**Oxidation with CAN.** Typically, α-substituted *p*-xylene (1) (3.3 mmol) and CAN (3.3 mmol) in acetic acid (100 mL) were made to react at 60 °C under nitrogen atmosphere until the orange color faded. The mixture was cooled and extracted with light petroleum, and the collected organic extracts were washed with aqueous $NaHCO_3$ then with water and finally dried with anhydrous $Na_2SO_4$.

**Anodic Oxidation.** The electrochemical experiments were performed in a thermostated microcell at 25 °C with platinum electrodes (12 $cm^2$ effective area). The magnetically stirred solution of the α-substituted xylene (2.1 mmol) in 3:1 v/v acetic acid/acetonitrile mixture were electrolyzed at constant potential (between 1.7 and 2.3V, vs SCE) by using an AMEL system 5000 potentiostat until 1 F/mol, in some cases 0.2 F/mol, of charge were passed. Some experiments were carried out at constant current (5 $mA/cm^2$). The reaction mixture was then worked up as above. The current yields, determined by GC or by $^1H$ NMR analysis using, respectively, *tert*-butylbenzene and diphenylmethane as internal standard, ranged from 40 to 100%.

**Determination of the Isomeric Distribution.** The isomeric distribution of Z-substituted benzyl acetates obtained from the anodic and CAN-promoted oxidations of 1 was determined by GC analysis. The isomer ratio was calculated against a calibrated solution of authentic specimens.

**Determination of $E_p$ values.** $E_p$ values (vs SCE) have been determined by cyclic voltammetry (100 mV/s) under nitrogen, at a platinum disk electrode in acetonitrile (HPLC grade) with ca. 0.1 M tetra-*n*-butylammonium tetrafluoborate as the supporting electrolyte, using an Amel System 5000 potentiostat.

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**Registry No.** 1 (Z = OH), 589-18-4; 1 (Z = $OCH_3$), 3395-88-8; 1 (Z = $CH_3$), 622-96-8; 1 (Z = CN), 2947-61-7; 1 (Z = COOMe), 23786-13-2; 1 (Z = OAc), 2216-45-7; 1 (Z = *t*-Bu), 24797-40-8; $1^{\bullet+}$ (Z = OH), 105639-65-4; $1^{\bullet+}$ (Z = $OCH_3$), 136708-11-7; $1^{\bullet+}$ (Z = $CH_3$), 73089-22-2; $1^{\bullet+}$ (Z = CN), 130932-66-0; $1^{\bullet+}$ (Z = COOMe), 136708-12-8; $1^{\bullet+}$ (Z = OAc), 136708-13-9; $1^{\bullet+}$ (Z = H), 34510-22-0; $1^{\bullet+}$ (Z = *t*-Bu), 136708-14-0; 2 (Z = $CH_3$), 19759-40-1; 2 (Z = CN), 75599-81-4; 2 (Z = COOMe), 136707-99-8; 2 (Z = OAc), 2929-93-3; 2 (Z = *t*-Bu), 136708-00-4; 3 (Z = $CH_3$), 67035-84-1; 3 (Z = CN), 80364-28-9; 3 (Z = COOMe), 119991-78-5; 3 (Z = OAc), 14720-70-8; 3 (Z = *t*-Bu), 136708-03-7; 4 (R = $CH_3$), 136707-98-7; 4 (R = H), 1075-22-5; 5 (R = $CH_3$), 136708-07-1; 5 (R = H), 136708-04-8; 6 (R = $CH_3$), 136708-02-6; 6 (R = H), 136708-01-5; ceric ammonium nitrate, 10139-51-2; *cis*-1,3-diacetoxy-5,6-dimethylindan, 136708-05-9; *trans*-1,3-diacetoxy-5,6-dimethylindan, 136708-06-0; α-hydroxy-*p*-tolylacetonitrile, 4815-10-5; α,α′-dibromo-*p*-xylene, 4076-57-7; *p*-tolyl *tert*-butyl ketone, 30314-44-4; 5-methylindan-1,3-dione, 50919-77-2; 5-methylindan, 874-35-1; 5-bromo-6-methylindan, 136708-08-2; 4-bromo-5-methylindan, 136708-09-3; 4-(acetoxymethyl)-5-methylindan, 136708-10-6.

# Friedel–Crafts Alkylation of Benzenes Substituted with Meta-Directing Groups

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In protonic acids, benzaldehyde, acetophenone, benzophenone, and ethyl benzoate were ring-alkylated by alcohols. Benzonitrile was N-alkylated rather than ring-alkylated. Ethyl *n*-propyl, isopropyl, and *n*-butyl alcohol were effective alkylating agents, whereas methyl and *tert*-butyl alcohol were not. Alkylations with *n*-propyl and *n*-butyl alcohol gave products in which the alkyl group was completely rearranged. Sulfuric, polyphosphoric, and 85% phosphoric acid were effective catalysts. The alkylation apparently proceeds via the reaction of an alkyl cation with the unprotonated substrate.

## Introduction

Benzenes substituted with meta-directing groups are usually considered to be inert toward Friedel–Crafts alkylation. In an earlier paper[1] we showed that the reason for the apparent inertness is that the most widely used catalysts, e.g., $AlCl_3$, preferentially coordinate with substrate rather than with the reagent. The catalyst thus loses its activity and the substrate is further deactivated by the presence of a positive charge, which is partially distributed on the ring. However, with a properly selected catalyst, one which preferentially coordinates with the reagent rather than with the substrate, benzenes substituted with meta-directing groups are reactive toward Friedel–Crafts alkylation. In fact, in sulfuric acid, even nitrobenzene can be alkylated by ethanol.[1]

Here we will describe how the natures of the substrate, the alcohol, and the catalyst affect the alkylation. Benzaldehyde, acetophenone, benzophenone and ethyl benzoate were all ring-alkylated. Ethyl, *n*-propyl, isopropyl, and *n*-butyl alcohol were effective alkylating agents, whereas methyl and *tert*-butyl alcohol were not. Sulfuric acid, PPA, and 85% phosphoric acid were effective catalysts.

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## Experimental Section

The reagents were all chemically or analytically pure and were obtained commercially. Benzaldehyde was distilled, and a small amount of hydroquinone was added before use.

Typically, substrate (20 mmol), alcohol (40 mmol), and catalyst (15–20 mL) were mixed and the mixture was heated at 90–110 °C for 12–48 h. The cooled mixture was then poured into water and the whole was extracted thrice with $CHCl_3$. After evaporation of the solvent the product composition and yield were determined by GC/MS. The results were verified by $^1H$ NMR. The alkylation of benzaldehyde was performed under nitrogen. In the alkylation of ethyl benzoate the first step of workup was to pour the reaction mixture into a mixture of ice, water, and a slight excess of $NaHCO_3$.

## Results and Discussion

**A. Alkylation of Benzophenone by Various Alcohols.** Benzophenone was alkylated by ethyl, *n*-propyl, isopropyl, and *n*-butyl alcohol. The results are summarized

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Table I. Composition of the Products from the Alkylation of Benzophenone with Various Alcohols

| alcohol | EtOH | *n*-PrOH | *i*-PrOH | *n*-BuOH |
|---|---|---|---|---|
| catalyst (amount) | $H_2SO_4$ (20 mL) | $H_2SO_4$ (20 mL) | PPA (15 mL) | PPA (15 mL) |
| temp (°C) | 110 | 90 | 100 | 100 |
| time (h) | 12 | 1.2 | 26 | 26 |
| composition | | | | |
| unalkylated (%) | 66.95 | 74.53 | 41.66 | 98.21 |
| ortho-alkylated (%) | 1.49 | 0.58 | 2.77 | 0.09 |
| meta-alkylated (%) | 19.69 | 18.87 | 28.44 | 1.48 |
| para-alkylated (%) | 4.74 | 3.20 | 6.63 | 0.22 |
| dialkylated (%) | 5.75 (7)[a] | 2.38 (6)[a] | 17.33 (6)[a] | |
| trialkylated (%) | 0.27 (5)[a] | 0.08 (3)[a] | 1.28 (6)[a] | |
| AN[b] | 0.39 | 0.28 | 0.78 | 0.02 |
| "yield"[c] (%) | 93 | 89 | 91 | 92 |

[a] The number in parentheses is the number of isomers detected by GC/MS. [b] AN is the average number of alkyl groups introduced into the substrate. [c] The "yield" is the sum of the yield of the substituted products and the recovered substrate.

in Table I. However, no products of alkylation were detected after a mixture of benzophenone, methanol, and sulfuric acid had been heated at 160 °C for 72 h. Similarly, *tert*-butyl alcohol was unreactive under various conditions.

In $H_2SO_4$ solution, at 110 °C, ethyl alcohol readily alkylated benzophenone. However, under the same conditions, when other alcohols were used the reaction mixtures darkened quickly and black particles formed. This undesirable behavior could be suppressed by employing lower temperatures and shorter reaction times because the other alcohols proved to be more reactive than ethanol. Alternatively, a less active catalyst, PPA or 85% $H_3PO_4$, could be used. Thus, heating a mixture of benzophenone, isopropyl alcohol, and 85% $H_3PO_4$ at 110 °C for 48 h gave products with an average alkylation number, AN, of 0.20. On the other hand, with PPA as the catalyst, products with an AN of 0.78 were formed in a shorter time at a lower temperature. Thus, PPA is a more active catalyst than is 85% $H_3PO_4$.

Alkylation with *n*-propyl alcohol gave exclusively isopropyl derivatives. In support of this statement are the observations that products from the reaction of both *n*-propyl and isopropyl alcohol gave the same GC/MS spectra, which showed a strong M − 15 peak, but a weak, if any, M − 29 peak. The high field portion of the $^1H$ NMR spectra of the products show characteristic isopropyl peaks at $\delta$ 1.17 (6 H, d, $J$ = 6.5 Hz) and 2.80 (1 H, m, $J$ = 6.5 Hz). Similarly, alkylation with *n*-butyl alcohol gave exclusively *sec*-butyl derivatives.

The mixture of products from the alkylation of benzophenone by isopropyl alcohol contained seven components, the molecular weight of which are 2 Da too low to be either a mono-, di-, or triisopropylbenzophenone. The total yield of such products was 1.53%. These products of a dehydrogenative side reaction that occured during Friedel–Crafts isopropylation have been described by Yoneda et al.,[2] who also proposed a mechanism to explain their formation.

**B. Ethylation of Other Substrates.** In $H_2SO_4$, benzaldehyde, acetophenone, benzophenone, and ethyl benzoate were all ring-alkylated by ethanol. The results are summarized in Table II. When benzonitrile was treated with ethanol in sulfuric acid, no products of ring alkylation could be detected. In addition to products of the hydrolysis of benzonitrile, i.e., benzoic acid, benzamide, and ethyl benzoate, there appeared *N*-ethylbenzamide, a product of the Ritter reaction.

Table II. Composition of the Products from the Ethylation of Benzaldehyde, Ethyl Benzoate, Acetophenone, Benzophenone,[a] and Nitrobenzene[b]

| substrate | PhCHO | $PhCO_2Et$ | PhCOMe | $Ph_2CO$ | $PhNO_2$ |
|---|---|---|---|---|---|
| unalkylated (%) | 71.12 | 24.20 | 36.75 | 66.59 | 51.85 |
| ortho-alkylated (%) | 4.71 | 2.22 | 0.62 | 1.49 | 9.51 |
| meta-alkylated (%) | 15.09 | 38.15 | 27.17 | 19.69 | 28.19 |
| para-alkylated (%) | 4.99 | 8.36 | 5.65 | 4.74 | 4.62 |
| dialkylated (%) | 1.00 (3)[c] | 15.96 (5)[c] | 10.26 (3)[c] | 5.75 (7)[c] | 5.20 (6)[c] |
| trialkylated (%) | | 2.70 (6)[c] | 0.56 (2)[c] | 0.27 (5)[c] | 0.58 (5)[c] |
| tetralkylated (%) | | 0.44 (2)[c] | | | 0.04 (2)[c] |
| AN | 0.28 | 0.98 | 0.69 | 0.38 | 0.55 |
| "yield" (%) | 85 | 38 | 75 | 78 | 91 |

[a] $H_2SO_4$ catalyst, 110 °C, 12 h. [b] From ref 1. The reaction time was 6 h. [c] The number in parentheses is the number of isomers detected.

When benzaldehyde was ethylated in the presence of air the predominant products were benzoic acid, ethyl benzoate, and their ring-alkylated derivatives. Under nitrogen, the side reaction that gave such products was almost completely suppressed.

The ethylation of acetophenone also gave some ethyl benzoate and its ring-alkylated derivatives. The total yield of such products was 5.79%. Surprisingly, the side reaction was not suppressed when the ethylation was performed under nitrogen. In addition to products of ethylation and oxidation there appeared four dehydrogenated compounds derived from mono- and diethylacetophenone (13.07%). Such dehydrogenation did not occur during the ethylation of the other substrates.

When the reaction mixture from the ethylation of ethyl benzoate was worked up in the usual manner the main products were benzoic acid and its ring-ethylated derivatives. In an attempt to suppress what was apparently a hydrolytic side reaction, the mixture was instead poured carefully into a stirred mixture of ice, water, and a slight excess of $NaHCO_3$. The "yield" of ring-ethylated products was only 38% but the products showed an AN of 0.98. The aqueous layer was then acidified and was extracted with $CHCl_3$. A 13% yield of benzoic acid and ring-ethylated benzoic acid was obtained. The AN of this products was only 0.41, much lower than that of the ring-ethylated ester. It was thus obvious that hydrolysis still occurred to a significant extent and that the less highly alkylated ester hydrolyzed more readily.

**C. Mechanism of Alkylation.** Evidently, the reaction involves carbocations because *n*-propyl and *n*-butyl alcohol yield isopropyl and *sec*-butyl derivatives, respectively. The methyl cation is a high-energy species and is most difficult to form. Therefore, methanol is not a good alkylating agent. The ethyl cation is also a high-energy species, and consequently ethanol shows lower reactivity than the other alcohols. The *tert*-butyl cation, on the other hand, is a low-energy species and is easily formed. However, its electrophilicity is low[2] and it is readily deprotonated to yield isobutylene.

It is well-known that most of the substrates that were employed in this study are protonated upon dissolution in sulfuric acid. Protonation, by introducing positive charge into the ring, further deactivates the substrate, especially toward the substitution at the ortho and para positions. Therefore, there must be two alternative routes that lead to the products: Reaction of the more abundant but less reactive protonated state and reaction of the less

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Table III. Isomer Ratio of the Products of Friedel-Crafts Monoethylation and Mononitration

| | ethylation | | | | nitration | | | |
|---|---|---|---|---|---|---|---|---|
| substrate | ortho | meta | para | m/p | ortho | meta | para | m/p |
| PhCHO | 19.0 | 60.9 | 20.1 | 3.0 | 19 | 68 | 9 | 7.6 |
| $PhCO_2Et$ | 4.6 | 78.3 | 17.2 | 4.6 | 28.3 | 68.4 | 3.3 | 20.7 |
| PhCOMe | 1.9 | 81.0 | 16.9 | 4.8 | 30 | 68 | | >30 |
| $PhNO_2$ | 22.5 | 66.6 | 10.9 | 6.1 | 6.4 | 93.3 | 0.3 | 311 |

abundant but more reactive unprotonated state. Because Friedel-Crafts alkylation is the least selective of the electrophilic aromatic substitutions,[3] the meta to para ratio, m/p, of the products should be relatively small if the reaction proceeds via the unprotonated state. If, however, the reaction proceeds via the protonated state, the products should consist almost solely of the meta isomer, as is found in Friedel-Crafts alkylation in the presence of large excesses of $AlCl_3$[4] or in super acids.[2] From a comparison of the m/p ratios of the products of the monoethylation and mononitration[5] (Table III), it is evident that alkylation by alcohols in protonic acids proceeds mainly via the unprotonated state.

During the ethylation of acetophenone a small amount of crystalline substance formed on the wall of the condenser. It was collected and was identified as acetophenone. This observation suggested that some unprotonated acetophenone exists in equilibrium with the more abundant protonated acetophenone.

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**Registry No.** $CH_3OH$, 67-56-1; *tert*-BuOH, 75-65-0; $H_2SO_4$, 7664-93-9; $H_3PO_4$, 7664-38-2; PhCHO, 100-52-7; $PhCO_2Et$, 93-89-0; PhCOMe, 98-86-2; $PhNO_2$, 98-95-3; *o*-$EtC_6H_4CHO$, 22927-13-5; *m*-$EtC_6H_4CHO$, 34246-54-3; *p*-$EtC_6H_4CHO$, 4748-78-1; *o*-$EtC_6H_4CO_2Et$, 56427-44-2; *m*-$EtC_6H_4CO_2Et$, 136569-05-6; *p*-$EtC_6H_4CO_2Et$, 36207-13-3; *m*-$EtC_6H_4COMe$, 22699-70-3; *p*-$EtC_6H_4COMe$, 937-30-4; *o*-$EtC_6H_4NO_2$, 612-22-6; *m*-$EtC_6H_4NO_2$, 7369-50-8; *p*-$EtC_6H_4NO_2$, 100-12-9; EtOH, 64-17-5; *n*-PrOH, 71-23-8; *i*-PrOH, 67-63-0; *n*-BuOH, 71-36-3; *m*-$EtC_6H_4COPh$, 66067-43-4; *m*-*i*-$PrC_6H_4COPh$, 32388-73-1; $Ph_2CO$, 119-61-9; benzonitrile, 100-47-0; *N*-ethylbenzamide, 614-17-5.

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# Cascade Polymers:[1] Syntheses and Characterization of One-Directional Arborols Based on Adamantane

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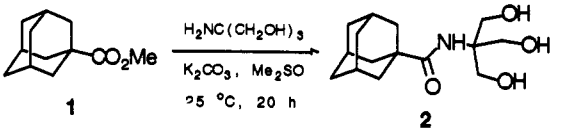
Several methods for the synthesis of cascade polymers (dendritic macromolecules) on adamantane have been investigated. The synthesis of two novel, branched monomers, 4-amino-4-(3-acetoxypropyl)-1,7-diacetoxyheptane and di-*tert*-butyl 4-amino-4-[2-(*tert*-butoxycarbonyl)ethyl]heptanedioate, possessing 3-fold symmetry and branches emanating from a tetrahedral carbon branch point, is described. These monomers were reacted with a monofunctional adamantane core to evaluate the reaction efficiency, ease of purification of products, and spectral characteristics.

## Introduction

The syntheses and spectral features of cascade polymers (arborols)[3] possessing two-,[4,5] three-,[6] and four-directional[7-10] microenvironments with functionalized polar outer surfaces have been recently reported from our laboratories; related work on these dendritic macromolecules has been reviewed.[11] Depending on their molecular shape, many of these macromolecules aggregate to form aqueous gels[5] or show novel micellar characteristics in aqueous solution.[9,10] In view of our continued interest in generating a spherical hydrophilic surface with a compact lipophilic core,[12] we herein probe the development of a cascade system emanating from a central adamantane core. The

Scheme I

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