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Electrophilic Aromatic Substitution. 8.[1] A Kinetic Study of the Friedel–Crafts Benzylation Reaction in Nitromethane, Nitrobenzene, and Sulfolane. Substituent Effects in Friedel–Crafts Benzylation

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Abstract: Kinetic studies have been made of the reaction of benzyl chloride with benzene and/or toluene catalyzed by $TiCl_4$ in nitromethane and in nitrobenzene and catalyzed by $SbCl_5$ in nitromethane and sulfolane. The reactions are all zero order in aromatic, first order in benzyl chloride, and either second order in $TiCl_4$ or first order in $SbCl_5$. Competitively determined k_T/k_B values range from 2.1 to 3.1 and product toluene isomer percentages were ortho 42–46%, meta 4.7–6.4%, and para 48–52% for all four reactions. The reactions do not fit Brown's selectivity relationship (BSR), giving slope *b* values in the range 0.6–0.8. Competitive or noncompetitive kinetic studies are reported for Friedel–Crafts benzylation reactions with *p*-chloro, 3,4-dichloro, *p*-methyl, and *p*-nitrobenzyl chlorides in nitromethane. The $AlCl_3$-catalyzed reactions of *p*-chloro- and 3,4-dichlorobenzyl chloride are both zero order in aromatic and do not follow BSR. However, the $TiCl_4$-catalyzed *p*-xylyl chloride reaction fits Brown's relationship even though it is also zero order in aromatic. The *p*-nitrobenzyl chloride reaction catalyzed by $AlCl_3$ is first order in aromatic hydrocarbon and also obeys Brown's relationship. These mchanistic differences are rationalized in terms of Jencks' approach: the xylyl cation is diffusionally equilibriated and shows relatively high substrate selectivity, the less stable *p*-chloro- and 3,4-dichlorobenzyl cations react faster than they diffuse thus exhibiting little selectivity, while with *p*-nitrobenzyl chloride an S_N2 displacement mechanism is preferred.

In recent years Professor G. A. Olah and various co-workers have reported kinetic data for a number of reactions which do not appear to fit the Brown selectivity relationship[2] or for which the fit appears to be a function of the electrophilic character of the species attacking the aromatic hydrocarbon.[3,4]

In his many papers on alkylation Olah has properly placed great stress on the question of kinetic vs. thermodynamic (concomitant isomerization and/or disproportionation side reactions) control in the determination of rate constants or product isomer distributions. Since his benzylation results[4b] in excess aromatic hydrocarbon and in nitromethane indicate the reaction to be moderate in rate and free of undesirable side reactions, this would seem to be an ideal system to test Brown's selectivity relationship.

Olah has reported noncompetitive as well as competitive kinetic data for the benzylation reaction.[4b] However, as pointed out earlier,[5] the consistency between these results is open to question in that his noncompetitive k_T and k_B values were calculated from first-order plots which are markedly curved (Figures 6 and 7 of ref 4b) toward early reaction times. A restudy of this reaction could be crucial.

In this contribution, we describe our systematic examination of the $SbCl_5$- and $TiCl_4$-catalyzed benzylation of benzene and toluene with benzyl chloride in nitromethane, nitrobenzene, and sulfolane.

For these reactions the question of substituent effects on the electrophile ring is a natural and important one. For solvolysis and substitution reactions of benzylic compounds, it is also of much current interest.[6]

The literature abounds with published studies of substituent effects in Friedel–Crafts benzylation.[6-11] However, with one exception,[11] the competitive kinetic approach was used. As we will show, this method does not establish aromatic rate order dependence despite claims to the contrary.[4b,7,9,10] Absolute kinetic data were reported by Brown and Grayson for the $AlCl_3$-catalyzed reaction of 3,4-dichlorobenzyl chloride with benzene or toluene in nitrobenzene at 25 °C.[11] A value of k_T/k_B was determined but unfortunately not product toluene isomer percentages.

Thus we decided to undertake absolute kinetic studies of Friedel–Crafts benzylation using a variety of substituted benzyl chlorides. Our goals were to determine the rate law in each case, with particular attention paid to the order with respect to the aromatic hydrocarbon. Product isomer percentages and k_T/k_B were also determined, the latter competitively if zero order in aromatic and both competitively and noncompetitively when the aromatic order was one.

Experimental Section

Materials. The analysis, purification, drying, apportionment, and storage procedures of reagents benzene, toluene, benzyl chloride, catalysts

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$AlCl_3$ and $TiCl_4$, solvent nitromethane and internal standards *m*-nitrotoluene and *o*-dichlorobenzene were as described earlier.[12,13] Catalyst $SbCl_5$, reagent grade, was vacuum distilled,[14] poured (under vacuum) into "solvent" tubes (ref 12, Figure 3, insert), and then apportioned into small tubes via vacuum transfer with liquid nitrogen. Aldrich tetramethylene sulfone (sulfolane), 99.2% pure (GC analysis with 25 meter OV101 glass capillary column), was first dried with stirring for a few days at 35–40 °C with one or more batches of molecular sieve 3A pellets and then vacuum distilled as such, or from P_2O_5,[15] into a manifold (flamed out under vacuum) for subsequent apportionment through pouring into the usual solvent tubes. Subsequent GC analysis indicated the same or higher purity and water concentration (Poropak Q column-thermal conductivity detector) of 0.002 M. *p*-Chloro-, 3,4-dichloro-, *p*-methyl-, and *p*-nitrobenzyl chlorides were commercial products which were used without further purification. Each was checked for purity by GC analysis. *NOTE*: *p*-Xylyl chloride decomposes readily in stainless-steel injection ports at 150–250 °C. The compound's true purity (>99%) was determined by IR and GC with glass capillary column and a glass mixing chamber in the injection port. To identify GC product peaks and to establish calibration factors, we usually prepared the reaction products by a Friedel–Crafts synthesis of the analagous ketone followed by reduction of the carbonyl group.[12]

Kinetic Procedures. General procedure for mixing of reagents, aliquot removal and quenching, GC analysis, and data evaluation were given earlier.[12] The following minor changes are noted. Sulfolane transfer from its tube (Figure 3, insert, ref 12) to the reaction manifold was accomplished by tipping the manifold and pouring most of it over. The transfer was completed by flaming. Because it is a solid, a known solution of *p*-nitrobenzyl chloride in nitromethane was prepared in the dry box. A corked syringe containing this solution was weighed and preequilibrated to reaction temperature, injected to start the reaction, then reweighed to determine the amount of RCl and extra solvent added. Syringes used to remove aliquots were preequilibrated to reaction temperature. Kinetic reactions at −27 °C were stirred with an in-house designed D.C. motor driven, submersible stirrer. Nitromethane reactions were quenched with saturated NaCl solution as usual. Sulfolane reactions were quenched with distilled water; a small amount of cyclohexane was then added for extraction purposes. Distilled water was used as a nitrobenzene reaction quench.

Gas Chromatographic Analysis. Benzylation reactions at 30 °C were analyzed with a column packed with 5% diisodecylphthalate and 5% bentone 34 on Chromosorb W under conditions given earlier.[12] GC analysis of other runs involved the use of a HP 5880 gas chromatograph and either a 10-m or a 25-m glass capillary OV 101 column. With the latter and the following settings—detector 250 °C, injection port 300 °C, oven 150 °C, and helium carrier gas 22 cm/s—typical retention times were (min) benzyl chloride 4.4, *o*-dichlorobenzene 4.6, sulfolane 6.2, diphenylmethane 11.4, and *m*-, *o*-, *p*-methyldiphenylmethanes 15.7, 16.0, 16.5, respectively. In all cases except *p*-nitrobenzyl chloride reactions, the internal standard/product peak area ratio was independent of injection size in the range of $^1/_2$ to 3 μL. With the injection port temperature at 300 °C, the ratio of *o*-dichlorobenzene to toluene product (*p*-NO_2) peak areas *decreased* markedly with increased injection size. This fractionation effect, which was much less pronounced for benzene products, was minimized by the use of small injection sizes (1-μL maximum), Supelco Pyrosep S-1 septa, and an injection port temperature of 375 °C.

Results

Effects of Catalysts and Solvents on the Kinetics of Benzylation of Benzene and Toluene with Benzyl Chloride. Titanium Tetrachloride/Nitromethane. The $TiCl_4$ catalyzed benzylation reaction

$$PhCH_2Cl + ArH \xrightarrow{TiCl_4} PhCH_2Ar + HCl \qquad (1)$$

in nitromethane was readily followed at 30 °C. There were no difficulties with phase separation as was encountered in a similar study with excess aromatic hydrocarbon as solvent.[12] Titanium tetrachloride dissolves readily in nitromethane to form a clear, yellow solution. This color did not seem to change as the reagents were added or as the reaction progressed.

Table I. First-Order Rate Constants for the $TiCl_4$-Catalyzed Benzylation of Benzene in Nitromethane at 30 °C

reactants, M			reactant based[a]	product based[b]
$[C_6H_6]$	$[PhCH_2Cl]$	$[TiCl_4]$	10^4k_1, s^{-1}	10^4k_1, s^{-1}
0.0703	0.0676	0.0408	12.7 ± 0.9	3 ± 1
0.0711	0.0695	0.0274	38 ± 1	1.7 ± 0.4
0.0730	0.0411	0.0433	10.9 ± 0.6	3.9 ± 0.4
0.5679	0.0283	0.0392	6.2 ± 0.6	5.6 ± 0.9
0.5733	0.0523	0.0310	3.0 ± 0.3	3.1 ± 0.2

[a] Calculated from the benzyl chloride gas chromatographic peak areas. [b] Calculated from diphenylmethane gas chromatographic peak areas.

The reaction does have its complications, however. Benzyl chloride undergoes polymerization whenever its concentration is comparable to that of the aromatic (first three reactions, Table I). This is avoidable if at least a 10-fold excess of aromatic is present (last two reactions, Table I).

Nitromethane dryness and purity were also important factors. When dry (0.005 wt % H_2O) but impure nitromethane was used and the solvent was transferred from a self-contained ampule (Figure 3, ref 12), the initial rate data were consistent with the rate order dependence of zero for the aromatic, one for benzoyl chloride and three for $TiCl_4$. After the nitromethane was purified via cryocrystallization and transferred by the second method (Figure 3, insert, ref 12) which minimized moisture, new initial rate data yielded a catalyst rate order of two (Table II). This is supported by the constancy of the third-order rate constants—where k_3 is defined as $k_1/\{TiCl_4\}_0{}^2$. These results support a rate law of the form

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

Individual product isomer concentrations were evaluated with gas chromatography for each toluene run. Typical values, expressed in percentages, are given in Table IV. The percentages as well as the meta/para and ortho/para ratios remain essentially constant throughout the course of the reaction, even after injection of water.[16] Calculated averages for all toluene runs are % ortho = 44.3 ± 0.2, % meta = 6.8 ± 0.3, and % para = 48.9 ± 0.3 (± standard deviation).

Occasionally the gas chromatogram gave evidence of secondary benzylation reaction products. These small peaks appeared for late reaction times and were not analyzed. However, secondary reaction is undoubtedly helping to cause downward curvature of the first-order plots at longer times. These observations do support Olah's suggestion that whenever more basic solvents such as nitromethane are used, isomerization and disproportionation side reactions are minimal or nonexistent.

A series of competitive runs were also made with $TiCl_4$. The first two were carried out with impure nitromethane and the original solvent addition technique and the rest with purified solvent and the improved solvent-addition technique. The initial concentrations and the calculated k_T/k_B ratios obtained are summarized in Table V. Again typical product isomer percentages remain reasonably constant throughout the course of the reaction from run to run, even after the addition of water. Average values for all competitive runs are k_T/k_B = 2.5 ± 0.3, % ortho = 45 ± 3, % meta = 6 ± 1, and % para = 49 ± 2. These product isomer percentages are in satisfactory agreement with values obtained by noncompetitive means.

Rate constants were determined for a series of benzylation reactions at 55, 40, and 20 °C (Table II). These were used with the average value of $k_1/\{TiCl_4\}_0{}^2$ at 30 °C to determine Arrhenius/Eyring parameters. A regression analysis of a plot of ln

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[15] A gradual darkening of the P_2O_5– sulfolane mixture was observed but the distillate was purer (99.9%, GC).

[16] For example, a toluene run yielded the following: average percent before H_2O addition, 44.4 ortho, 7.3 meta, 48.2 para; average percent after H_2O addition, 43.8 ortho, 6.7 meta, 49.5 para; overall average percent; 44.1 ortho, 7.0 meta, 48.8 para. We added sufficient H_2O to obtain a concentration of about 0.05, which is our estimate of the H_2O content in nondehydrated nitromethane. Olah does not report having dried his nitromethane solvent.[4b,17] Instead, he injected small amounts of H_2O in an attempt to standardize its effect upon the reaction.

Table II. Initial Rates and Rate Constants for the $TiCl_4$-Catalyzed Benzylation of Benzene and Toluene in Nitromethane[a]

	reactants, M				initial rate ×	initial rate/			
temp, °C	$[C_6H_6]$	$[C_6H_5CH_3]$	$[PhCH_2Cl]$	$[TiCl_4]$	10^5 M s^{-1}	$[TiCl_4]_0^2$ $[PhCH_2Cl]_0$	$10^4 k_1$,[b] s^{-1}	$k_1^b/[TiCl_4]_0^2\cdot$ $[arom]_0$, M^{-3} s^{-1}	$k_1^b/$ $[TiCl_4]_0^2$, M^{-1} s^{-1}
30	0.5679		0.0283	0.0392	1.5 ± 0.3[c]	0.34	5.6 ± 0.9[c]	0.63 ± 0.10	0.36 ± 0.06
	0.5733		0.0523	0.0310	1.7 ± 0.3	0.34	3.1 ± 0.2	0.56 ± 0.04	0.32 ± 0.02
	0.5719		0.0512	0.0587	9.8 ± 0.5	0.56	14 ± 1	0.72 ± 0.05	0.41 ± 0.03
	0.5915		0.0680	0.0124	0.55 ± 0.02	0.53	0.67 ± 0.04	0.74 ± 0.04	0.44 ± 0.03
					av ± SD[d]	0.44 ± 0.12		0.66 ± 0.08	0.38 ± 0.05
		0.4741	0.0286	0.0310	1.8 ± 0.2	0.65	7.1 ± 0.5	1.56 ± 0.11	0.74 ± 0.05
		0.4265	0.0539	0.0279	4.4 ± 0.6	1.05	7.5 ± 0.3	2.25 ± 0.09	0.96 ± 0.04
		0.4253	0.0268	0.0636	9 ± 2	0.8	36 ± 2	2.09 ± 0.12	0.89 ± 0.05
		0.8114	0.0310	0.0328	32 ± 6	0.90	78 ± 3	0.84 ± 0.03	0.68 ± 0.03
		0.8195	0.0328	0.0265	1.9 ± 0.2	0.82	6.0 ± 0.2	1.05 ± 0.04	0.86 ± 0.03
					av ± sd[d]	0.85 ± 0.14		1.56 ± 0.62	0.83 ± 0.11
55	0.5622		0.0226	0.0385			24.5 ± 1.3		1.66 ± 0.09
40	0.6269		0.0554	0.0318			7.8 ± 0.2		0.77 ± 0.02
20	0.6383		0.0504	0.0329			1.5 ± 0.1		0.14 ± 0.01

[a] Purified, dried (molecular sieve, P_2O_5) nitromethane transferred by the second (Figure 3, insert, ref 12) method. [b] Product based. [c] 95% confidence limits. [d] Standard deviation.

Table III. Linearity of First-Order Benzylation Kinetic Plots

reactants, M		extent of reaction, %			
$[C_6H_6]$	$[C_6H_5CH_3]$	linear[a]	total[b]	no. of points[a]	r (coef)[b]
0.5679		24	79	8	0.988
0.5733		27	67	10	0.997
0.5719		50	78	12	0.997
0.5915		28	>61	12	0.996
	0.4741	40	82	12	0.995
	0.4265	62	88	12	0.998
	0.4253	41	93	8	0.998
	0.8114	80	99	9	0.999
	0.8195	62	99	9	0.999

[a] The extent of the reaction for which the first-order plot was linear. [b] Based on product diphenylmethane or methyldiphenylmethane GC peaks [c] Linear correlation coefficient.

Table IV. Product Isomer Distribution for Benzylation of Toluene[a] Catalyzed by $TiCl_4$ in Nitromethane, 30 °C

time, s	% rxn	% ortho	% meta	% para
9	7.5	43.6	7.0	49.5
21	16.7	43.7	6.9	49.4
31	22.5	44.9	6.8	48.3
40	27.5	44.4	6.3	49.3
48	34.7	44.9	7.5	47.6
58	37.8	44.3	6.7	49.0
70	44.4	44.2	6.5	49.3
97	55.2	44.5	7.1	48.4
203	79.6	44.9	7.1	47.9
503	96.9	45.2	7.2	47.6
999	99.9	45.5	7.1	47.4
av ± sd[b]		44.6 ± 0.6	6.9 ± 0.3	48.5 ± 0.8

[a] Fourth toluene run, Table II. [b] Standard deviation.

($k_1/\{TiCl_4\}_0^2$) vs. $1/T$ produced a slope of -6.7 (± 2.6) × 10^3, an intercept of 21 ± 8, and an r(coef) of -0.992 (± 95% confidence limits). For $TiCl_4$-catalyzed reaction, the calculated values are $E_a = 56 \pm 11$ kJ/mol, $\Delta H^{\ddagger} = 53 \pm 11$ kJ/mol, $\Delta G^{\ddagger} = 77.5 \pm 0.4$ kJ/mol, and $\Delta S^{\ddagger} = -78 \pm 35$ J/(mol deg) (± standard deviation).

Titanium Tetrachloride/Nitrobenzene. To see if the known acidity of nitromethane[18] might be affecting k_T/k_B, we did a competitive study of this reaction in nitrobenzene, Table V. The results are consistent with those in nitromethane.

Antimony Pentachloride/Nitromethane. Since Olah reported competitive and noncompetitive results for the benzylation reaction catalyzed by $SbCl_5$ in nitromethane at 30 °C, we initially attempted to do likewise. However, with thoroughly dried nitromethane (molecular sieves, P_2O_5), the $SbCl_5$-catalyzed reaction between benzyl chloride and benzene was found to be too fast to follow even at 0 °C. Meaningful kinetic data (Table VI) were obtained only when this reaction was studied in a Lauda TK-30 Kryomat at −27 °C.

Even at this temperature the $SbCl_5$ concentrations had to be reduced to a range uncomfortably close to the water concentration in nitromethane (0.003 M) in order to follow the reaction. Because of possible significant removal of $SbCl_5$ activity through interaction with water, the noncompetitive rate constants may be unrealistically low. However, under these circumstances doubling the $SbCl_5$ concentration might increase the apparent rate constant, k_1, by more than a factor of 2 (assuming first-order catalyst dependence). Thus the results of Table VIII do indicate zero order benzene rate dependence. Although the $SbCl_5$ rate order was not determined, these data suggest the rate expression

$$\text{rate} = k_2\{SbCl_5\}_0\{PhCH_2Cl\} \tag{3}$$

Competitive results for this reaction are given in Table VII.

Antimony Pentachloride/Sulfolane. Since at this point we wondered if the zero order aromatic dependence for benzylation with benzyl chloride happened only in nitro solvents, the possibility of sulfolane as a solvent was investigated. In comparison to nitromethane, sulfolane is quite similar with respect to dielectric constant (nitromethane 35.9, sulfolane 42.0), but it is a considerably more basic solvent (donor number of nitromethane 2.7, sulfolane 14.8).[19a] Thus sulfolane, like nitromethane, was expected to give homogeneous solutions throughout the reaction but because of complexation with Friedel–Crafts catalysts reactions would be considerably slower.

These predictions proved to be correct. After 3 days in 40 °C sulfolane in the presence of $AlCl_3$ no reaction between benzyl chloride and benzene or toluene was observed (GC analysis). Furthermore, the peak area ratio of benzyl chloride and internal standard *o*-dichlorobenzene also remained constant, indicating no benzyl chloride polymerization either.

When the very strong catalyst, $SbCl_5$, was dissolved in sulfolane a clear light purplish-black color formed and remained essentially unchanged as reagents were added and the reaction proceeded. At 40 °C the reaction occurred at a reasonable pace provided the

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Table V. Kinetic Data for the Competitive Benzylation of Toluene and Benzene Catalyzed by $TiCl_4$

$[C_6H_6]$	$[C_6H_5CH_3]$	$[PhCH_2Cl]$	$[TiCl_4]$	$(k_T/k_B)^a$	% ortho[b]	% meta[b]	% para[b]
A. In Nitromethane, 30 °C							
0.3136	0.7014	0.1336	0.0572	2.6 ± 0.1	46.2 ± 1.0[c]	5.6 ± 0.4[c]	48.2 ± 0.4[c]
0.7887	0.6582	0.1688	0.0480	2.5 ± 0.1			
0.2534	0.2161	0.0693	0.0401	2.4 ± 0.1	46.9 ± 1.5	5.7 ± 0.4	47.4 ± 1.5
0.0487	0.0498	0.0486	0.0324	2.5 ± 0.3	46.2 ± 0.6	7.1 ± 0.5	46.7 ± 0.2
0.0117	0.2369	0.0426	0.0386	2.7 ± 0.2	45.6 ± 0.8	5.7 ± 0.2	48.7 ± 0.7
0.2335	0.0049	0.0452	0.0484	2.2 ± 0.2	38.1 ± 1.7	7.8 ± 0.4	54.1 ± 2.0
0.0945	0.1144	0.1002	0.0480	3.0 ± 0.5	41.3 ± 5.4	8.1 ± 2.3	50.6 ± 5.5
0.0950[d]	0.1208[d]	0.1208[d]	0.0533[d]	2.1 ± 0.2[d]	47.2 ± 2.5[d]	6.0 ± 0.9[d]	46.8 ± 1.9[d]
			av ± sd[c]	2.5 ± 0.3	45 ± 3	6 ± 1	49 ± 2
B. In Nitrobenzene, 30 °C							
0.2190	0.1870	0.0395	0.0190	2.6 ± 0.2	42.1 ± 0.9	6.4 ± 0.4	51.5 ± 0.9

[a] (k_T/k_B) = ([toluene products]/[benzene products])($[\text{benzene}]_0/[\text{toluene}]_0$), evaluated at various times after reaction had begun. Average values are reported along with standard deviations. [b] Product methyldiphenylmethanes. Average values are reported along with standard deviations. [c] Standard deviation. [d] High-speed stirrer.

Table VI. Rate Constants for the $SbCl_5$-Catalyzed Benzylation of Benzene in Nitromethane at -27 °C

reactants, M					
$[C_6H_6]$	$[PhCH_2Cl]$	$[SbCl_5]$	10^3k_1, s^{-1}	$k_1/[SbCl_5]_0$, $M^{-1}\ s^{-1}$	$k_1/[SbCl_5]_0\ [C_6H_6]_0$, $M^{-2}\ s^{-1}$
0.5904	0.0197	0.0169	4.5 ± 2.4	0.27 ± 0.14	0.45 ± 0.24
0.3350	0.0206	0.0089	2.4 ± 0.5	0.27 ± 0.06	0.80 ± 0.17

Table VII. Competitively Determined Rate Constant Ratios and Product Isomer Percentages for the Friedel-Crafts Benzylation Reaction

$XC_6H_4CH_2Cl$	catalyst	solvent	temp, °C	k_T/k_B	% ortho	% meta	% para	b^a
p-NO_2	$AlCl_3$	CH_3NO_2	35	2.5 ± 0.1[b]	43.6 ± 0.7[b]	21.5 ± 1.2[b]	34.9 ± 0.8[b]	1.4
3,4-Cl_2	$AlCl_3$	CH_3NO_2	25	1.9 ± 0.2	45.5 ± 0.9	15.8 ± 0.7	38.7 ± 1.2	0.93
p-Cl	$AlCl_3$	CH_3NO_2	20	2.2 ± 0.2	46.5 ± 1.1	9.1 ± 0.2	44.5 ± 1.2	0.78
H	$TiCl_4$	CH_3NO_2	30	2.3 ± 0.4	46.2 ± 0.5	6.0 ± 0.6	47.7 ± 0.8	0.68
H	$TiCl_4$	$C_6H_5NO_2$	30	2.6 ± 0.1	42.1 ± 0.9	6.4 ± 0.4	51.5 ± 0.9	0.75
H	$SbCl_5$	CH_3NO_2	-27	2.1 ± 0.1	44.5 ± 0.6	4.7 ± 0.6	51.2 ± 0.8	0.61
H	$SbCl_5$	sulfolane	40	3.1 ± 0.3	44.0 ± 0.3	6.0 ± 0.7	50 ± 0.8	0.79
p-CH_3	$TiCl_4$	CH_3NO_2	0	40.2 ± 1.6	27.2 ± 0.2	1.9 ± 0.3	70.9 ± 0.4	1.2

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

Table VIII. Kinetic Data for the $SbCl_5$-Catalyzed Benzylation of Benzene and Toluene in Sulfolane

	reactants, M							
temp, °C	$[C_6H_6]$	$[C_6H_5CH_3]$	$[PhCH_2Cl]$	$[SbCl_5]$	10^3k_1, s^{-1}	$k_1/[SbCl_5]$, $M^{-1}\ s^{-1}$	$k_1/[SbCl_5]^2$, $M^{-2}\ s^{-1}$	$k_1/[SbCl_5][\text{arom}]$, $M^{-2}\ s^{-1}$
40	0.1157		0.0043	0.0124	(0.78 ± 0.07)	(0.063 ± 0.006)		
	0.2710		0.0149	0.0104	(0.062 ± 0.007)	(0.00059 ± 0.00007)		
	0.2603		0.0142	0.0503	5.0 ± 1.0	0.10 ± 0.02	2.0 ± 0.4	0.38 ± 0.08
	0.1860		0.0105	0.0209	2.7 ± 0.5	0.13 ± 0.02	6.2 ± 1.1	0.69 ± 0.13
	0.5106		0.0102	0.0314	5.4 ± 1.0	0.17 ± 0.03	5.5 ± 1.0	0.34 ± 0.06
	0.1771		0.0131	0.0299	3.5 ± 0.4	0.12 ± 0.01	3.9 ± 0.4	0.66 ± 0.08
	0.1624		0.0134	0.0448	6.5 ± 1.1	0.15 ± 0.06	3.2 ± 0.5	0.89 ± 0.15
	0.1638		0.0137	0.0781	12 ± 2	0.15 ± 0.02	1.9 ± 0.3	0.94 ± 0.15
					av ± sd	0.14 ± 0.03	3.8 ± 1.8	0.65 ± 0.25
		0.1465[a]	0.0131	0.0380	8.1 ± 0.8	0.21 ± 0.08		
30	0.2276		0.0157	0.0438	3.9 ± 0.9	0.089 ± 0.020		
50	0.2507		0.0154	0.0234	4.5 ± 0.3	0.19 ± 0.01		
60.1	0.2273		0.0136	0.0379	10.7 ± 0.15	0.28 ± 0.04		

[a] Based on eight aliquots the average product methyldiphenylmethane isomer percentages were (± standard deviation) ortho 43.8 ± 0.4, meta 6.8 ± 0.7, para 49.4 ± 0.9.

Table IX. Rate Constants for the $AlCl_0$-Catalyzed Reaction of *p*-Chlorobenzyl Chloride and Benzene in Nitromethane at 20 °C

reactants, M					
$[C_6H_6]$	$[ClC_6H_4CH_2Cl]$	$[AlCl_3]$	10^2k_1, s^{-1}	$(k_1/[AlCl_3]_0) \times 10$, $M^{-1}\ s^{-1}$	$k_1/[AlCl_3]_0$-$[C_6H_6]_0$, $M^{-1}\ s^{-1}$
0.1400	0.0410	0.0251	1.35 ± 0.29[a]	5.4 ± 1.1[a]	3.8 ± 0.8[a]
0.2435	0.0402	0.0190	1.25 ± 0.12	6.6 ± 0.6	2.7 ± 0.3

[a] ± 95% confidence limits.

catalyst concentration was greater than 0.02 M. At lower $SbCl_5$ concentrations the reaction rate was found to be well below that expected from the rate law (first two reactions, Table VIII) probably because of a quenching interaction with solvent water (within ~20% of $SbCl_5$ concentration in the first two reactions) or solvent impurities.

Reactions at higher $SbCl_5$ concentrations point consistently to a rate order dependence of one for $SbCl_5$ and benzyl chloride and again zero for aromatic (Table VIII and rate expression 3).

Since it would not be possible under the circumstances to determine whether this reaction fitted Brown's selectivity relationship with noncompetitively determined k_T/k_B value, a competitive study

Table X. Initial Rates and Rate Constants for the $AlCl_3$-Catalyzed Reaction of 3,4-Dichlorobenzyl Chloride and Benzene in Nitromethane and Nitrobenzene at 25 °C

reactants, M			initial rate × 10^5, M s^{-1}	(initial rate/ $[AlCl_3]_0[RCl]_0$) × 10^2, M^{-1} s^{-1}	10^3k_1, s^{-1}	$(k_1/[AlCl_3]_0)$ × 10^2, M^{-1} s^{-1}	$(k_1/[AlCl_3]_0 \cdot [C_6H_6]_0)$ × 10^2, M^{-1} s^{-1}
$[C_6H_6]$	[RCl]	$[AlCl_3]$					
				A. In Nitromethane			
0.4549	0.0330	0.0539	2.7 ± 0.1[a]	1.52 ± 0.06[a]	0.89 ± 0.09[a]	1.6 ± 0.2[a]	3.6 ± 0.4[a]
0.3249	0.0436	0.0761	5 ± 2	1.5 ± 0.6	1.1 ± 0.2	1.4 ± 0.3	4.4 ± 0.8
0.1845	0.0236	0.1026	3.5 ± 0.8	1.45 ± 0.33	1.7 ± 0.1	1.61 ± 0.09	8.7 ± 0.5
					av ± sd[b]	1.54 ± 0.12	
				B. In Nitrobenzene			
0.5249	0.0222	0.0438	0.204 ± 0.005	0.210 ± 0.005	0.095 ± 0.001	0.217 ± 0.002	0.413 ± 0.004
0.2789	0.0241	0.0926	0.409 ± 0.024	0.183 ± 0.011	0.167 ± 0.003	0.180 ± 0.003	0.645 ± 0.011
					av ± sd[b]	0.199 ± 0.026	

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

Table XI. Rate Constants for the $TiCl_4$-Catalyzed Reaction of p-Xylyl Chloride and Benzene in Nitromethane

	reactants, M							
temp, °C	$[C_6H_6]$	[p-xylyl-Cl]	$[TiCl_4]$	10^3k_1, s^{-1}	$(k_1/[TiCl_4]_0)$ × 10, M^{-1} s^{-1}	$k_1/[TiCl_4]_0^2$, M^{-2} s^{-1}	$k_1/[TiCl_4]_0 \cdot [C_6H_6]_0$, M^{-2} s^{-1}	$k_1/[TiCl_4]_0^2 \cdot [C_6H_6]$, M^{-3} s^{-1}
0	0.3872	0.0321	0.0336	3.9 ± 1.3[a]	1.2 ± 0.4[a]	3.5 ± 1.2[a]	0.30 ± 0.10[a]	8.9 ± 3.0[a]
	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[b]	4.6 ± 1.0		
15	0.5642	0.0187	0.0213	7.1 ± 1.5		15.5 ± 3.3		
−15	0.3522	0.0247	0.0364	2.0 ± 0.2		1.5 ± 0.1		
−27	0.2214	0.0174	0.0256	0.194 ± 0.008		0.30 ± 0.01		

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

was undertaken. The results are given in Table VII.

Arrhenius/Eyring activation parameters were calculated from experimentally determined $k_1/\{SbCl_5\}_0$ values at 30, 50, 60.1, and the averaged value at 40 °C (Table X). A plot of ln $(k_1/\{SbCl_5\}_0)$ vs. $1/T$ yielded a slope of -3.82 (± 0.64) × 10^3, an intercept of 10 (± 2) and linear correlation coefficient of -0.998 (± 95% confidence limits). These data produced $E_a = 32 \pm 2$ kJ/mol, $\Delta H^\ddagger = 29 \pm 2$ kJ/mol, $\Delta G^\ddagger = 83 \pm 1$ kJ/mol, and $\Delta S^\ddagger = -170 \pm 9$ J/(deg mol) (± standard deviation).

Substituent Effects on the Kinetics of Benzylation of Benzene and Toluene with Substituted Benzyl Chlorides. *p*-Chlorobenzyl Chloride. Low-temperature polymerization of substituted benzyl halides has been reported.[19b] To check the possibility of polymerization a mixture consisting of p-chlorobenzyl chloride, $TiCl_4$, and internal standard m-nitrotoluene was run in nitromethane at 30 °C. Over a reaction time of 10 000 s, no apparent change in the GC p-chlorobenzyl chloride peak was observed. Benzene and toluene were then injected into the solution. After another 10 000 s only minor amounts of toluene product were produced.

With the stronger catalyst $AlCl_3$ the reaction was faster—to the point that good initial rate data (<10% reaction) could not be obtained. However, the first-order (in benzyl halide) plots were linear through 50% reaction and suggest a kinetic rate order of zero for benzene (Table IX) and the overall rate law

$$\text{rate} = k[AlCl_3]_0[p\text{-}ClC_6H_4CH_2Cl] \qquad (4)$$

Under this circumstance[1] only the competitive approach yields a meaningful k_T/k_B value. This is reported along with product isomer percentages in Table VII.

3,4-Dichlorobenzyl Chloride. The $AlCl_3$-catalyzed reaction between 3,4-dichlorobenzyl chloride and benzene is slower than with the p-chloro halide. Thus the rate law was established both through the initial rate method and by dividing the first-order rate constants (defined in terms of the benzyl halide) by various powers of initial concentrations of $AlCl_3$ and benzene (present in excess). The data (Table X) clearly support the rate law

$$\text{rate} = k_2[AlCl_3]_0[3,4\text{-}Cl_2C_6H_3CH_2Cl] \qquad (5)$$

Again k_T/k_B had to be determined competitively (Table VII).

Brown and Grayson[11] found this reaction in nitrobenzene to be first order in aromatic as well as $AlCl_3$ and RCl. Considering the similarity in solvents, a different rate dependence upon aromatic appears surprising. Therefore the reaction in nitrobenzene was reinvestigated. The results, which support zero order aromatic dependence, are given in Table X. The first-order plots were very linear (correlation coefficients of 0.9997 and 0.9996) through 73% reaction, the extent of the analyses.

The discrepancy between our results is difficult to explain. Brown and Grayson used catalyst and benzyl halide concentrations which were a factor of 10 higher; however, this should not affect aromatic rate order dependence. In that they followed the production of HCl, their evidence for aromatic rate order dependence is less direct than ours, in which product 3,4-dichlorodiphenylmethane was determined via gas chromatography.

The reaction is about eight times faster in nitromethane than in nitrobenzene. This is consistent with the higher donor number of nitrobenzene[19] and IR[20] and NQR[21] analyses of the $AlCl_3$ and $GaCl_3$ complexes but not with an earlier cryoscopic study with $AlBr_3$.[22]

***p*-Methylbenzyl Chloride (*p*-Xylyl Chloride).** Since an electron-donating substituent on the benzyl ring was expected to speed up the reaction rate, $TiCl_4$ was chosen as the catalyst for p-xylyl chloride. Even with the milder catalyst the reaction was fast but followable in the temperature range between 15 and −27 °C.

When benzene and internal standard m-nitrotoluene were added to a solution of $TiCl_4$ in nitromethane the yellow color did not appear to change. Upon injection of p-xylyl chloride the solution became yellow-brown and darkened with time.

Because of the activating effect of the methyl group, the reaction analysis is complicated by the appearance of secondary reaction products,[23] seen as four GC peaks with reproducible retention times

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[20] Jones, D. E. H.; Wood, J. L. *J. Chem. Soc. A* **1971**, 3132–3135.

[21] Tong, D. A. *J. Chem. Soc., Chem. Commun.* **1969**, 790–791.

[22] Gorenbein, E. Y. *Zh. Neorg. Khim.* **1959**, *4*, 1643–1648.

[23] Conceivably these could be disproportionation (transbenzylation) products. However, this is unlikely since no disproportionation was observed when either (2-methyldiphenyl)methane or (2,2′-dimethyldiphenyl)methane was heated at 50 °C with $AlCl_3$–O_2NCH_3 in benzene. Tashiro, M.; Yamato, T.; Fukata, G. *J. Org. Chem.* **1978**, *43*, 1413–1420.

Table XII. Initial Rates and Rate Constants for the $AlCl_3$-Catalyzed Reaction of *p*-Nitrobenzyl Chloride and Benzene or Toluene in Nitromethane

	reactants, M								
temp, °C	$[C_6H_6]$	$[C_6H_5CH_3]$	[RCl]	$[AlCl_3]$	initial rate × 10^7, M s^{-1}	(initial rate/ $[cat.]_0[RCl]_0\cdot[arom]_0$) × 10^4, M^{-2} s^{-1}	10^5k_1 s^{-1}	$(k_1/[AlCl_3]_0)$ × 10^4, M^{-1} s^{-1}	$(k_1/[AlCl_3]_0\cdot[arom]_0)$ × 10^4, M^{-2} s^{-1}
35	0.5756		0.0782	0.0404	3.5 ± 0.5[a]	1.9 ± 0.3[a]	0.53 ± 0.015[a]	1.31 ± 0.03[a]	2.28 ± 0.06[a]
	0.3160		0.0407	0.1056	3.3 ± 0.6	2.4 ± 0.5	0.77 ± 0.16	0.73 ± 0.15	2.3 ± 0.5
	0.3060		0.0349	0.1441	4.3 ± 0.4	2.8 ± 0.3	1.43 ± 0.34	0.99 ± 0.24	3.2 ± 0.8
	1.042		0.0293	0.0281	1.6 ± 0.2	1.9 ± 0.2	0.58 ± 0.04	2.06 ± 0.14	2.0 ± 0.1
					av ± sd[b]	2.25 ± 0.4		av ± sd[b]	2.4 ± 0.5
		0.4263	0.0458	0.0819			1.10 ± 0.11	1.34 ± 0.13	3.2 ± 0.3
		0.9556	0.0395	0.0705			1.70 ± 0.10	2.41 ± 0.14	2.5 ± 0.1
								av ± sd[b]	2.85 ± 0.5
50	0.4647		0.0326	0.0642			3.19 ± 0.18	4.97 ± 0.28	10.7 ± 0.6
60	0.6153		0.0364	0.0450			4.62 ± 0.33	10.3 ± 0.7	16.7 ± 1.2
69.2	0.4937		0.0192	0.1060			25.1 ± 1.3	23.6 ± 1.2	47.9 ± 2.5

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

in the 15–18 min range. Since it was possible to obtain good kinetic data before appreciable secondary product production, no attempt was made to include them in the analysis. However, the first two benzene runs (Table XI) had the lowest benzene:*p*-xylyl chloride ratios and predictably showed early formation of secondary products. This undoubtedly is the prime reason for their somewhat lower rate constant values.

Programmed temperature gas chromatography also indicated two small peaks caused by the two isomeric *p*-xylyl chloride dimers. However, corrections for this small amount of halide polymerization had a negligible effect on rate constant values.

Even without these corrections, the data are consistent with the rate law

$$\text{rate} = k_3[TiCl_4]_0{}^2[p\text{-xylyl chloride}] \qquad (6)$$

Again k_T/k_B had to be determined competitively, and it is reported in Table VII.

A plot of ln $(k_1/[TiCl_4]_0{}^2)$ vs. $1/T$ using data at four temperatures (Table IV) yields a straight line with slope −6.5 (± 1.9) × 10^3, intercept 25 ± 7 (± 95% confidence limits), and *r*(coef) −0.995. The calculated Arrhenius/Eyring parameters are E_a = 54 ± 8 kJ/mol, $\Delta H^‡$ = 52 ± 8 kJ/mol, $\Delta G^‡$ = 62.9 ± 0.6 kJ/mol, $\Delta S^‡$ = −41 ± 32 J/(deg mol) (± standard deviation).

***p*-Nitrobenzyl Chloride.** Using a differential titration method to determine the hydrogen chloride produced, Brown and Grayson.[11] briefly studied the $AlCl_3$-catalyzed reaction between *p*-nitrobenzyl chloride and benzene. They found the reaction to be third order but too slow (25% reaction after 48 h at 25 °C in nitrobenzene) to be convenient for study by their method. However, because of the pivotal importance of strongly electron-withdrawing substituent effects in benzylation, a study of this reaction in nitromethane was undertaken.

When benzene or toluene is added to a colorless solution of $AlCl_3$ and internal standard *o*-dichlorobenzene in nitromethane, the solution turns light yellow to yellow. This color is enhanced somewhat when the reaction is initiated by the injection of the *p*-nitrobenzyl chloride solution. The reaction proceeds homogeneously with no perceptible color change until long reaction times, when it exhibits a greenish tinge. The reaction proved to be slow but followable in the range 10–60 °C.

Noncompetitive results appear in Tables XII and XIII. Product toluene isomer percentages were constant and virtually identical for all aliquots of the two noncompetitive toluene reactions, and in excellent agreement with those determined competitively (Table VII). They are decidely different from those reported by Olah:[4b] ortho 59.6%, meta 6.2%, para 34.2%. However, Olah's competitive reaction involved a different catalyst ($TiCl_4$), different solvent (excess aromatic hydrocarbon), and GC analysis with stainless-steel capillary columns which necessitated reduction of the products to amines and then diazotization before GC injection.

Table XIII. Product Isomer Distribution for the $AlCl_3$-Catalyzed Reaction of *p*-Nitrobenzyl Chloride and Toluene[a] in Nitromethane at 35 °C

no.	time, s	% rxn	% ortho	% meta	% para
1	3612	5.4	43.3	22.0	34.7
2	5573	8.4	43.6	22.1	34.2
3	8404	12.9	43.9	21.8	34.3
4	10883	14.6	43.3	21.7	34.9
5	14400	22.7	44.3	22.1	33.6
6	18000	23.3	43.6	22.3	34.1
7	25283	29.5	43.2	22.2	34.6
8	28801	37.3	43.6	21.9	34.5
9	36423	40.2	43.7	22.3	34.0
10	94566	77	44.0	22.0	33.9
	av ± sd		43.6 ± 0.3	22.0 ± 0.2	34.3 ± 0.4

[a] Second toluene run, Table XII.

Unlike the previous reactions, benzylation with a *p*-nitro substituent is clearly first order in either benzene or toluene. This can be seen from the initial rate data by dividing the pseudo-first-order rate constant k_1 by the initial concentrations of *both* $AlCl_3$ and aromatic (present in ≥10-fold excess over benzyl halide). Thus the overall rate law is

$$\text{rate} = k[AlCl_3]_0[pO_2NC_6H_4CH_2Cl][\text{arom}] \qquad (7)$$

In this case k_T/k_B may be calculated directly from the average absolute values of k_T $(=k_1/[AlCl_3]_0[tol]_0)$ and k_B. This value is 1.2 ± 0.5 (± standard deviation).

The competitively determined value (Table VII) is 2.5 ± 0.1 (± standard deviation).

When data gathered at various temperatures (Table XII) are used, a plot of ln $(k_1/[AlCl_3]_0[C_6H_6]_0)$ vs. $1/T$ produced a straight line with slope −8.8 (± 3.7) × 10^3, intercept 20 ± 11 (± 95% confidence limits), and *r*(coef) −0.991. The resulting parameters are E_a = 73 ± 15 kJ/mol, $\Delta H^‡$ = 71 ± 15 kJ/mol, $\Delta G^‡$ = 98.5 ± 0.3 kJ/mol, and $\Delta S^‡$ = −85 ± 46 J/(deg mol).

Discussion

In a previous paper[12] we reported difficulties with phase separation when the benzylation reaction was run in excess aromatic hydrocarbon as solvent. No such difficulties occurred in nitromethane. Solution homogeneity was maintained even after small amounts of water were purposefully injected in an effort to reproduce reaction conditions reported by Olah and co-workers.[4b,17] In these cases there appeared momentarily a grey flock, possibly a σ-complex formed from HCl produced by the reaction of $TiCl_4$ with added water, that quickly dissolved. The injection of 0.05% H_2O into noncompetitive reaction mixtures after reaction had begun decreased the reaction rate markedly—by factors of 8 to 25. However, both k_T/k_B and product isomer percentages of competitive reactions were unaffected by H_2O injections.

The role of small amounts of water in Friedel–Crafts reactions should not be underestimated.[24] Our initial attempts to evaluate rate constants were frustrated by inconsistent results. Only after lowering the H_2O content of the nitromethane to 0.003 M (0.005 wt %) by several successively better drying methods were satisfactory results obtained. Even then the rate order of $TiCl_4$ appeared to be three. Only after the nitromethane was purified by cryocrystallization *and* dried to 0.003 M *and* transferred by a method which minimized moisture (Figure 3, insert, ref 12) did $TiCl_4$ rate order revert to the more reasonable value of two.

Through the use of vacuum line techniques, purified, dried solvents, and catalyst concentrations a factor of 10 or more higher than the residual solvent water concentration, we now consistently obtain reproducible absolute kinetic rate data. Rate constants determined by different undergraduates using totally different batches of purified, dried solvent now agree usually within a few percent error.

These results indicate different catalytic rate orders for $TiCl_4$ and $SbCl_5$. This is not unexpected. It is known that $AlCl_3$ preferentially coordinates with nitrobenzene over benzoyl chloride[25] and $GaBr_3$ preferentially coordinates with nitrobenzene over ethyl bromide.[26] By analogy, we expect both $SbCl_5$ and $TiCl_4$ to select nitromethane (or sulfolane) over benzyl chloride. Thus for either catalyst a competition should exist between solvent and benzyl chloride. With $TiCl_4$:

$$C_6H_5CH_2Cl + S\text{–}TiCl_4 \rightleftharpoons C_6H_5CH_2Cl{:}TiCl_4 + S$$

$$C_6H_5CH_2Cl{:}TiCl_4 + S\text{–}TiCl_4 \xrightleftharpoons{\text{slow}} C_6H_5CH_2^+Ti_2Cl_9^- + S$$

$$C_6H_5CH_2^+Ti_2Cl_9^- + C_6H_6 \xrightarrow{\text{fast}} \text{products}$$

and with $SbCl_5$:

$$C_6H_5CH_2Cl + S\text{–}SbCl_5 \xrightleftharpoons{\text{slow}} C_6H_5CH_2^+SbCl_6^- + S$$

$$C_6H_5CH_2^+SbCl_6^- + C_6H_6 \xrightarrow{\text{fast}} \text{products}$$

This competition would account for the apparent shift of the rate-determining step from attack of a benzyl chloride catalyst complex upon aromatic hydrocarbon to the formation of the electrophile itself. Indeed, in any solvent more basic than benzyl chloride, the competition for catalyst may become the rate-determining step.[25,27]

Although, as Olah has pointed out,[28] "in all probability in Friedel–Crafts type reactions no simple monotonic series of catalytic activity of Lewis acid and related proton acid catalysts is possible", the evidence indicates $SbCl_5$ to be a considerably stronger catalyst than $TiCl_4$.[4b,28,29,30] Thus apparently two molecules of the weaker catalyst $TiCl_4$ are necessary to bring about the formation of the benzyl cation (or ion pair) electrophile. This also follows from our earlier study of this reaction in excess benzene or toluene. Even though the aromatic hydrocarbon should offer much less competition than nitromethane, the reaction was again second order in $TiCl_4$.[12]

As a further illustration of the importance of moisture control and the difficulties encountered in obtaining reproducible data, the pseudo-first-order rate constant for the $SbCl_5$-catalyzed reaction in nitromethane at −27 °C is a factor of 10 *larger* than that reported[4b] at 30 °C for the same reaction!

To make sure these reactions were kinetically controlled, i.e., that the rate of stirring was greater than the rate of reaction, $TiCl_4$-catalyzed competitive benzylation with benzyl chloride was studied with a high-speed stirrer. No change in k_T/k_B was observed, Table V.

The zero-order aromatic rate dependence in all but one of these reactions is significant for two reasons. First, it illustrates that the competitive method may *not* be used to infer first-order dependence.[31] Second, as with the case of the desulfonylative benzylation reaction,[1] it indicates that the rate-determining step is the formation of the electrophile.

Thus the ratio k_T/k_B, where k_T and k_B are absolute rate constants determined by noncompetitive studies, cannot be used to test Brown's selectivity relationship because neither reaction should reflect the activity of the aromatic. It also follows that the ratio k_T/k_B determined noncompetitively should be essentially one. For the $SbCl_5$-catalyzed reaction in sulfolane (Table VIII) this appears to be the case: $k_T/k_B = 1.5 \pm 1.2$ (standard deviation). However, the $TiCl_4$-catalyzed reaction in nitromethane yields $k_T/k_B = 2.2 \pm 0.6$ (standard deviation).

The reason for the "high" latter value is unclear. With $AlCl_3$ dissolved in nitromethane, the addition of benzene or toluene results in a solution color change from colorless to light yellow or yellow, respectively. Thus even though the solvent $AlCl_3$ complex should be far more stable than one between the catalyst and aromatic, there are indications of perhaps ternary complex formation. Although the yellow color of CH_3NO_2–$TiCl_4$ solutions did not seem to deepen with the addition of benzene or toluene, similar ternary complex formation is plausible. Possibly this "solvent effect" by the aromatic is stronger with toluene and produces $k_T/k_B > 1$.

With the exception of *p*-nitro benzylation our competitive results (Table VII) agree fully with those reported by Olah.[4b,33,34] Takematsu, Sugita, and Nakane[15] have also studied substituent effects in Friedel–Crafts benzylation using BF_3 as catalyst and in nitromethane solvent. The competitive method was used exclusively. Their results for *p*-chlorobenzyl, *p*-methylbenzyl, and unsubstituted benzyl chloride appear to be within experimental error of ours. Clearly for benzylation with benzyl chloride, *p*-chlorobenzyl chloride, 3,4-dichlorobenzyl chloride, and benzyl sulfonyl chloride[1] in polar solvents, the rate laws do *not* involve aromatic nor do they fit Brown's relationship. The calculated slope values of the slope b for Brown's equation

$$\log p_f = bS_f$$

are all outside of Brown and Stock's least-squares slope of $b = 1.31 \pm 0.20$ (95% confidence limits), Table VII.

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[24] The influence of small amounts of water on the rate of the chlorination of benzene catalyzed by iron trichloride has been determined and quantified. Vanden Berg, H.; Westernick, R. M. *Ind. Eng. Chem. Fundam.* **1976**, *15*, 164–71. The authors reported significant and rapid variations in observed rates with increased H_2O concentrations. The rate changes were correlated to distribution of hydrated iron(III) chloride species.

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[30] From the Arrhenius equation slope and intercept values, we calculate a third-order rate constant for the $TiCl_4$-catalyzed reaction of benzyl chloride and benzene in nitromethane at −27 °C to be $k_3 = k_1/[TiCl_4]_0^2 = 2 \times 10^{-3}$. From the value of $k_2 = k_1/[SbCl_5]_0 = 0.27$ at this temperature the relative rate of $SbCl_5$ to $TiCl_4$ is 135.

[31] In ref 4b, Table IX, "evidence" is given for first-order aromatic dependence. This argument is readily seen to be incorrect. For example, in the case of 3:1, toluene:benzene, the 17.9 toluene product/benzene product ratio must be divided by three, not because the reaction is first order in aromatic but because this is a *statistical* correction which must always be applied, regardless of reaction order. Even if the reaction was zero order in aromatic, a 3:1 toluene:benzene ratio must be corrected for, since there is 3 times the chance of toluene product formation.

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[33] Olah, G. A.; Kuhn, S. J.; Flood, S. H. *J. Am. Chem. Soc.* **1962**, *84*, 1688–1695.

[34] This may seem surprising in light of the discrepancy in our absolute rate constants. However, we have shown[16] that the injection of H_2O does not change our competitive results *in nitromethane*.

Table XIV. Absolute Rate Data for Friedel-Crafts Benzylation Reactions in Nitromethane and Sulfolane

$XC_6H_4CH_2Cl$	catalyst	solvent	rate constant, benzene reaction	temp, °C	relative rate	$\Delta H^{\ddagger}$, kJ/mol	$\Delta S^{\ddagger}$, J/(deg mol)
p-NO_2	$AlCl_3$	CH_3NO_2	6×10^{-5}[a]	20	1	71 ± 15[b]	-85 ± 46[b]
3,4-diCl	$AlCl_3$	CH_3NO_2	0.015[c]	25	250		
p-Cl	$AlCl_3$	CH_3NO_2	0.6[c]	20	10,000		
H	$TiCl_4$	CH_3NO_2	0.38[d]	30	1	53 ± 11	-78 ± 35
p-CH_3	$TiCl_4$	CH_3NO_2	35[d]	30	92	52 ± 8	-41 ± 32
H	$SbCl_5$	sulfolane	0.14[e]	40	1	29 ± 2	-170 ± 9
H	$SbCl_5$	CH_3NO_2	0.27[d]	-27	62[f]		

[a] For a reaction 1 M in benzene. [b] ± standard deviation. [c] $k_1/[AlCl_3]_0$, $M^{-1}\ s^{-1}$. [d] $k_1/[TiCl_4]_0^2$, $M^{-2}\ s^{-1}$. [e] $k_1/[SbCl_5]_0$, $M^{-1}\ s^{-1}$. [f] At -27 °C.

In all cases except *p*-nitro benzylation, the formation of the electrophile, *E*, is rate determining. Thus the competitive method measures k_T/k_B from product concentrations for the reactions

$$E + C_6H_6 \rightarrow$$
$$E + C_6H_5CH_3 \rightarrow$$

For benzylation with benzyl chloride or benzylsulfonyl chloride all the competitively determined k_T/k_B values and isomer percentages agree closely, regardless of catalyst chosen. This supports the concept of a fast step involving the attack of the benzyl cation (or possibly benzyl cation–catalyst anion pair) on the aromatic.

Benzylation involving *p*-xylyl chloride is also zero order in aromatic. The rate-determining formation of the electrophile is about 90 times faster than that for benzyl chloride (Table XIV), yet the substrate selectivity has increased markedly (Table VII) to the point that the *p*-xylyl chloride reaction fits Brown's relationship ($b = 1.2$).

Why should the presence of a methyl group in the para position of the electrophile increase the substrate selectivity by a factor of 20? Why do reactions involving the benzyl, p-chlorobenzyl and 3,4-dichlorobenzyl electrophiles not fit Brown's relationship? We do not know the rate constants for the electrophile–aromatic reactions. However, the rate data for electrophile formation supply a clue as to their relative stability (Table XIV). Electron donation should stabilize the formation of a benzyl carbonium ion and thus the *p*-xylyl ion should be more stable than a benzyl cation.[36]

Following Jenck's approach,[37] the change in substrate selectivity may be explained by the following argument. Quite possibly the xylyl cation is diffusionally equilibrated in solution and thus can selectively choose a partner. The benzyl, *p*-chlorobenzyl, and 3,4-dichlorobenzyl cations, being less stable (more reactive), may react faster than they can diffuse and thus show little selectivity. This model is illustrated in Figure 1 (from Jencks, ref 37, Figure 4).

It might be argued that ions reacting at the diffusion-controlled rate should show no positional selectivity. This may not necessarily be so. The following argument has been given by Rys.[38] "To avoid misinterpretation of the kinetic data one must specify clearly the influence of these diffusion effects on the substrate and positional selectivity. Whereas the *substrate selectivity* can depend on these diffusional effects, the *positional selectivity* ... is to a first approximation *independent* of mass diffusion occurring *prior* to the encounter complex formation. (This holds in *nonionic* systems if one assumes that no long-range interaction is operating on the reactants. However, in diffusion-limited reactions between *ions* this assumption would seem to be violated, as coulombic interaction might already influence the direction of the approach of the reagent before the solvent cage is formed.)

In order to understand positional selectivities in diffusion-limited reactions, we must appreciate the difference between gas-phase and liquid-phase chemical transformations. Whereas in gas-phase reactions the lifetime of an encounter complex lasts only for one collision, it is estimated that an encounter complex of two reactants in most solvents at room temperature survives as many as 10 to 1000 collisions between the reactants before they separate again (cage effect).... It is for this reason that, in solution, even when the formation of the encounter complex is the rate-limiting step, positional selectivity is still determined by the different chemical reactivities of the various reaction positions. Only if, in the very extreme case, every collision within the encounter complex were successful in giving the reaction products would we find a statistical distribution of isomers as is found in collision-limited gas-phase reactions."

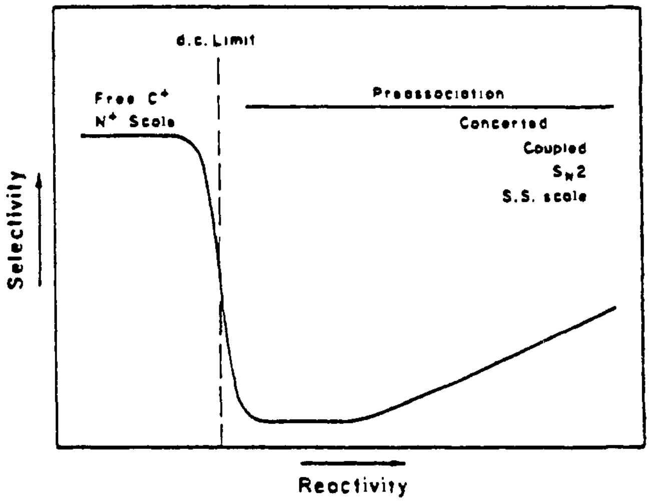

Figure 1. Diagram from ref 37 (with permission of the American Chemical Society) showing the changes in selectivity with changing reactivity of a carbocation. A stable intermediate will show a large selectivity toward nucleophiles; a less stable intermediate will react at a diffusion-controlled rate and show essentially no selectivity; a still less stable intermediate will show a small selectivity by stabilization of the transition state of a preassociation mechanism by the entering reagent; and a concerted reaction with an "intermediate" that is too unstable to exist will show a larger selectivity in an S_N2 reaction.

Continuing with Jencks' model, decreasing the stability of the carbocation further should lead eventually to a mechanism in which an S_N2 displacement path is preferred. This appears to be the case for the reaction of *p*-nitrobenzyl chloride. It is clearly first order in aromatic for both benzene and toluene (Table XII). The calculated slope $b = 1.4$ is in excellent agreement with Brown's selectivity relationship.[39] Furthermore, the $\Delta S^{\ddagger}$ value of -85 J/(deg mol) is quite typical of S_N2-type reactions.

The kinetic results for the *p*-nitro compound are crucial because although they apparently fit Jencks' approach they are inconsistent with Olah's mechanism. Benzylation reactions involving strong electrophiles such as the benzyl, p-chlorobenzyl, and 3,4-dichlorobenzyl species do not fit Brown's relationship and may well

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(35) Takematsu, A.; Sugita, K.; Nakane, R. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2082–2085.

(36) Van Pelt, P.; Buck, H. M. *J. Am. Chem. Soc.* **1976**, *98*, 5864–5870. They found benzyl cation stability to depend strongly on para substituents. The stability order was found to be $OCH_3 > CH_3 > F > Br = H > NO_2$.

(37) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161–169.

(38) Rys, P. *Acc. Chem. Res.* **1976**, *9*, 345–351. For another example of positional selectivity in an encounter controlled reaction, see: Perrin, C. L.; Schiraldi, D. A.; Arrhenius, G. M. L. *J. Am. Chem. Soc.* **1982**, *104*, 196–201.

(39) Less can be said concerning the noncompetitively determined k_T/k_B of 1.2. This ratio is surprisingly low, possibly because the rate dependence on $AlCl_3$ may be higher than one (Table VII) but more likely because of appreciable data scatter in only six runs.

involve early transition states resembling π complexes. However, this must also be predicted for the stronger electrophile in the p-nitro benzylation reaction. Yet the reaction fits Brown's relationship and this implies a transition state resembling a Wheland (σ complex) intermediate. Thus it appears that the data are more satisfactorily explained with Jencks' approach.

Olah has suggested that in the case of p-nitro benzylation meta substitution may have been enhanced through para–meta migration of the σ complex prior to deprotonation. While isomerization is a common Friedel–Crafts side reaction, the following is offered as evidence of its relative unimportance in this reaction: first, if isomerization were occurring, *some* change in product isomer distribution would be expected.[40] None was seen (Table XIII) in *any* run. Second, since the stability of the benzyl cation is a prime factor in intramolecular or intermolecular (disproportionation) migration, the p-nitro benzyl group would seem to be the *least* likely to undergo either side reaction. If the p-nitro product meta percentage was raised to 22% by isomerization, there should have been some evidence of high meta percentages and/or disproportionation in the other cases.

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Registry No. $TiCl_4$, 7550-45-0; $SbCl_5$, 7647-18-9; $AlCl_3$, 7446-70-0; C_6H_6, 71-43-2; $C_6H_5CH_3$, 108-88-3; $C_6H_5CH_2Cl$, 100-44-7; p-$ClC_6H_4CH_2Cl$, 104-83-6; 3,4-$Cl_2C_6H_3CH_2Cl$, 102-47-6; p-$NO_2C_6H_4CH_2Cl$, 100-14-1; p-$CH_3C_6H_4CH_2Cl$, 104-82-5.

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(40) Olah's idea (Olah, G. A.; Olah, J. A.; Ohyama, T. *J. Am. Chem. Soc.* in press) of deuterium labeling as a test of isomerization is an excellent one. However, even this may not be definitive due to acid-catalyzed hydrogen–deuterium exchange in these systems.

Study of ^{1}H Chemical Shifts and Couplings with ^{19}F in 9α-Fluorocortisol. Application of a Novel ^{1}H–^{13}C Chemical Shift Correlation Technique with Homonuclear Decoupling

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Abstract: ^{1}H–^{13}C chemical shift correlation, selective flip of distant protons, and distortionless enhancement by polarization transfer are combined into a new pulse sequence which eliminates most homonuclear J couplings. Correlation maps facilitate easy assignments and accurate measurements of ^{1}H chemical shifts, geminal couplines ($^2J_{HH}$), and heteronuclear couplings with additional spins. The results are obtained without having to resolve the complicated homonuclear multiplets. The study of 9α-fluorocortisol demonstrates the advantages of this method over the conventional chemical shift correlation method. The values of proton chemical shifts, geminal couplings ($^2J_{HH}$), and heteronuclear couplings with fluorine are explained by substitution effects as well as the conformational change of the A ring.

One-dimensional (1-D) ^{1}H spectra of steroids are very complicated, since resonances of over 20 protons are distributed mostly in a narrow spectral region between 0.5 and 2.5 ppm downfield from Me_4Si. Assignment was possible only for methyl, olefinic, and some other protons shifted signficiantly downfield due to substitution.[1] Therefore, the spectra did not provide much information about the molecular conformation in solution. Recently, Hall and Sanders[2,3] and Barrett et al.[4] used a combination of ^{1}H two-dimensional (2-D) J resolved spectroscopy, NOE differences, and selective homonuclear decoupling to assign the proton spectra of several steroids.

Further information can be obtained from heteronuclear chemical shift correlation NMR[5-8] which separates ^{1}H and ^{13}C resonances along the F_1 and F_2 dimensions, thus avoiding overlap of peaks and establishing an indispensable link between the spin systems. Although one-bond coupling $^1J_{CH}$ unambiguously correlates chemical shifts and simplifies assignments, the experiments require acquisition of weak ^{13}C signals and measuring times may become unacceptably long. Efficiency of heteronuclear 2-D spectroscopy can be improved by selective proton flips or other spin manipulations[9-13] which suppress "unimportant" interactions.

Table I. Relative Phases of Radio-Frequency Pulses in A and C

step	ϕ_1	ϕ_2	ϕ_3
1	$-y$	x	x
2	$-x$	$-y$	$-x$
3	y	$-x$	x
4	x	y	$-x$

In a previous paper[14] we utilized a combination of ^{1}H–^{13}C chemical shift correlation and indirect homonuclear decoupling to determine

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