted by Jencks' approach.[2,3] To the extent the mechanism is truly S_N2, i.e., concerted, Olah's π-complex model may not apply. In any event it does not fit the data in that it predicts a further *drop* in substrate selectivity with the stronger electrophile. Olah's model would also not predict the *p*-nitrobenzylation reaction to fit BSR since a still stronger electrophile would produce an early transition state resembling a π-complex. Clearly, our anisole data are best explained by Jencks' model.

Finally, the low k_A/k_B ratio of 1.2 calculated from absolute rate constants is noted. A similar low noncompetitively determined k_T/k_B value was obtained for $AlCl_3$-catalyzed *p*-nitrobenzylation of toluene and of benzene.[2] The color change of the $TiCl_4$ solution upon anisole addition suggests ternary anisole–$TiCl_4$–nitromethane complexation, which may produce these low results. Such complexation might hinder the speed of the anisole reaction, thus lowering noncompetitively determined k_A/k_B, but might not affect k_A/k_B ratios obtained competitively, since both anisole and benzene reaction rates would be slowed by $TiCl_4$–anisole interaction.

Kinetic Results in Solvent Dichloromethane. Dichloromethane has proven to be an appropriate choice as a solvent with lower polarity and complexing ability than nitromethane. Besides being easier to purify and dry, it affords no solubility problems with $TiCl_4$-catalyzed benzylation reactions. However, the lack of strong complexation between $TiCl_4$ and CH_2Cl_2 (relative to $TiCl_4$ and nitromethane) often added kinetic complications not seen in results obtained with nitromethane. Others have observed these complications; Kobayashi and co-workers found the $AlCl_3$-catalyzed sulfonylation of anisole to be extremely slow in CH_2Cl_2.[25] Their attribution of this effect to anisole–$AlCl_3$ complexation is supported by NMR and IR evidence. However, when our data are interpreted with allowance for such complexation, the conclusions are relevant to the discussion.

Different reaction pathways, as we find for the $TiCl_4$-catalyzed reactions of benzyl chloride with anisole and with benzene in CH_2Cl_2, are not uncommon for Friedel–Crafts reactions. Apparently two $TiCl_4$ molecules are needed to weaken the C–Cl benzyl chloride bond in the case of benzene whereas one $TiCl_4$ is sufficient for the stronger nucleophile anisole (note that *both* reactions do show first-order arene dependence).

Our attempts to force a common mechanism through the use of 2,4-dichloro-3,5,6-trimethylanisole were unsuccessful. Although this compound has essentially the same methoxy oxygen Lewis basicity as anisole, its presence at considerable concentrations did not change the rate law for either benzene (Table IX) or anisole (unreported data).

Our discovery of different rate laws for benzylation of anisole and benzene in CH_2Cl_2 underscores the danger of interpretation based solely on competitive results. Because they follow different rate laws, neither competitive nor noncompetitive data for this system may be used to refute or support either Brown's or Olah's theories. Until rate laws are established, the same must be said for Olah's competitive benzylation data in 50/50 anisole/benzene.[4]

Both anisole and benzene are *p*-xylylated through the same rate law, eq 6. Both reactions involve arene in the rate law; therefore, a Brown slope value may be calculated from either competitive or noncompetitive data. From the average product isomer percentages (for both competitive and noncompetitive runs), Table XI, the calculated Brown slope values are 0.53 and 0.89 for noncompetitive and competitive k_A/k_B ratios, respectively. Our competitive data fit Brown's relationship exactly (Stock and Brown's *b* value is 0.89 ± 0.03 for anisole reactions[6]) whereas noncompetitively determined k_A/k_B ratios do not. This also makes sense; noncompetitive k_A's are probably anomalously low due to $TiCl_4$–anisole complexation. However, in competitive reactions in CH_2Cl_2 the $TiCl_4$–anisole complex is common to *both* benzene and anisole. Both reactions are slowed to the same extent as long as only a minor fraction of the anisole is complexed to the $TiCl_4$. Under these circumstances competitively determined k_A/k_B ratios are valid if benzene and anisole follow the same rate law, as they do in the *p*-xylylation reaction.

The precise fit of the competitive *p*-xylylation data to Brown's relationship is particularly germane to the longstanding debate regarding the mechanisms of electrophilic aromatic substitution. For this reaction meta isomer percentages consistently hovered about 0.18%; i.e., the reaction is clearly a kinetically controlled process. Even though the mechanism of *p*-xylylation in CH_2Cl_2 is different from that in nitromethane in that arene involvement is rate determining,[26] it is further evidence that Brown's one-step mechanism rather than Olah's two-step mechanism applies when isomerization is avoided.

The benzylation of anisole with *p*-nitrobenzyl chloride proceeds at a very slow pace in CH_2Cl_2 when catalyzed by $TiCl_4$. The $TiCl_4$-induced conversion of anisole to phenol, followed by *p*-nitrobenzylation of phenol, occurs at a similar speed. As a consequence we were not able to obtain useful kinetic data. Although the solvent systems are not the same (CH_2Cl_2 vs a 50/50 mixture of anisole and benzene), our results do bring into question the validity of Olah's competitive *p*-nitrobenzylation results in the latter solvent system.[4]

Conclusions

The $TiCl_4$-catalyzed reactions of benzyl and *p*-methyl- and *p*-nitrobenzyl chlorides with anisole and benzene in solvents nitromethane and dichloromethane were shown through absolute and competitive kinetic studies (1) to be under kinetic control (minimal meta product percentages in all cases) and (2) to fit Brown's relationship applied through Jencks' model of carbocation activity in all but one case—benzylation with benzyl chloride in CH_2Cl_2—which involves different rate laws for anisole and benzene and therefore cannot be used to test any model.

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(26) A reasonable mechanism for the $TiCl_4$-catalyzed *p*-xylylation reaction in CH_2Cl_2 would involve a rate-determining reaction of either a polar p-$CH_3C_6H_4CH_2Cl$–$TiCl_4$ complex or a p-$CH_3C_6H_4CH_2^+TiCl_5^-$ intimate ion pair with the arene. Intimate ion-pair electrophiles were proposed earlier for isopropylation[14] and *tert*-butylation.[22]

matograph. We are indebted to Dr. David Schubert of UCLA for his assistance with NMR analysis.

Registry No. CH_2Cl_2, 75-09-2; $TiCl_4$, 7550-45-0; $AlCl_3$, 7446-70-0; Ph_2CH_2, 101-81-5; *p*-$PhCH_2C_6H_4CH_3$, 620-83-7; *p*-$PhCH_2C_6H_4NO_2$, 1817-77-2; *o*-$PhCH_2C_6H_4OMe$, 883-90-9; *p*-$MeC_6H_4CH_2$-*o*-C_6H_4OMe, 57076-34-3; *p*-$NO_2C_6H_4$-*o*-C_6H_4OMe, 92199-93-4; $PhCH_2$-*m*-C_6H_4OMe, 23450-27-3; *p*-$MeC_6H_4CH_2$-*m*-C_6H_4OMe, 123594-82-1; *p*-$NO_2C_6H_4CH_2$-*m*-C_6H_4OMe, 123594-83-2; *p*-$PhCH_2C_6H_4OMe$, 834-14-0; *p*-$MeC_6H_4CH_2$-*p*-C_6H_4OMe, 22865-60-7; *p*-$NO_2C_6H_4CH_2$-*p*-C_6H_4OMe, 22865-59-4; 2,4-dichloro-3,5,6-trimethylanisole, 123594-81-0; benzene, 71-43-2; anisole, 100-66-3; benzyl chloride, 100-44-7; *p*-xylyl chloride, 104-82-5; *p*-nitrobenzyl chloride, 100-14-1; 2,4-dichloro-3,5,6-trimethylphenol, 6965-74-8.

Kinetic and Thermodynamic Effects in the Thermal Electrocyclic Ring-Openings of 3-Fluorocyclobutene, 3,3-Difluorocyclobutene, and 3-(Trifluoromethyl)cyclobutene

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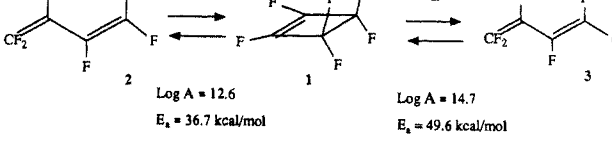
Abstract: The synthesis and thermal electrocyclic ring-opening of 3-fluorocyclobutane, **4**, 3,3-difluorocyclobutane, **5**, and 3-(trifluoromethyl)cyclobutane, **6**, are reported. Activation energies for their ring-openings were found to be 28.1, 45.0, and 36.3 kcal/mol, respectively. **6** was found to form both the (*E*)- and the (*Z*)-5,5,5-trifluoro-1,3-butadienes, in a 95:5 ratio. Thermal equilibrations of the diene products from **4** and **6** were also carried out. The results demonstrate that a CF_3 group exhibits only a slight preference for outward rotation (ΔE_a = 1.2 kcal/mol), while a fluorine substituent gives rise to a much more dramatic outward rotational preference (ΔE_a = 13.8 kcal/mol). These results were consistent with those previously reported for perfluorinated systems and with theoretical expectations.

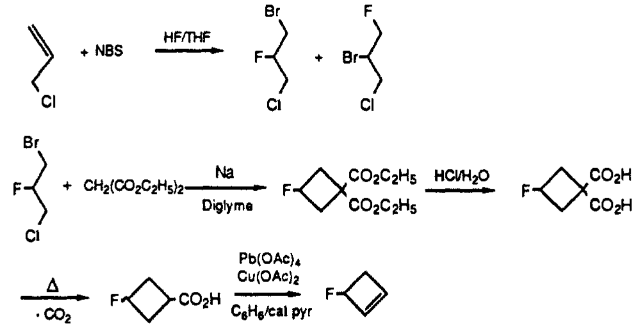
Recently we have published a number of papers on the thermal electrocyclic interconversion of a series of perfluorinated dienes and their cyclobutene isomers.[1-3] The kinetic and thermodynamic behavior of these systems along with related experimental work of Stevens,[4] Houk, and Kirmse[5] and theoretical work of Rondan and Houk[5,6] have led to a better understanding of the dramatic kinetic effects of substituents in the 3-position of cyclobutene on the *stereochemistry* of cyclobutene ring-opening.

In effect it has been found that single substituents at the 3-position of cyclobutene *decrease* the energy of the transition state for ring-opening and that electron-donating substituents prefer to undergo that conrotatory process which will rotate the substituent outward, while electron acceptors prefer the contrary conrotatory process which leads to inward rotation of the substituent. For the most part these potent electronic effects are found to overwhelm potential steric effects.

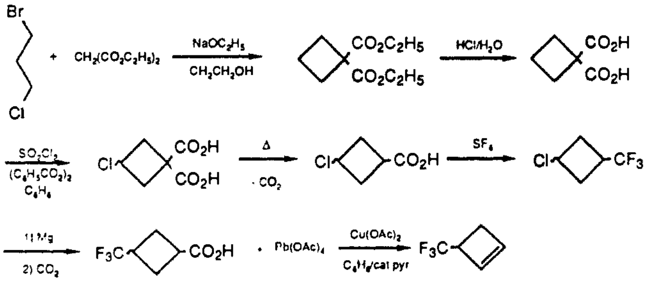
In our earlier studies, for example, we found that in perfluoro systems, such as the perfluoro-3-methylcyclobutene (**1**) system,[2,3] there was a dramatic kinetic preference (ΔE_a = 12.9 kcal/mol) for that conrotatory ring-opening of **1** which led to inward rotation of the very bulky trifluoromethyl substituent, the prime kinetic motivation for such a seemingly sterically unfavorable process being the dominant, very energetically favorable *outward* rotation of the fluorine substituent which was also at the 3-position.



Scheme I. The Synthesis of 3-Fluorocyclobutanecarboxylic Acid



Scheme II. The Synthesis of 3-(Trifluoromethyl)cyclobutanecarboxylic Acid



In such a perfluoro system, while an overall accurate picture of the net kinetic effect of a fluorine substituent and a trifluoromethyl substituent can be reasonably surmised, it is not possible to determine unambiguously and quantitatively the effect of a *lone* fluoro or trifluoromethyl substituent from these results.

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