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Acylation of aromatic substrates with ketenes. An example of vinyl oxocation reactivity

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Acylations of aromatic substrates with ketenes involve the reactivity of species similar to vinyl cations. Resonance stabilization of ketene – aluminum chloride complexes seems to make these complexes less reactive than corresponding vinyl cations.

The kinetic isotope effect of the reaction with dimethylketene and benzene is 1.06, compatible with vinylcation cases, but not with acylation with CH_3COBF_4 types of electrophiles.

Substrate specificity was determined from *k* (toluene)/*k* (benzene) values. It was 47.2 for dimethylketene and 173.7 for diphenylketene. The diphenylketene – aluminum chloride complex could be isolated.

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L'acylation de substrats aromatiques au moyen de cétènes fait intervenir la réactivité d'espèces semblables aux cations vinyliques. La stabilisation par résonance des complexes cétène – chlorure d'aluminium semble rendre ces complexes moins réactifs que les cations vinyliques correspondants.

L'effet isotopique cinétique de la réaction entre le diméthylcétène et le benzène est de 1.06. Il est compatible avec l'existence de cations vinyliques, mais il n'est pas compatible avec une acylation au moyen d'agents électrophiles du type CH_3COBF_4.

La spécifité du substrat est déterminée à partir des valeurs de *k* toluène/*k* benzène. Elle est de 47.2 pour le diméthylcétène et de 173.7 pour le diphénylcétène. On a pu isoler le complexe cétène – chlorure d'aluminium.

[Traduit par le journal]

Although acylations of aromatic rings with ketene have been known (1–4) for over forty years, no serious mechanistic study of this reaction has been undertaken. We report in this paper the results of experiments showing positional selectivity, the substrate selectivity, the intermolecularity of the transfer of the proton from the site of attack to the α position of the ketone, and the kinetic isotope effect. Experiments with both dimethyl and diphenyl ketenes were explored.

We used dimethylketene (DMK) prepared by Staudinger's method, pyrolysis of dimethylmalonic anhydride (5); it was redistilled before use. Diphenylketene (DPK) was prepared by the triphenylphosphine catalysed dehalogenation of 2-bromo-2,2-diphenylacetylbromide (6), and distilled before use. The yields from dimethylketene acylation with a variety of substrates are summarized in Table 1. (The low yields with benzene, in neat hydrocarbon, are in contrast to the modest yields of up to 45.0% reported by earlier workers for ketene (4).) The reaction mixtures for the reaction with benzene, by gas chromatography, revealed seven compounds besides the authentic ketone. These compounds were due to the reaction of dimethylketene with itself in the presence of aluminum chloride to give dimers, as was shown by comparing the nmr spectrum of the reaction mixture with a sample of dimethylketene which had been allowed to dimerize at room temperature. Other ill-defined materials which were nonaromatic (nmr) were not further examined. The low yields of isobutyrophenone obtained with benzene as a substrate are due to the faster rate of these side reactions compared to the rate of acylation of the aromatic nucleus. These side products were a constant feature of the reactions with less active aromatic substrates. They completely vanished in the cases of more active substrates such as toluene, which were exceptionally clean, giving only one ketone in most cases.

TABLE 1. Yields of ketones from acylation with dimethylketene at 25°C in neat hydrocarbon

Substrate	%Yield (based on dimethylketene)
1. Benzene	5 [a]
2. Toluene	28.7
3. *o*-Xylene	40.0[a]
4. Anisole	65.2[b]

[a] Yield determined by gas chromatography.
[b] *ortho*/*para* (*o*/*p*) ratio 4.47×10^{-3} by gas chromatography; no *meta* isomer (0.1% of isomers could be detected).

Position Selectivity

The dimethylketene – aluminum chloride complex is highly positionally selective even though one might suspect that it should be highly reactive.

The position selectivity of dimethylketene was contrasted to that of isobutyryl chloride by analyzing the isomer distribution of reactions of the

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TABLE 2. Comparison of *o*/*p* ratios for acylations with isobutyryl chloride and dimethylketene

	ortho/*para* $\times 10^2$	
Substrate	Isobutyryl chloride	Dimethylketene
1. Toluene	4.33	0.00
2. Anisole	1.30	0.447
3. Ethylbenzene	0.0734	0.000
4. Cumene	0.000	0.000

acid chloride with aromatic substrates at 25°C. The results are shown in Table 2 in which *ortho*/*para* (*o*/*p*) ratios are given. No *meta* isomers were observed. Control experiments showed that no isomerization of products occurred under the reaction conditions, and as little as 0.1% of the isomers could be detected.

The nmr spin patterns of the *ortho* isomers, collected by preparative scale gc, displayed ABCD patterns similar to that of *o*-methylacetophenone (7) and had carbonyl bands at 1680 cm^{-1}. With dimethylketene only *para* isomers in yields of 15–50% were observed except with anisole and *o*-methylanisole. With anisole the *o*/*p* ratio was 4.47×10^{-3}. With *o*-methylanisole a mixture of the 4-isomer and 5-isomer in the ratio of 29:5 was obtained. It was observed that allowing pure samples of these ketones to stand in contact with aluminum chloride caused no changes to include *ortho* or *meta* isomers. Hence, it is likely that these mixtures represent the products of kinetic control and are not thermodynamically controlled mixtures. Since the selectivity of a reagent in discriminating between *ortho*- and *para*-positions depends not only on polar but also on steric interactions (8), one may thus infer that the reagents involved in acylation with $AlCl_3$ (dimethyl or diphenylketene) have a larger steric requirement than for an ordinary acid chloride acylation.

In no case of acylation with ketene did we find any *meta* isomers. This is unexpected because an acylating agent consisting of an oxovinyl cation should be a reactive species similar to an acylium ion. Such selectivity from reagents thought to be highly reactive has recently been reported by Stang and Anderson from alkylations with the stereoelectronically similar vinyl cations (9). Their product distributions are given in Table 3.

Except for toluene no *meta* isomer was observed. The *ortho*, *para* selectivity was lower for these vinyl cations than for the ketenes of this study. Both vinyl cation selectivity and ketene selectivity are higher than for acylations in general.

TABLE 3. Isomer distribution of vinyl triflate with monosubstituted benzenes (C_6H_5X) at 120°C

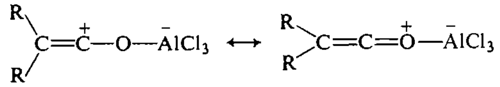
X	*ortho*	*meta*	*para*
CH_3O	11.3	0.0	88.7
CH_3	27.6	8.0	63.6
F	21.1	0.0	78.6
Cl	29.7	0.0	70.3

Substrate Selectivity

An indication of the substrate specificity of dimethylketene was obtained by competition experiments with benzene and toluene. In this case it was necessary to use an excess of benzene in the substrate mixture to ensure adequate detection of the isobutyrophenone in the rather complex gas chromatogram which arose due to the side products. The data on these experiments are summarized in Table 4. In each experiment a ratio of moles $AlCl_3$/moles dimethylketene of 2.5:1 was used.

The substrate specificity of 47.2[6] for dimethylketene found in this work contrasts with that found by Olah *et al.* (10) for acylation with $CH_3CO^+SbF_6^-$ or $CH_3CO^+SbCl_6^-$ which had toluene/benzene ratios of 125 and 121, respectively, for acylation in nitromethane at 25°C, and with acetyl chloride in nitromethane (11) which had a toluene/benzene ratio of 134. The dimethylketene – aluminum chloride reagent is thus actually more reactive than the other acylating agents cited in spite of the low yields with benzene and other moderately activated aromatic substrates. This finding supports the idea that the dimethylketene reacts more rapidly with itself in the presence of aluminum chloride than with a nonactivated or only moderately activated aromatic ring.

Our relative rates for toluene–benzene competitions compared with the value of 6.76 for vinyl cation alkylations (9) indicate that the substituted ketene – aluminum chloride complex is a great deal more substrate selective than the stereoelectronically similar vinyl cations. One might rationalize this greater substrate selectivity on the basis of structure **1** in which a mode of delocalization of charge is shown for the substituted ketene –



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[6] 51.69 was corrected to a mole per mole ratio by multiplying by mol. wt. phenyl ketone/mol. wt. tolyl ketone.

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TABLE 4. Substrate selectivity for dimethylketene

Substrate ratio benzene/toluene	Substrate mols/ ketene mols	Ratios of areas (tolyl/phenyl)	Substrate ratio g/tolyl ketene: g/phenyl ketone
1:1	99	52.340	52.34
3:1	184	16.980	50.95
5:1	257	10.372	51.80
			Av. = 51.69

TABLE 5. Yields of ketones from acylation with diphenylketene

Substrate	Yield (%)
1. Benzene	10.0
2. Toluene	11.1
3. *o*-Xylene	47.0
4. Ethylbenzene	19.6
5. Cumene	6.26
6. Anisole	59.1
7. *o*-Methylanisole	49.1 (76.6 corrected)[a]
8. Chlorobenzene	1.07

[a] In this experiment an aliquot showed that only a 64% yield of the diphenylketene was obtained.

aluminum chloride complex which is not available for the analogous vinyl cation. Analogous "resonance" arguments are advanced for the known stability of carbocations from α-haloethers (12).

Diphenylketene Studies

Our study of acylation of various aromatic substrates with diphenylketene supports the picture of a ketene – aluminum chloride complex as a site selective reagent prone to react with other ketene molecules rather than aromatic rings. Table 5 shows the yield data. All of these reactions were found to produce polymeric tar from which the ketones had to be removed.

We examined the nature of the ketene–$AlCl_3$ complex as follows. To a 2.4 g solution of diphenylketene in 300 mL of ligroin was added one equivalent of aluminum chloride plus 10% excess, assuming reaction [1]. The mixture became cloudy and a ring of brown precipitate formed on the bottom. An additional 10% excess of $AlCl_3$ was added and a white solid was noted. A small aliquot of this solid was removed, rapidly filtered, and an ir spectrum taken (Nujol). The absence of ketene was noted by the lack of absorption at 2100 cm^{-1}. Instead, a medium band at 1620^{-1} appeared. The solution above this precipitate contained diphenylketene as shown by the yellow color and ir spectrum. To this mixture was then added 50 mL of anisole and the solution allowed to stand overnight. Decantation of the ligroin from the resultant brown complex was followed by dissolving the complex in CH_2Cl_2 and treatment with ice–HCl. Solvent removal yielded 2.16 g (58.3%) of the anisyl ketone. This compares very well with 59.1% of this ketone obtained by slowly adding an excess of aluminum chloride to anisole and diphenylketene.

These data are consistent with formulation of the $AlCl_3$–diphenylketene adduct **2** as in [1].

[1] $$(C_6H_5)_2C{=}C{=}O + AlCl_3 \rightarrow \underset{\mathbf{2}}{(C_6H_5)_2C{=}C{-}O{-}AlCl_3}$$

The lack of any ketene bands in the precipitate and the appearance of a band at 1620 cm^{-1} would indicate that coordination to the O atom does indeed occur. These results parallel those reported by Hurd, who isolated a similar $AlCl_3$–ketene complex in CS_2 which also gave acylations with benzene and anisole (1).

The substrate specificity of the diphenylketene – aluminum chloride complex differs from that of dimethylketene as seen by comparing the data in Table 4 with those in Table 6. We regard the value from the 10:1 experiment as more valid because of difficulties in comparing greatly different areas with our integrator.

The value of 173.7 for the relative rate of toluene to benzene indicates the greater kinetic stability of the diphenylketene – aluminum chloride complex over that of the dimethylketene – aluminum chloride complex, as we observed in the isolation of the DPK complex. No isolation of the dimethylketene – aluminum chloride complex was possible. When we attempted to assay its relative stability by first adding $AlCl_3$ to a solution of dimethylketene in carbon disulfide, then adding anisole, no acylated anisole was found (96% recovery of starting anisole).

If one takes the relative rates of a toluene–benzene competition experiment as a measure of the kinetic stability of a species, one can order the vinyl type cations in the sequence below. This order allows one to think about structural variations

$$C_6H_5{-}\overset{+}{C}{=}CMe_2 < Cl_3\overset{-}{Al}{-}O{-}\overset{+}{C}{=}CMe_2 < Cl_3\overset{-}{Al}{-}O{-}\overset{+}{C}{=}C(C_6H_5)_2$$

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TABLE 6. Substrate specificity for diphenylketene

Benzene/toluene	Substrate moles/ketene moles	Area ratio (mols/mol)	k(toluene)/k(benzene)
1:1	25	18.9	189
10:1	110	17.37	173.7

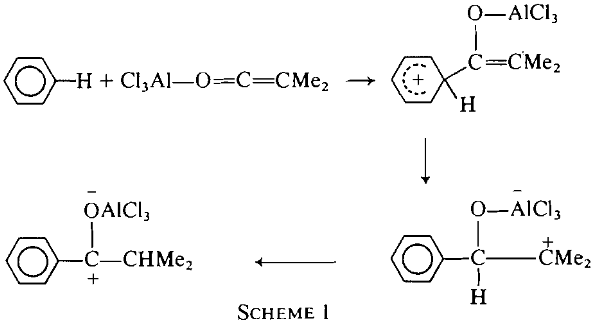
within the series in a consistent way. One can say that the phenyl ring attached directly to the charged carbon atom in the vinyl cation is less able to stabilize the charge than is the oxygen atom in the ketene complexes. This is certainly the order one would expect from consideration of the constants, say using σ^+ for OCH_3 as a model for —O—$AlCl_3$, and the σ^+ for C_6H_5(-0.78 vs. -0.18) (10).

The Intermolecularity of Proton Transfer

The unique stereoelectronic requirements of the dimethylketene – aluminum chloride complex, (if one accepts that coordination occurs at the oxygen as in **3**) allow intramolecular transfer of the proton on the benzene ring to the α-position in the final

$$(CH_3)_2C{=}C{=}\overset{+}{O}{-}\overset{-}{A}lCl_3$$

ketone as in Scheme 1 to be formally considered. The driving force could be a combination of formation of a stable carbocation and rearomatization. Such 1,2 shifts are well known in carbonium ion chemistry. Despite early workers' claims (1–4) that evolution of HCl occurred with ketene, the present reactions with dimethylketene or diphenylketene showed no tendency to evolve HCl although a careful check was made to observe it. The question of how the ketone arises via proton transfer is thus an important one if one is to determine a kinetic isotope effect. When toluene-d_8 was acylated with dimethylketene, the label was retained to the extent of 98 ± 2% (by nmr integration) indicating that the α-proton in the final product ketone does not enter the molecule in the work-up step as would be necessary if aluminum chloride formed a complex like **4** as suggested by early workers for the case of ketene (2). Likewise acylating benzene-d_6 with diphenylketene gave 97 ± 1% retention of deuterium.



SCHEME 1

$$Cl_2Al{-}CH_2{-}COCl$$

Control experiments using ketones labeled in the α-position showed that exchange under work-up conditions could have been 7 ± 5%.

It was desirable to perform a crossover experiment in which one aromatic substrate was deuterated and the other was nondeuterated because the substrate itself in the foregoing experiments was the only source of deuterium (protium), hence allowing the probability that the result was predetermined. Accordingly, a 50:50 molar mixture of anisole and toluene-d_8 was acylated with dimethylketene with the result that each ketone was found to have deuterium at the α-position. The *p*-tolylketone was found to have ca. 70% protium at the α position. When *p*-toluene-*d* alone was acylated, label retention (D) occurred only to about 80% by nmr integration. These results clearly eliminate the formally possible Scheme 1 and point to a transfer of the proton via excess aromatic substrate as in Scheme 2.

When diphenylketene was used to acylate *p*-deuteriotoluene, the resulting ketone had a value of 72% protium at the α-position. This enhances the conclusions found for dimethylketene acylation in that extensive scrambling of the label occurs as in Scheme 2.

This mechanism is interesting because it allows the possibility of the observation of a large kinetic isotope effect. It is well documented that the absence of a base of sufficient strength to remove a proton easily leads to high kinetic isotope effects (13). One expects a high kinetic isotope effect in the present work due to the low basicity of the aromatic substrates (14, 15), i.e., more S_E3 character.

Following the method of Olah *et al.* (10), we determined the k_H/k_D for benzene acylation by comparing ratios of products from competition reactions with toluene–benzene and toluene – benzene-d_6. The reactions were run on mixtures having molar ratios of 5 mols of benzene-d_6 to one mol of toluene and 5 mols of benzene to one mol of toluene to circumvent difficulties in the analysis (see Experimental). The results are given in Table 7. The low value of 1.06 is contrasted with Olah's

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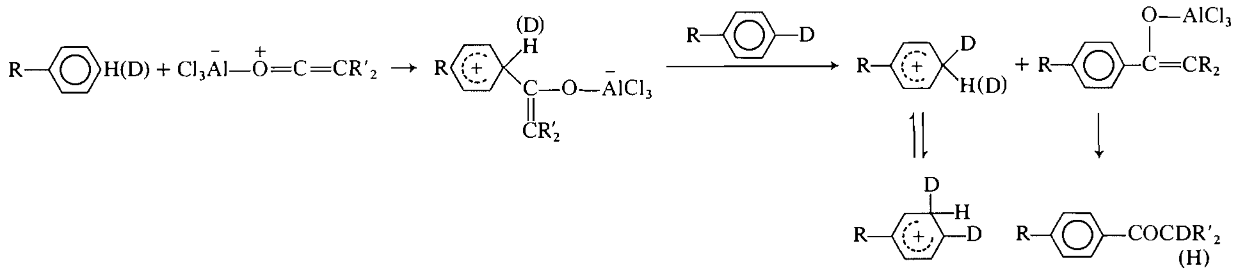

SCHEME 2

value of 2.27 for acetylation with $CH_3CO^+SbF_6^-$ and CH_3COBF_4 complexes. This value is consistent with the great selectivity shown by the acylating agents from ketenes and is entirely consistent with the value of 0.98 ± 0.026 found by Stang and Anderson (9) for alkylation with vinyl cations.

A second paper reporting on Hammett–Brown (16) treatments of dimethylketene and diphenylketene acylations is in preparation.

Experimental

General

Infrared spectra were neat or Nujol mulls except where noted, and were run on a Beckman IR4. The nmr measurements were run in the solvents noted with TMS or DSS as internal standards. All chemicals were reagent grade Eastman or Aldrich products.

Preparation of Ketenes

Dimethylketene was prepared by the pyrolysis of dimethylmalonic anhydride as per Staudinger *et al.* (5). The material thus obtained was distilled twice before use and opened only to a dry nitrogen atmosphere.

Diphenylketene was made by debromination of α-bromodiphenylacetylbromide (7) with triphenyl phosphine in ligroin. The dibromotriphenyl phosphorane was filtered through a sintered glass funnel and hydroquinone (0.1 g) was added. The ligroin was removed by distillation under reduced pressure and the residue distilled to give yields of 60–85% of diphenylketene.

Preparation of Authentic Aryl Isopropyl Ketones

All authentic ketones were made by acylation with isobutyryl chloride and $AlCl_3$ in the aromatic substrate in excess as the solvent. The reactions were all at 25°C, and were catalysed by the addition of 2.5 equivalents of aluminum chloride per equivalent of acid chloride (4). The known isobutyrophenones were made into appropriate derivatives which were recrystallized to constant melting points. These compounds are summarized with their references in Table 8. The new isobutyrophenones synthesized in this work were also made into derivatives, and their analytical data appear below.

4-Methoxy-3-methylphenyl Isopropyl Ketone

Analysis for 2,4-DNP (mp 194–196°C). *Anal.* calcd. for $C_{18}H_{20}N_4O_5$: C 58.06, H 5.41, N 15.05; found: C 57.96, H 5.57, N 15.01.

3-Chloro-4-methylphenyl Isopropyl Ketone

Analysis for 2,4-DNP (mp 146–148°C). *Anal.* calcd. for $C_{17}H_{17}ClN_4O_4$: C 54.19, H 4.55, N 14.87; found: C 54.11, H 4.52, N 14.78.

4-Isopropylphenyl Isopropyl Ketone

Analysis for 2,4-DNP (mp 131–131.5°C). *Anal.* calcd. for $C_{19}H_{22}N_4O_8$: C 61.61, H 5.99, N 15.13; found: C 61.48, H 5.91, N 15.04.

4-Methoxy-3-bromophenyl Isopropyl Ketone

This material was a solid and was analyzed as obtained (mp 66.5–68.8°C). *Anal.* calcd. for $C_{11}H_{13}BrO_2$: C 51.38, H 5.10; found: C 51.37, H 5.12.

Procedure for Acylation with Dimethylketene

Typically the reaction was run at 25°C in a flask fitted for mechanical stirring with excess hydrocarbon as the substrate. The best results were obtained when, following Williams and Osborne (4), aluminum chloride was added portionwise to a mixture of hydrocarbon and dimethylketene under an N_2 atmosphere. Accordingly, in each case the pure dimethylketene was mixed with a 20-fold excess of hydrocarbon and a 2.5 molar excess of $AlCl_3$ added slowly. The reactions were stirred for an hour after the addition was completed, then the reaction mixtures were poured onto ice and 6 *M* HCl. Extracting with equal volumes of dichloromethane, water washing, 5% sodium bicarbonate washing, water washing, then drying over magnesium sulfate, gave oils in each case after solvent removal. When distilled, these oils gave derivatives which were identical to those from the known ketones from acid chloride preparations.

Spectral data include ir at 1680–1690 cm^{-1}, ν (C═O) for all ketones (neat), and nmr signals at δ ($CDCl_3$): 3.6–3.8 (broad heptet 1H), and 1.13–1.25 (doublet, 6H).

Deuterium Labelling Experiments

A 1.5 g (0.021 mol) sample of doubly distilled dimethylketene was treated with 10 g (0.075 mol) of anhydrous aluminum chloride from a fresh bottle and 10 g (0.1 mol) of toluene-d_8 (99+% isotopically pure). After the reaction had subsided, it was stirred for an additional hour and worked up by pouring onto H_2O–HCl (6 *M*) in ice and extracting with dichloromethane. Washing with water twice and drying over $MgSO_4$ gave the ketone, after solvent removal. The ketone was purified by preparative scale gc (Varian 920 Autoprep) using a 20 ft × $\frac{3}{8}$ in. 15% SE 30 on 30/60 Chromosorb W column. The nmr showed only a singlet at 1.2 ppm with a trace of heptet at 3.40 ppm which corresponded to an exchange of 4.5% (ratio of 3.4 to 1.2 was 3/66). The amount of exchange during workup was determined as follows. The parent unlabelled ketone was treated with a 2.5 molar excess of aluminum chloride (4.0 g of ketone + 10.0 g of aluminum chloride) in toluene, and stirred for one hour. It was then poured into 25 mL of D_2O–DCl (from $SOCl_2$ and D_2O). The workup then proceeded as for the other experiments. The nmr integration gave for the parent compound, before exchange, the ratios 88:66.5 for the signals at 1.1–1.25 and 7.0 ppm for a ratio of 1.32 (theory 1.2). After the exchange, the ratio was 84:63.5 = 1.32. Taking the signal at 1.1–1.25 as worth 6H, one obtains a

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TABLE 7. k_H/k_D Values for benzene

Experiment	Area ratio = (tolyl ketone/benzene ketone)	k_H/k_D
Benzene–toluene 5:1	10.371	1.06
Benzene-d_6 – toluene 5:1	11.051	

TABLE 8. Derivatives of ketones

Ketone	Derivative	Melting point (°C) Found	Melting point (°C) Lit.	Reference
Isobutyrophenone	2,4 DNP	162–163	163	Ref. 17
4-Methoxyisobutyrophenone	Semicarbazone	211–212	212–213	Ref. 18; II, **8**, 118
4-Methylisobutyrophenone	Oxime	90–91	90–91	Ref. 18; II, **7**, 254
3,4-Dimethylisobutyrophenone	Oxime	67–68	68	Ref. 18; **7**, 335

ratio of 14.0 units/proton. In the parent compound before the exchange the signal at 3.4 due to α-C—H was 14.5 ± 0.5 units. After the exchange, experimental ratios for three experiments gave an average of 0 ± 3% exchange. The worst case gave 9% exchange with two experiments giving no exchange. (Ratios of 3.4 signal were 14.6, 14.5, and 13.2.)

When 4.11 g (0.021 mol) of diphenylketene was treated with aluminum chloride in 20 mL of benzene-d_6 (99.9% isotopically pure), and the reaction worked up by washing only with water, the nmr showed the ratio of the signal at 5.95 ppm to the aromatic signal to be 1:35 (1:10 theory). One can say that exchange to the extent of ~3% occurred in workup. This was entirely consistent with our results from dimethylketene.

Reactions with p-*Deuteriotoluene*

With Dimethylketene

A 2.0 g (0.0280 mol) sample of dimethylketene was treated with 22 g (0.233 mol) of *p*-deuteriotoluene (see below) and 5.7 g (4.29×10^{-2} mol) of aluminum chloride. The workup was as described above. After separation via preparative scale gc the nmr of the ketone showed 20% protium signal at 3.4 ppm (compared to the signals at 1.2). The signal at 1.25 had three components corresponding to the methyl groups of the deuterated and undeuterated ketones. The yield of ketone was 25%.

With Diphenylketene

A 1.78 g (9.18×10^{-3} mol) sample of diphenylketene was dissolved in 25 mL of *p*-deuteriotoluene with mechanical stirring. A sample of 3.33 g ($2.5 \times 9.18 \times 10^{-3}$ mol) of anhydrous aluminum chloride was added portionwise through the reflux condenser. The workup was as recorded above, omitting the base wash. The nmr spectrum showed 20 integral units for the signal at 2.32 ppm and 5 units for the proton at 6.0 ppm (the α-proton). This corresponds to ~72% protium content at the α position. The yield was ca. 10%.

Preparation of p-*Deuteriotoluene*

A 1 mol sample of *p*-bromotoluene was dropped onto 1.5 g-atoms of magnesium in ether. After the reaction had subsided, the mixture was stirred 24 h, then quenched by addition of 99+% deuterium oxide. Distillation gave 80 g of hydrocarbon. The nmr consisted of an A_2B_2 signal at 7.38 (4H) and a singlet at 2.38 (3H) (in $CDCl_3$ and neat). The ratios of integration were 130:96 (4.06 protons). This corresponds to ~94% deuteration.

Competition Experiments with Dimethylketene

General Procedure

Dimethylketene generated and purified as reported above was added to a 20-fold excess of a 50 mol% mixture of each substrate. Aluminum chloride was added portionwise with stirring of the reaction, and the reactions were stirred one hour after the addition was completed. Workup was as recorded above.

Gas chromatographic analysis was done on a Perkin-Elmer 3920 instrument (TC Bridge) with a 6 ft 10% Carbowax 20 m on 80/100 Chromosorb W column at a temperature of 190°C, He flow rate of 30 mL/min.

Relative response factors (RRF) were determined by mixing known concentrations of ketones (in g/100 mL) and determining the ratios of areas. This procedure gives a relative response factor (RRF) of area per g of ketone I/area per g of ketone II. The RRF for tolyl ketone/phenyl ketone was 1.3250. All competitions were done by comparing the rates of reaction with toluene for experimental convenience (12). The rate constant ratios were determined by the formula

$$\frac{k_a}{k_b} = \frac{[AX]}{[BX]} \Big/ \frac{[A_0]}{[B_0]}$$

In all cases the substrate ratios to ketene were large enough to ensure small errors in the rate ratios. Integration was performed by a Spectra Physics electronic integrator.

Authentic samples of ketones were used in artificial mixtures as a check on the accuracy of the integration technique. It was found that at very high ratios the integrator consistently overestimated the amount of the smaller component. Corrections were applied where appropriate or the reaction run was redone using a larger amount of less active substrate.

The benzene/toluene ratios were determined in this way using ratios of benzene/toluene of 1:1, 3:1, and 5:1. These results are summarized in Table 4.

Reactions of Diphenylketene with Aromatic Substrates

A typical procedure is given using ethyl benzene as a substrate at 25°C. A 9.7 g (0.05 mol) sample of distilled diphenylketene was dissolved in 50 mL of pure ethyl benzene. While this solution was magnetically stirred, a 2.5-fold excess of aluminum chloride (16.6 g) was added portionwise through the reflux condenser. The reaction mixture was stirred overnight, then poured into HCl – ice water and washed with water repeatedly until the

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TABLE 9. Analytical data for diphenylacetophenones

Compound	Melting point (°C)	Analysis				Yield (%)
		Calculated		Found		
		C	H	C	H	
α,α-Diphenylacetophenone	134–136[a]					>10
α,α-Diphenyl-*p*-methylacetophenone	98–99	88.08	6.33	87.81	6.38	11.1
α,α-Diphenyl-3,4-dimethylacetophenone	97–98	87.97	6.71	87.71	6.90	47.0
α,α-Diphenyl-4-methoxyacetophenone	126–128	83.45	6.00	83.18	6.12	59.1
α,α-Diphenylisopropyl acetophenone	116–119	87.86	7.05	87.62	6.96	6.26
α,α-Diphenyl-4-ethylacetophenone	101–103	87.97	6.71	87.82	6.88	19.6
α,α-Diphenyl-4-ethoxy-3-methylacetophenone	104–106	83.51	6.31	83.46	6.50	49.1 (76.6 corrected)[b]
α,α-Diphenylchloroacetophenone	140–145	78.30	4.93	78.49	5.18	1.07

[a] Literature (ref. 18, vol. 7, p. 522) mp 135–136°C.
[b] In this experiment an aliquot showed that only a 64% yield of the ketene was obtained.

washings gave a pH of six by pHydrion paper. The excess ethyl benzene was removed by distillation. The residual brown tar was extracted repeatedly with hot pentane. The combined extracts were concentrated to ~50% of their volume and allowed to stand. Crystals of the product formed slowly and were collected. They showed v(Nujol): 1675 (C=O) cm^{-1}. This procedure was used for all the ketones. The effectiveness of this technique for recovery was tested by dissolving a known amount of a ketone in pentane at the boiling point, concentrating it, and collecting crystals.

In the case of more active substrates very little polymerization occurred and recovery with pentane (subsequent to distillation of most of the substrate–solvent) was simple, since the polar ketone is not very soluble in the cold pentane solvent. Recovery of pure anisyl ketone from hot pentane was 98.3%. In the case of cumenyl ketone, however, which turned out to be soluble in pentane, the solid was recovered by triturating it out of the polymer with pentane, and recrystallizing the crude solid which was contaminated with cumene, from ethanol. As a check on the recovery method some pure cumenyl ketone was dissolved in cumene and as much of the cumene was distilled off as possible. Subsequently recrystallization from ethanol was effected. Recovery of the pure ketone was 80%.

The yields, melting points, and microanalytical data are recorded in Table 9.

Competition of Toluene and Benzene for Diphenylketene

These experiments were performed in an analogous manner to those for dimethylketene except that the analysis of the reaction mixtures was done using a Waters high performance liquid chromatography apparatus consisting of two Model 6000 pumps, a U6K loop injector, a Model 440 Absorbance Detector connected to a Soltec Model 252A recorder, and a Model 660 Solvent programmer. Integrations were performed as with the dimethylketene experiments. The column was a Whatman ODS – Magnum 9 C_{18} reverse phase column. Flow rate was 2.5 mL/min of 25% water – methanol.

The relative response factor for the tolyl ketone relative to the phenylketone was 1.296 as determined by artificial mixtures. The values corrected by the relative response factor appear in Table 6 along with the relative rates.

Crossover Experiment with Anisole and Toluene-d_8

A mixture of 15 g (0.14 mol) of anisole and 15 g (0.15 mol) of toluene-d_8 was treated with 1.56 g of clean, triple distilled dimethylketene (0.022 mol) and 10 g (0.075 mol) of anhydrous aluminum chloride in a three-necked flask equipped with a drying tube, mechanical stirrer, and addition funnel. After the reaction had subsided the mixture was poured onto 300 g of 6 *M* HCl – ice water and extracted with three 100-mL portions of dichloromethane. After drying over magnesium sulfate the solvent was removed and the higher boiling excess organic substrates were removed under reduced pressure. The residue was fractionally distilled through a 3 in. Vigreux column to give ketone materials in fractions two and three (bp 98–140°C; 10.5 Torr). These ketones were separated by preparative scale gc and analyzed by mass spectra (Varian EM 600 calibrated by perfluorokerosine-H) and nmr.

The nmr spectrum of the anisyl isopropyl ketone showed considerable incorporation of D at the isopropyl group. The mass spectrum had (average of 5 scans) a ratio of M to *M* + 1 of $0.380 \pm 5.53 \times 10^{-2}$ (standard deviation). The expected M to *M* + 1 ratio was 0.122. These figures indicate a protium/deuterium value of 3.83 in the anisyl ketone.

The nmr spectrum of the tolyl ketone showed retention of only about 70% of the deuterium label at the position as indicated by a septet at $\delta = 3.4$ (compared to the methyl signal at 1.1–1.25). These data indicated that proton transfer from the aromatic ring to the α-position was intermolecular.

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