Parameters Affecting the Variable Isomer Distribution in the Friedel–Crafts Acetylation of Hemimellitene

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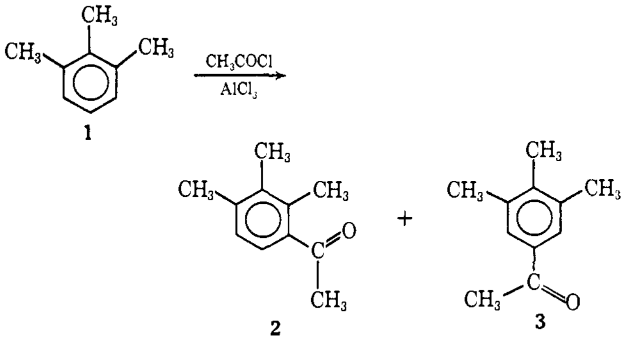
Abstract: The ratio of isomers derived from the aluminum chloride catalyzed acetylation (acetyl chloride) of hemimellitene (**1**) (1,2,3-trimethylbenzene) is strongly dependent upon (1) the mode of addition of reagents, (2) over-all concentration of reactants, (3) the Lewis acid catalyst, and (4) solvent. Under appropriate conditions, formation of either isomer (>95% purity) can be readily achieved. Utilizing the same reaction parameters, other representative aromatic hydrocarbons were acetylated, and their isomer distributions determined. The mechanistic implications of the results of acetylation are discussed.

Acetylation of the xylenes, trimethylbenzenes (with the exception of hemimellitene), and tetramethylbenzenes by acetyl chloride–aluminum chloride in ethylene dichloride solution gives isomer distributions of products which agree extremely well with predicted values calculated from partial rate factors obtained from the acetylation of toluene.[1] For hemimellitene, calculations predict large amounts (~65%) of the *ortho* isomer, 2,3,4-trimethylacetophenone. Experimentally, however, greatly diminished *ortho* substitution was observed, and 3,4,5-trimethylacetophenone is the major product. This discrepancy and the essential absence of *ortho* isomers from toluene and other monoalkylbenzenes[2] have been attributed to the bulkiness of the acetylating agent, *i.e.*, the acetyl chloride–aluminum chloride complex.

In benzoylation of naphthalene, the presence of aluminum chloride complexing agents (*e.g.*, nitrobenzene and benzoyl chloride) decreases the amount of α-ketone.[3] This was also attributed to the steric bulk of these complexes.[4] However, the addition of excess acid halide in acetylation of benzene derivatives has not been found to cause observable changes in rates or isomer distributions. Even in the case of the benzoylation of *p*-xylene, where all available positions are *ortho*, no change in rate is observed. The amount of *ortho* isomer (relative to *para* isomer) obtained in the benzoylation of toluene is nearly identical in benzoyl chloride,[5] nitrobenzene,[6] and ethylene dichloride[7] solution. Similarly, the amount of *o*-methylacetophenone obtained from acetylation of toluene (acetyl chloride) is identical in ethylene dichloride[8] and nitromethane[9] solvents. Obviously, the observed changes in isomer distribution with naphthalene, concurrent with changing reaction conditions, cannot be wholly attributed to a steric effect of the attacking species.

Results and Discussion

We have found that hemimellitene can be acetylated in excellent yield to give either the 4- or 5-substituted isomer in greater than 95% purity, by utilizing appropriate reaction conditions. The product distribution is extremely sensitive to the mode of addition of reagents, changes in reactant concentration, solvent, and the Lewis acid catalyst.[10]



It had been reported by Marino and Brown that the acetylation of hemimellitene gave 21% 2,3,4-trimethylacetophenone (**2**) and 79% 3,4,5-trimethylacetophenone (**3**).[1,11] As stated earlier, the "predicted" amount of **2** is 65%. This discrepancy was described as a "decreased tendency to substitute *ortho* to the strongly buttressed assembly of three methyl groups," implying a large steric effect. In our efforts to effect the acetylation, we inadvertently used a procedure described by Scharwin for the acetylation of tetralin.[12] To our surprise, **2** not **3** was found to be the major product.

Initially this result was thought to be a concentration effect, since the final concentrations *via* Scharwin's procedure are approximately ten times that of the procedure of Marino and Brown. A number of reactions were therefore carried out under a variety of conditions (concentration, solvent, temperature) using both of the

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(1) G. Marino and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 5929 (1959).

(2) H. C. Brown and G. Marino, *ibid.*, **81**, 5611 (1959).

(3) H. F. Bassilias, S. M. Maker, and A. Y. Salem, *Bull. Soc. Chim. France*, 72 (1954).

(4) The benzoylation of naphthalene is reviewed by F. R. Jensen and G. Goldman in "Friedel Crafts and Related Reactions," Vol. III, Part 2, G. A. Olah, Ed., Interscience Publishers, New York, N. Y., 1964, pp 1024–1032.

(5) H. C. Brown and F. R. Jensen, *J. Am. Chem. Soc.*, **80**, 2296 (1958).

(6) H. C. Brown, B. A. Bolto, and F. R. Jensen, *J. Org. Chem.*, **23**, 417 (1958).

(7) H. C. Brown and G. Marino, *J. Am. Chem. Soc.*, **81**, 3308 (1959).

(8) H. C. Brown, G. Marino, and L. M. Stock, *ibid.*, **81**, 3310 (1959).

(9) G. A. Olah, M. E. Moffatt, S. J. Kuhn, and B. A. Hardie, *ibid.*, **86**, 2198 (1964).

(10) Our interest in the acetylation of hemimellitene originated with attempts to prepare pure bromo isomers of this hydrocarbon. It was felt that acetylation, and separation of the trimethylacetophenones by distillation, would provide a solid stepping stone for the proposed syntheses.

(11) Marino and Brown's acetylation procedure involves the addition of a preformed acetyl chloride–aluminum chloride complex in ethylene dichloride to the hydrocarbon in the same solvent, at room temperature.

(12) W. Scharwin, *Chem. Ber.*, **35**, 2511 (1902). This procedure involves the addition of a solution of acetyl chloride and the hydrocarbon in carbon disulfide to a slurry of aluminum chloride in the same solvent at 0°. We have utilized ethylene dichloride and carbon disulfide in this investigation.

Table I. The Effect of Reaction Conditions on the Isomer Distribution in the Acetylation of Hemimellitene

Run no.	Initial molarity			Mole ratio	Final concn of $AlCl_3$, M	Solvent	Temp, °C	% acetophenones	
	1	AcCl	$AlCl_3$	1:AcCl:$AlCl_3$				2	3
Scharwin's procedure[a]									
1	4.64	5.07	2.60[c]	1.0:1.1:1.2	1.80	$C_2H_4Cl_2$	0	69	31
2	3.00	3.33	1.90[c]	1.0:1.1:1.2	1.25	$C_2H_4Cl_2$	0	83	17
3	1.50	1.67	0.95[c]	1.0:1.1:1.2	0.63	$C_2H_4Cl_2$	0	91	9
4	0.75	0.83	0.48[c]	1.0:1.1:1.2	0.32	$C_2H_4Cl_2$	0	>95	<5
5	0.75	0.83	0.48[c]	1.0:1.1:1.2	0.32	$C_2H_4Cl_2$	25	92	8
6[b]	1.50	3.33	1.90	1.0:1.1:1.2	1.25	$C_2H_4Cl_2$	0	91[g]	9
7[b]	0.38	0.83	0.48	1.0:1.1:1.2	0.32	$C_2H_4Cl_2$	0	94	6
8	3.00	3.33	1.90[c]	1.0:1.1:1.2	1.25	CS_2	0	>95	<5
9	1.50	1.67	0.95[c]	1.0:1.1:1.2	0.63	CS_2	0	100	0
10	0.75	0.83	0.48[c]	1.0:1.1:1.2	0.32	CS_2	0	100	0
11	0.75	0.83	0.48	1.0:1.1:1.2	0.32	$PhNO_2$	0	20	80
Marino and Brown's procedure[d]									
12	3.33	3.33	3.33	1.0:1.0:1.0	1.67	$C_2H_4Cl_2$	25	45	55
13	1.67	1.67	1.67	1.0:1.0:1.0	0.83	$C_2H_4Cl_2$	25	47	53
14	1.25	0.63	0.63	1.0:1.0:1.0	0.42	$C_2H_4Cl_2$	25	38	62
15	0.80	0.40	0.40	1.0:1.0:1.0	0.26	$C_2H_4Cl_2$	25	31	69
16	0.40	0.20	0.20	1.0:1.0:1.0	0.13	$C_2H_4Cl_2$	25	8	92
17	0.20	0.10	0.10	1.0:1.0:1.0	0.067	$C_2H_4Cl_2$	25	5	95
18	0.10	0.05	0.05	1.0:1.0:1.0	0.034	$C_2H_4Cl_2$	25	3	97
19	3.33	6.66	3.33	1.0:2.0:1.0	1.67	$C_2H_4Cl_2$	25	43	57
20	0.10	0.10	0.05	1.0:2.0:1.0	0.034	$C_2H_4Cl_2$	25	9	91
21[e]	0.10	0.05	0.05	1.0:1.2:2.0	0.067	$C_2H_4Cl_2$	25	69	31
22[f]	0.20	0.10	0.10	1.0:1.0:1.0	0.067	$C_2H_4Cl_2$	25	38	62
23[f]	0.20	0.20	0.10	1.0:2.0:1.0	0.067	$C_2H_4Cl_2$	25	33	67
24[f]	0.20	0.40	0.10	1.0:4.0:1.0	0.067	$C_2H_4Cl_2$	25	26	74
25	0.10	0.05	0.05	1.0:1.0:1.0	0.034	$PhNO_2$	25	10	-90

[a] For the Scharwin procedure, see ref 12. [b] The acetyl chloride was added to a solution of hemimellitene and aluminum chloride. [c] A slurry of aluminum chloride in the solvent. [d] For the Marino and Brown procedure, see ref 11. [e] The hemimellitene solution contained an additional equivalent of aluminum chloride. [f] Inverse Marino and Brown addition sequence. [g] Includes "rearranged ketone, 2,4,5-trimethylacetophenone (27%), which was formed from acetylation of pseudocumene resulting from the concomitant aluminum chloride catalyzed isomerization of hemimellitene.[b]

aforementioned procedures. The isomer distributions obtained are listed in Table I. Interconversion of **2** and **3** does not occur under these reaction conditions. It is apparent that while solvent and concentration are important factors, they do not explain the anomalous isomer ratios in a straightforward manner. As total reactant concentrations decrease, higher ratios of **2** (relative to **3**) are obtained *via* Scharwin's procedure (ethylene dichloride or CS_2, runs 1-4 and 8-10), whereas under Marino and Brown's conditions (runs 12-18) **3** becomes the exclusive isomer. This trend is illustrated in Figure 1.

Arguments for a large steric effect of the attacking species are groundless, since from Scharwin's procedure the most sterically hindered ketone is obtained, while from Marino and Brown's procedure, at a given concentration, isomer ratios that are essentially independent of excess acetyl chloride result. (Compare run 12 with 19 and run 18 with 20.)

Jensen and Goldman have advanced an explanation for the variable isomer distribution in the benzoylation of naphthalene.[4] They proposed that the acylation occurs by both a second- and third-order process and that the isomer distribution from each process is different.[13] The kinetics of the benzoylation of naphthalene were further studied by Oziomek[14] and concurrent second- and third-order reaction processes were demonstrated. The nature of the attacking species was not specified[15] but reaction mechanisms (second and third order) incorporating (1) an oxonium complex, (2) an acylium complex, and (3) an acylium ion were presented. In either mechanism, the initially formed α or β σ complexes can decompose directly (unimolecularly) or decomposition may be aided by a molecule of aluminum chloride (present in solution as a donor-acceptor complex) leading to over-all third-order kinetics. Why the

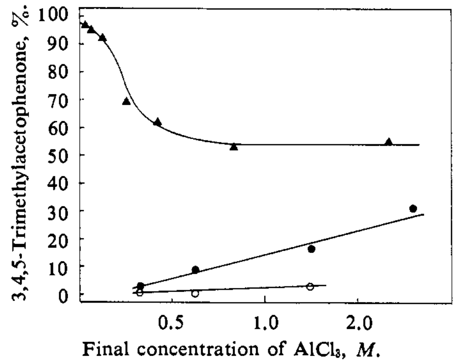

Figure 1. The effect of solvent and reactant concentration on the isomer distribution in the acetylation of hemimellitene: ▲, Marino and Brown procedure in $C_2H_4Cl_2$; ●, Scharwin procedure in $C_2H_4Cl_2$; ○, Scharwin procedure in CS_2

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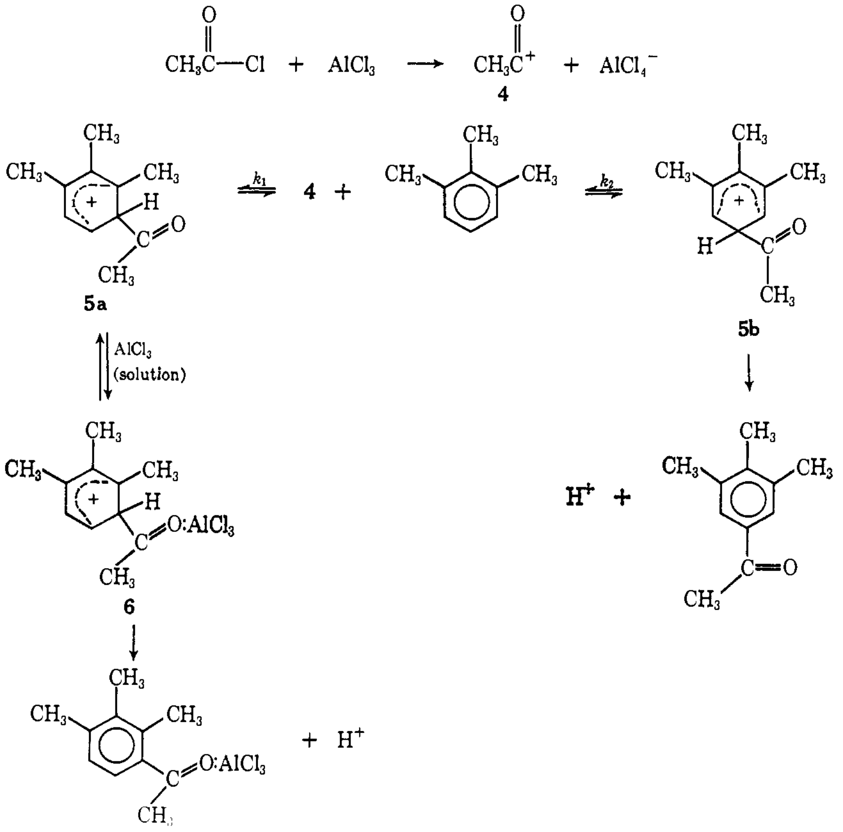
(13) An isomer distribution of 38% α and 62% β was calculated for the second-order process. An isomer distribution of 94% α and 6% β was calculated for higher addition compound concentrations, corresponding to the third-order reaction.

(14) J. Oziomek, Ph.D. Thesis, The University of California, Berkeley, Calif., 1968.

(15) Current feeling on the nature of the attacking species is based on the fact that isomer ratios of benzoylation and acetylation of toluene are essentially independent of aluminum chloride complexing species and that the kinetics of the benzoylation of *p*-xylene are also independent of excess benzoyl chloride. The logical species which would fit these experimental data is the "free" acylium ion.

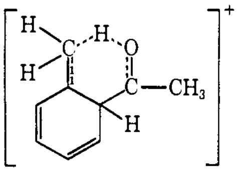
Scheme I



third-order process becomes energetically favorable was not known, but it was postulated that the stability of the intermediate σ complex must be involved.

It is our contention that the acetylation of hemimellitene also occurs by second- and third-order processes which yield respectively the 5 and 4 isomers (**3** and **2**). A possible mechanistic pathway is illustrated in Scheme I.[16] In keeping with current theory, we have postulated the initial formation of an acylium ion (**4**) in the reaction sequence.

The formation and fate of σ complexes **5a** and **5b** are dependent upon reaction conditions. In order for the third-order process to occur selectively, one of the σ complexes must be more stable than the other.[17] The more stable σ complex should be **5a**, since dispersal of the positive charge can occur adjacent to two methyl groups as compared to one methyl group in **5b**.[19] It is also conceivable that intramolecular coordination as suggested in **7** would give added stability to **5a**. Therefore, under conditions of acetylation (either procedure), formation of **5a** must be the more facile reaction. Since "free" $AlCl_3$[20] is always present in Scharwin's procedure, **5a** could then interact with the excess Lewis acid (**6**, Scheme I) to yield the ketone **2**. Apparently this *ortho* σ complex has sufficient stability at room temperature (run 5) as well as at 0°, since in each case ketone **2** is essentially the exclusive isomer produced. The concentration effect can be interpreted inasmuch as the extent of the third-order process is determined by the ratio of the gross amount of "free" aluminum chloride in solution[21] relative to **5a**. Under dilute conditions[22] this ratio is high, leading to the exclusive formation of the third-order reaction product. When reactant concentrations are high, the relative amount of $AlCl_3$ in solution is not sufficient to intercept **5a** and since σ complex formation is reversible, the reaction proceeds *via* **5b** which decomposes directly to give **3**.



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(16) We would like to thank Professor Jensen for making available to us a copy of Dr. Oziomek's Ph.D. Thesis. It has been a great aid in the interpretation of our data.

(17) **5a** and **5b** would be expected to be more stable than those formed from benzene or toluene since hemimellitene is much more basic than benzene or the lesser methylated aryls. Relative rates of acetylation of the methylbenzenes bear this out.[1] Also, the σ complex of hemimellitene and hydrogen fluoride has been found to be ~110 times more stable than that of toluene.[18]

(18) M. Kilpatrick and F. E. Luborsky, *J. Am. Chem. Soc.*, **75**, 577 (1953).

(19) The 2,4 arrangement of methyl groups increases the stability of σ complexes quite markedly. For example, the *o*-xylene–hydrogen fluoride σ complex is ~24 timess less stable than the *m*-xylene–hydrogen fluoride complex.[18]

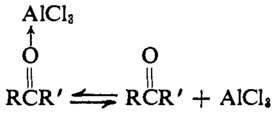
(20) Aluminum chloride is partially soluble in carbon disulfide. It is our belief that the third-order process is aided by free $AlCl_3$ in solution, rather than the donor–acceptor complex as proposed by Oziomek.[14]

(21) That free aluminum chloride is the actual species involved in the third-order mechanism is exemplified in runs 22–24. The addition of excess acetyl chloride in the inverse Marino and Brown procedure should decrease the amount of free $AlCl_3$ in the system if dissociation equilibria are involved, and the amount of 2,3,4-trimethylacetophenone should decrease. Experimentally this is observed.

(22) Reactant conditions in the Scharwin procedure are misleading. The initial concentration of $AlCl_3$ in solution is independent of the ratio of total $AlCl_3$ in the system to solvent. Under concentrated conditions the concentration of acetyl chloride is relatively high and the total amount of soluble $AlCl_3$ is not sufficient to maintain third-order kinetics. However, as greater amounts of solvent are utilized,the gross amount of $AlCl_3$ in solution is greater and the concentration of acetyl chloride is diminished, giving rise to a system where the rate of solution of $AlCl_3$ is sufficient to maintain essentially exclusive third-order kinetics.

In Marino and Brown's acetylation procedure the concentration of free $AlCl_3$ is minimized. The most stable σ complex must also be formed in this procedure, but since "free" aluminum chloride is not available, **5a** formation is reversed and the reaction proceeds *via* **5b**. Under high reactant concentrations some free $AlCl_3$ is made available *via* equilibria involving acceptor-donor complexes (Scheme II). The effect of excess aluminum chloride in Marino and Brown's procedure is shown in run 21. One additional equivalent of $AlCl_3$ in the hydrocarbon solution allows the third-order process to predominate (69% **2**). It must be emphasized that this reaction was carried out under conditions which without the added $AlCl_3$ gave 97% **3** (run 18). The inverse Marino and Brown procedure, in which the hemimellitene is added to the acetyl chloride-aluminum chloride complex (run 22), also effectively increases the aluminum chloride concentration (over the normal mode of addition); compare with run 17 giving greater amounts of **2**.

Scheme II



$$\overset{\overset{AlCl_3}{\uparrow}}{\underset{RCR'}{\overset{O}{\|}}} \rightleftharpoons \underset{RCR'}{\overset{O}{\|}} + AlCl_3$$

a, R = CH_3; R' = Cl
b, R = phenyl; R' = CH_3

When both Scharwin's and Marino and Brown's procedure are carried out in nitrobenzene solution, the reactions are homogeneous. Most of the aluminum chloride is complexed with the solvent, and as expected, second-order processes predominate (reactions 11 and 25).

To test this mechanistic hypothesis, the relative rates of acetylation of hemimellitene in the 4 position (which we will refer to as α) and 5 position (β position) were calculated, utilizing the inverse Marino and Brown procedure. By plotting per cent α (relative to β) as a function of per cent reaction for systems with $AlCl_3$-acetyl chloride ratios of 1.0 and 0.25, initial isomer ratios can be calculated. These data are plotted in Figure 2.

$$\frac{-\mathrm{d}(C_9H_{12})}{\mathrm{d}t} = \frac{\mathrm{d}\alpha}{\mathrm{d}t} + \frac{\mathrm{d}\beta}{\mathrm{d}t} \tag{1}$$

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = 2K_3[C_9H_{12}][CH_3CO^+][AlCl_3] \tag{2}$$

$$\frac{\mathrm{d}\beta}{\mathrm{d}t} = K_2[C_9H_{12}][CH_3CO^+] \tag{3}$$

Division of eq 2 by eq 3 yields

$$\frac{\mathrm{d}\alpha}{\mathrm{d}\beta} = \frac{2K_3[AlCl_3]}{K_2} \tag{4}$$

Equation 4 can be used in its differential form provided initial isomer ratios are employed.

$$\frac{\alpha_i}{\beta_i} = \frac{2K_3[AlCl_3]}{K_2}$$

Therefore

$$\frac{68}{32} = \frac{2K_3}{K_2}[X] \qquad \frac{47}{53} = \frac{2K_3}{K_2}[Y] \tag{5}$$

and

$$\frac{[X]}{[Y]} = 2.39 \text{ or } X = 2.39Y \tag{6}$$

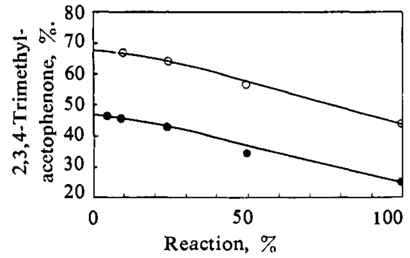


Figure 2. Per cent 2,3,4-trimethylacetophenone (α) as a function of per cent reaction in the inverse Marino and Brown procedure (initial concentration of $AlCl_3$, 0.10 *M;* hemimellitene, 0.20 *M*): ○, 1:1 $AlCl_3$:AcCl; ●, 1:4 $AlCl_3$:AcCl.

where X and Y are the concentrations of free $AlCl_3$ for each run at 0% reaction.

Utilizing the equilibrium expression for the dissociation of the acetyl chloride-aluminum chloride complex (this is the major equilibrium involving free $AlCl_3$ at 0% reaction)

$$K_{\text{dis}} = \frac{X^2}{0.10 - X} = \frac{[Y][0.30 + Y]}{[0.10 - Y]} = \frac{[AlCl_3][CH_3COCl]}{[CH_3COCl \cdot AlCl_3]} \tag{7}$$

Solving this equation with the aid of eq 6 yields $Y = 0.026$. Putting this value into eq 7 gives $K_{\text{dis}} = 0.115$ mole/l.

Utilizing eq 5

$$0.89 = \frac{2K_3}{K_2}[0.026] \qquad \frac{K_3}{K_2} = 17$$

This value, being greater than one, is significant in that it is consistant with the experimental data, namely, that formation of the third-order-process ketone, **2**, is more facile than formation of **3**. However, since K_3 and K_2 are the over-all rate constants, the ratio K_3/K_2 value tells us nothing about the relative stabilities of **5a** and **5b** (K_1 *vs.* K_2) or the relative rates of decomposition of these σ complexes to form product.

We were also interested in acetylating other aromatic hydrocarbons using Scharwin's and Marino and Brown's conditions (which gave >95% of either acetylhemimellitene) since the effect of hydrocarbon structure on the isomer distribution could serve as another test of this mechanistic hypothesis, and also that it might lead to general synthetic procedures for specific acetyl isomer formation. Compounds (naphthalene, tetralin, *o*-xylene, and toluene) were chosen which could yield at least two nonrearranged ketones. The isomer distributions obtained are listed in Table II.

Of the four compounds acetylated, only naphthalene gives results which are similar to hemimellitene. The anomalous isomer distributions obtained in the acetylation of naphthalene are well known and have been extensively investigated.[3,23] That the isomer distribution of the acetonaphthalenes is highly dependent upon the aluminum chloride concentration is quite evident. However, the same arguments used to interpret the selective acetylation of hemimellitene cannot be made in this instance, since benzylic cation structures can be drawn for both α and β σ complexes, **8** and **9**, respec-

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(23) (a) G. Baddeley, *J. Chem. Soc.*, S99 (1949); (b) H. F. Bassilios and A. Y. Salem, *Bull. Soc. Chim. France*, [5] 19, 586 (1952); (c) H. F. Bassilios, S. M. Makar, and A. Y. Salem, *ibid.*, 1430 (1958).

Table II. The Acetylation of Various Hydrocarbons Utilizing Scharwin's and Marino and Brown's Procedure

Hydrocarbon	Mode of reaction	Isomer distribution[c] (position of acetyl function) 1	2	3	4	5	6
Naphthalene	A[a]	99	1				
	B[b]	7	93				
Tetralin	A					8	92
	B					0	100
o-Xylene	A			0	100[d]		
	B			0	100		
Toluene	A		7.5[e]		92.5		
	B		2.2[e]		97.8		

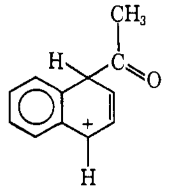
[a] Scharwin's procedure, using concentrations of run 5, Table I. [b] Marino and Brown's procedure, using concentrations of run 18, Table I. [c] As the percentage of total unrearranged ketone product. [d] The reaction product also contained 4% 2,4-dimethylacetophenone, which most likely arises *via* $AlCl_3$-catalyzed isomerization of *o*-xylene, followed by acetylation. See L. Friedman and R. Koca, *J. Org. Chem.*, **33**, 1255 (1968). [e] A small amount of 3-acetyltoluene was also formed.

Table III. The Effect of Lewis Acid Catalyst on the Isomer Distribution in the Acetylation of Hemimellitene

Run no.	Catalyst	Initial molarity[a] **1**	AcCl	Cat.	Mole ratio **1**:AcCl:$AlCl_3$	Final concn of cat., *M*	% acetylhemimellitene **2**	**3**
Scharwin's procedure[b]								
1	$FeCl_3$	3.00	3.33	1.90	1.0:1.1:1.2	1.25	19	81
2	$FeCl_3$	0.75	0.83	0.48	1.0:1.1:1.2	0.32	13	87
3	$SbCl_5$	0.75	0.83	0.48	1.0:1.1:1.2	0.32	25	75
4	$SnCl_4$	0.75	0.83	0.48	1.0:1.1:1.2	0.32	32	68
Marino and Brown's procedure[c]								
5	$FeCl_3$	0.10	0.05	0.05	1.0:1.0:1.0	0.034	10	90

[a] All reactions were carried out in ethylene dichloride. [b] Reaction temperature 0°. [c] Reaction temperature 25°.

tively. Although the acetylation of naphthalene may be proceeding *via* mixed-order kinetics, unfortunately, the isomer distributions of the acetonaphthalenes give no clue as to the reaction mechanisms involved.



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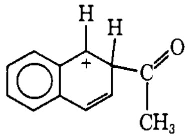

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On the other hand, tetralin, *o*-xylene, and toluene are less basic than hemimellitene. They would be expected to give rise to much less stable σ complexes under acetylating conditions. The relative stabilities of the possible σ complexes for each of these hydrocarbons must be small, since each position (*ortho* and *para* to a methyl group) is stabilized equally by only one methyl group. The isomer distributions for these hydrocarbons are therefore more dependent upon only the steric effect of the methyl group[24] and any *ortho*-directing acid–base type of interactions similar to **7**. This is exemplified in the low yields of *ortho*-acetyl derivative for each of these hydrocarbons utilizing the Scharwin procedure.

Utilizing Lewis acids other than aluminum chloride to effect the acetylation of hemimellitene also causes variations in the isomer distribution (Table III). Both acetylation procedures give **3** as the major product.

This trend could be due to a variety of factors. If these Lewis acids are less soluble in ethylene dichloride than aluminum chloride, second-order kinetics would be expected to prevail. Also, these catalysts may not be as effective as $AlCl_3$ in attacking the more stable σ complex.

We feel that the aforementioned data are strong evidence for the occurrence of concurrent second- and third-order reaction mechanisms for hemimellitene, in which the isomer distribution is dependent upon relative σ complex stabilities and the presence of free Lewis acid in the system. Steric factors, of the acetylating species, which have been proposed by earlier workers to explain such deviations in isomer distributions, do not appear to play an important role.

The only other possibility which could conceivably explain the experimental results is the interaction of the catalyst and aromatic hydrocarbon, namely, π complex formation. Polarization of the π cloud by a molecule of catalyst might decrease the resonance stability of the aromatic ring and lower the energy barrier to the formation of σ complexes. Such interactions could also lead to concurrent second- and third-order kinetics.

π-Complex formation was observed, utilizing Scharwin's procedure. When $AlCl_3$ and hemimellitene were combined in ethylene dichloride, the Lewis acid dissolved and the solution turned bright orange. Acetylation of this preformed π complex (runs 6 and 7, Table I) also gave high yields of **2**. However, no satisfactory explanation of how π complex formation might direct electrophilic substitution (steric?) has been proposed.

We feel that the strongest evidence against π complex formation directing acetylation is the fact that >95% of either isomer is obtained in the acetylation of hemimellitene. If π complex formation is invoked to direct electrophilic substitution, then it must direct acetylation into the 4 position (Scharwin's procedure) while acetylation of non-π-complexed hemimellitene should give an isomer ratio consistent with partial rate factors (≈34% 5-acetyl). Since it does not, but gives >95% 5-acetyl, this discrepancy leads us to believe that although π complex undoubtedly takes place to a great extent, it does not control the ratio of products in the reaction.

Experimental Section

Materials. Ethylene dichloride was purified by drying over anhydrous magnesium sulfate and distilling through an 18-in. glass-helices-packed column. Nitrobenzene was J. T. Baker purified quality and the carbon disulfide was Matheson Coleman and Bell spectroquality reagent. All of the hydrocarbons studied were examined by gas chromatography and found to be at least 99% pure. Anhydrous aluminum chloride and ferric chloric powder

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(24) The methyl groups of hemimellitene must also exert a steric effect. However, this is overcome by the stability of the *ortho* σ complex.

were Matheson Coleman and Bell reagent grade, stannic chloride and antimony pentachloride were "Baker Analyzed" reagents, and the acetyl chloride was Matheson Coleman and Bell practical grade.

Analytical. Infrared and nmr spectra were obtained on a Beckman IR 8 spectrophotometer and a Varian A-60 spectrometer, respectively. All chemical shifts are reported in parts per million (ppm) on the δ scale relative to an internal standard tetramethylsilane. Gas chromatographic data were obtained on an Aerograph Hy-Fi Model 600-D or, when preparative glpc was required, on an instrument equipped with gold-plated tungsten filaments.

Acetylation of Hemimellitene. Two representative acetylation procedures are described below: the Scharwin and the Marino and Brown procedures. The concentrations given are those which gave highest selectivity for either isomer (see runs 4 and 8, Table I). Since the other methods of acetylation used in this study are simple variations of these procedures, they are not described in detail.

Acetylation Procedures. Scharwin. Acetyl chloride (1.80 g) (0.023 mol) and 2.50 g of hemimellitene (0.021 mol) in 28 ml of ethylene dichloride were added (approximately 1 drop every 2 sec)[25] to a slurry of 3.45 g of aluminum chloride (0.026 mol) in 55 ml of ethylene dichloride. The reaction temperature was maintained at 0–5° by means of an ice bath. Fifteen minutes after the addition was complete, the reaction mixture was quenched with dilute HCl, and the organic layer was separated, dried over anhydrous magnesium sulfate, and analyzed. The acetylation products were separated on a 5 ft 5% SE-30 on Chromosorb W 60–80 column at 100° and 11 psi (nitrogen). The retention times are 2,3,4-trimethylacetophenone (13 min) and 3,4,5-trimethylacetophenone (17.0 min).

Marino and Brown. The donor–acceptor complex was formed by combining 0.98 g of acetyl chloride (0.0125 mol) and 1.67 g of aluminum chloride (0.0125 mol) in 250 ml of ethylene dichloride. This was added to a solution of 1.50 g of hemimellitene (0.0125 mol) in 125 ml of ethylene dichloride, maintaining the reaction temperature at 25°. Fifteen minutes after the addition was complete, the reaction mixture was worked up and analyzed as described above.

When an analysis was required at less than 100% reaction, a measured amount of reactant was added (using a calibrated dropping funnel), the reaction mixture was allowed to stand with stirring 5 min, and a 1-ml aliquot was withdrawn, quenched, and analyzed by glpc. Then another measured amount of reactant was added, etc.

Distillation of the acetylhemimellitenes was performed on a 4-ft metal-helices-packed column, yielding material which was >99% pure *via* gas chromatography; 2,3,4-trimethylacetophenone, bp 73° (0.5 mm), $n^{25}\mathrm{D}$ 1.5384; semicarbazone derivative, mp 207.5–209°, 3,4,5-trimethylacetophenone, bp 81° (0.5 mm), $n^{25}\mathrm{D}$ 1.5421; semicarbazone derivative, mp 215.5° (lit.[26] mp 217°).

Infrared and nmr analyses were run on the distilled products. The structures of the isomers were positively identified by their nmr spectra. 3,4,5-Trimethylacetophenone exhibited a singlet at δ 2.37 (3 H), acetyl methyl; a singlet at δ 2.24 (6 H), aromatic methyls in the 3 and 5 position; a singlet at δ 2.12 (3 H), aromatic methyl in the 4 position; and a singlet at δ 7.45 (2 H), aromatic hydrogen in the 2 and 6 positions. 2,3,4-Trimethylacetophenone gave a singlet at δ 2.37 (3 H), acetyl methyl; three singlets at δ 2.27 (3 H), 2.20 (3 H), 2.09 (3 H), aromatic methyls in the 2, 3, and 4 positions; and an AB pattern centered at δ 6.93 (2 H), aromatic hydrogen in the 5 and 6 positions.

Acetylation of Other Aromatic Hydrocarbons. Naphthalene, tetralin, *o*-xylene, and toluene were acetylated, using the procedures and concentrations described above for the acetylation of hemimellitene.

Naphthalene. Identification of the acetonaphthalenes was determined by comparison of glpc retention times with authentic samples. Separation of the isomers was effected on a 5-ft 5% SE-30 Chromosorb W 60–80 column at 150° and 11 psi; retention times: 1-acetylnaphthalene 4.9 min, 2-acetylnaphthalene 6.0 min.

Tetralin. Resolution of the isomeric ketones was effected on a 5-ft 5% SE-30 on Chromosorb W 60–80 column at 150° and 11 psi. The identity of 6-acetyltetralin was confirmed by oxidation[27] to 6-tetralincarboxylic acid, mp 153–154° (lit.[28] mp 153–156°); retention times: 5-acetyltetralin 4.4 min, 6-acetyltetralin 6.7 min.

Toluene. Separation of the isomeric ketones was effected on a 6ft 20% Carbowax 1500, 5% Bentone on Chromosorb W 60–80 column at 160° and 8 psi. Retention times were *o*-methylacetophenone 9.4 min, *m*- and *p*-methylacetophenones 13.4 min.

***o*-Xylene.** Identification of the acetylxylenes was determined by comparison of glpc retention times with authentic samples of 2,4-dimethylacetophenone, 2,3-dimethylacetophenone, and 3,4-dimethylacetophenone. The structure of 2,4-dimethylacetophenone was further verified by comparison of an infrared spectrum of glpc trapped material with that of the authentic isomer. Separation of the isomeric ketones was effected on a 5 ft 5% SE-30 on Chromosorb W 60–80 column at 75° and 11 psi. Retentions were 2,4-dimethylacetophenone 10.5 min, 2,3-dimethylacetophenone 14.5 min, and 3,4-dimethylacetophenone 16.8 min.

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(25) Isomer ratios of the acetylated hemimellitenes were dependent upon the rate of addition of reactants. Therefore, we standardized the addition rate of all experimental procedures to approximately one drop every 2 sec.

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