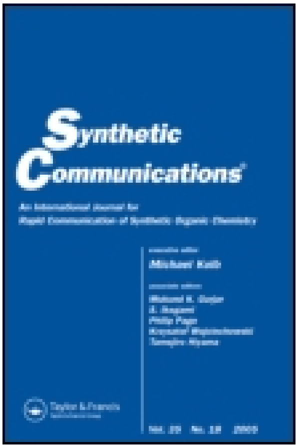

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Friedel-Crafts Alkylation and Acylation in the Absence of Solvent

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FRIEDEL-CRAFTS ALKYLATION and ACYLATION in the ABSENCE of SOLVENT

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A short and efficient synthetic route, for alkylation and acylation of aromatic compounds in the absence of solvent is developed. According to the reaction system and conditions used, different alkyl-, and acyl arenes are obtained in moderate to good yields. The structures are assigned by ^1H and ^{13}C NMR spectroscopy.

The Friedel-Crafts alkylation[1] and acylation[2] of aromatic compounds are important synthetic transformations. Although the mixed carboxylic sulfonic anhydrides, $RCOOSO_2CF_3$ are extremely reactive acylating agents and can smoothly acylate benzene without a catalyst[3], generally Friedel-Crafts alkylation and acylation reactions involve addition of a Lewis acid catalyst such as $AlCl_3$[4] to a well-stirred mixture of an alkyl or acyl halide and an aromatic compound under inert conditions.

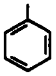
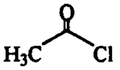
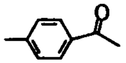
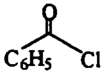
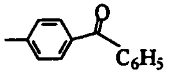
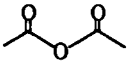
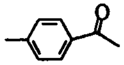
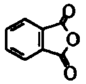
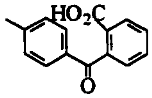
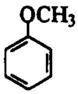
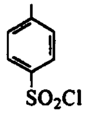
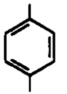
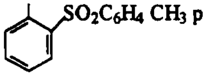
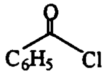
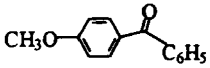
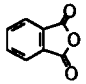
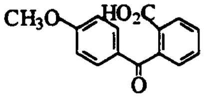
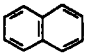
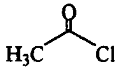
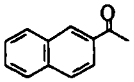
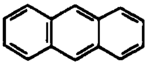
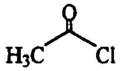
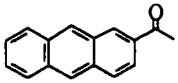
Most of these methods require very long reaction times, high temperature, and tedious work-up.

Recently, while exploring the scope and utility[5] of solid-phase conditions in organic synthesis, we observed that the no solvent conditions are also effective for the synthesis of alkyl-, and acylarenes. Herein, we report our results on these novel procedures.

In general, these no solvent reactions were carried out without any protection by mixing the corresponding aromatic compound, the respective alkyl- or acyl halo compound, and $AlCl_3$ in an agate mortor for 45 min. at room temperature followed by simple extraction of the product into an ether solution. The yields of the corresponding ketones or alkyl aromatic compounds obtained by this procedure are shown in Tables **1** and **2**, respectively. The yields obtained by this simplified procedure were either comparable or in some cases higher than in the reported solvent mediated methods. In a reported procedure[6] when naphthalene was reacted with acetyl chloride in nitrobenzene as solvent in the presence of $AlCl_3$ at 0°C, 1- and 2-acyl naphthalene were produced in 10% and 35%, respectively. Under our conditions by carrying out the reaction at room temperature for 45 min., only 2-acetyl naphthalene was obtained in 65%. The yield, for example, of 4-methyl benzophenone obtained in the no solvent reaction (75%) is better than that obtained by reacting benzoyl chloride with toluene in the presence of about 5 mol %, $ZnCl_2$ at 100-250°C (70%)[7].

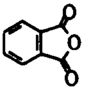
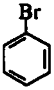
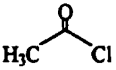
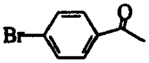
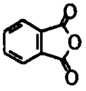
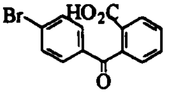
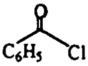
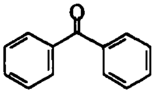
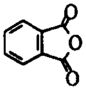
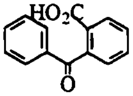
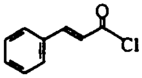
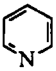
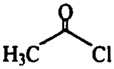
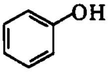
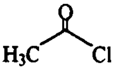
Alkylation of the aromatic compounds by the Friedel-Crafts alkylation can also be carried out in the absence of solvent. When benzene was treated with excess of

Table 1. Friedel-Crafts Acylation of aromatic Compounds in the Absence of Solvent

Entry	Substrate	Acylating Agent	Temp. (°C)	Time (min.)	Products	Yield[a] (%)
1			25	45		76
2			25	45		75
3			25	45		53
4			25	45		68
5			25	45	 (70%)  (30%)	90
6			25	45		75
7			25	45		72
8			25	45		65
9			25	45		85

(continued)

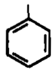
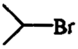
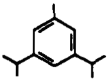
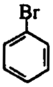
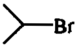
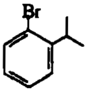
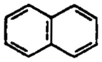
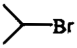
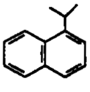
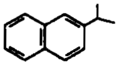
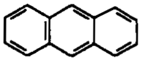
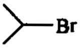
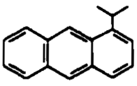
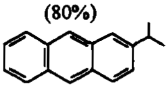
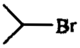
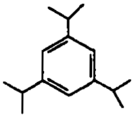
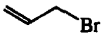
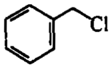
Table 1 Continued

10			25	45	no reaction	
11			25	45		66
12			25	45		60
13			25	120		60
14			25	2 days		75
15			25	45	polymerized	
16			25	45	no reaction	
17			25	45	O-Acylation	

[a] Yield of isolated products

isopropyl bromide in the presence of AlCl3 at room temperature for 45 min., surprisingly, 1,3,5-triisopropyl benzene was obtained in 95% yield (Table **2**). While a number of other successful alkylation reactions are also represented in Table **2**, but in a few cases we could obtain no reaction, or the reaction took undesirable paths, eg., by treating benzene or toluene with benzyl chloride in the presence of AlCl3, a polymeric

Table 2. Friedel-Crafts Alkylation of Aromatic Compounds in the Absence of Solvent

Entry	Substrate	Alkylating Agent	Temp (°C)	Time (min)	Products	Yield[a] (%)
1			25	45		80
2			25	45	 (5%)  (95%)	86
3			25	45	 (70%)  (30%)	92
4			25	45	 (80%)  (20%)	95
5			25	45		95
6			25	45	Polymerized	
7			25	45	Polymerized	

[a] Yield of isolated products

material was obtained that we were not able to separate any low-boiling product from the reaction mixture.

A plausible interpretation for having a faster reaction in no solvent condition might be related to the polar character of the alkylating and acylating complexes, $[R^{\sigma+}\text{--}X\text{----}{}^{\sigma-}AlCl_3]$ and $[RCO^{\sigma+}\text{--}X\text{----}{}^{\sigma-}AlCl_3]$, respectively. Formation of these complexes in the more polar condition (no solvent), in comparison with the less polar condition (having a high concentration of aromatic compound) is much more easier. Generation of local heat by grinding of substrate and reagent, and local distribution of the heat of reaction is also helpful.

Solvents were used directly as obtained from the suppliers. Reagents were employed as purchased from Aldrich or Merck. Thin layer chromatography (TLC) was carried out using glass sheets precoated with silica gel 60F. Melting points were determined on an Electro thermal Gallen Kamp apparatus and uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390 (60 MHz). IR spectra were obtained using a Shimatzo IR-435 spectrometer. The product ratio and purity of the products were determined by GC and ^{1}H NMR spectroscopy,and comparing with authentic samples.

General Procedure for the Friedel-Crafts Acylation Reaction in the Absence of Solvent.- A mixture of aromatic substrate, acylating reagent, and anhydrous $AlCl_3$ was throughly ground in an agate mortor and pestle for 45 min. The reaction mixture was mixed with crushed-ice and extracted with ether. The ether solution was washed with brine and dried over anhydrous $MgSO_4$. The solvent and volatile materials were removed in vacuo to give the corresponding product in the yields shown in Table **1**.

4-Methyl-benzophenone.- A mixture of toluene (2.3 g, 25 mmol), benzoyl chloride (2.81 g, 20 mmol) and $AlCl_3$ (5.43 g, 40 mmol) was ground in an agate mortar and pestle for 45 min., and the mixture was kept at room temperature for 1 h. The reaction mixture was mixed with crushed-ice and extracted with ether (25 mL). The ether solution was washed once with H_2O (10 mL), brine (5 mL), then dried over anhydrous $MgSO_4$. Evaporation of the solvent and volatile materials in vacuo gave the 4-methyl-benzophenone in pure form (75%). mp. 56-57°C, lit.[8] 56-57°. The purity of the product was also determined by ^1H NMR spectroscopy.

General Procedure for the Friedel-Crafts Alkylation Reaction in the Absence of Solvent.-A mixture of the aromatic substrate, alkyl bromide and $AlCl_3$ was throughly ground in an agate mortor and pestle for 45 min. The reaction mixture was mixed with crushed-ice and extracted with ether. The ether solution was washed with brine and dried over anhydrous $MgSO_4$. The solvent and volatile materials were removed in vacuo to give the corresponding product in the yields shown in Table **2**.

1,3,5-Triisopropyl benzene.- A mixture of benzene (2.6 g, 33 mmol), isopropyl bromide (16.4 g, 133 mmol), and $AlCl_3$ (8.86 g, 66 mmol) was throughly ground in an agate mortar and pestle for 45 min., and the mixture was kept at room temperature for 1 h. The reaction mixture was mixed with crushed-ice and extracted with ether(25 mL). The ether solution was washed once with H_2O (10 mL), brine (5 mL), then dried over anhydrous $MgSO_4$. Evaporation of the solvent and volatile aromatic compound in vacuo gave 1,3,5-triisopropyl benzene in pure form (95%). ^1H NMR ($CDCl_3$): $\delta = 6.84$ (s,3H), 3.2 (m, 3H), 1.2 (12H, d). ^{13}C NMR (DMSO-d_6): $\delta = 24.95$ (C_8), 35.5 (C_7), 123 (C_2), 150 (C_1). IR (KBr): $\nu = 3060$, 2956, 1600, 1450, 1370, 1365, 880, 715 cm^{-1}. MS (EI): *m/z* = 204 (M). $C_{15}H_{24}$ (204.19): Calculated: C, 88.15; H,11.85. Found: C, 88.19; H,11.90.

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