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Friedel-Crafts Alkylation Reactions of Benzene with Amide Bond Containing Compounds

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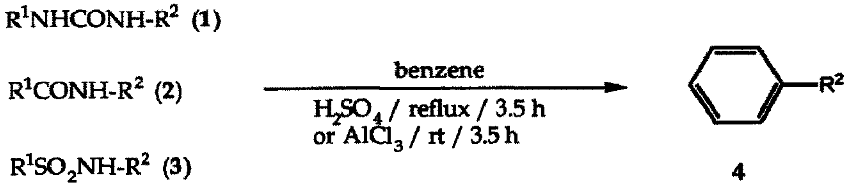
Abstract *: The reactions of benzene and various amide derivatives in the presence of anhydrous aluminium chloride or concentrated sulfuric acid have been examined, and found that these amide derivatives could be used as the electrophile sources in the Friedel-Crafts alkylation reactions.*

Friedel-Crafts and related alkylation reactions of arenes are most important in organic chemistry. Such carbon-carbon bond forming reactions between carbon electrophiles and arenes are well documented in the literature.[1] Recently, we have reported on the Friedel-Crafts cyclohexylation of arenes with 1,3-dicyclohexylcarbodiimide (DCC).[2] In the reaction, DCC served as cyclohexyl carbocation source in the presence of concentrated sulfuric acid or anhydrous aluminum chloride.

As a continuous study, we examined the reaction of 1,3-dicyclohexylurea (DCU) and neat benzene as a representative aromatic compound in the presence of sulfuric acid or aluminum chloride. And besides DCU, we have studied the feasibility using the amide bond containing compounds such as ureas **1**, amides **2**, and sulfonamides **3** in the Friedel-Crafts alkylation reactions. As expected, we could obtain the corresponding alkylated benzene derivatives **4** by using H_2SO_4 (5 eqiuv, reflux condition) or $AlCl_3$ (2 equiv, room temperature). The results are summarized in **Scheme 1** and **Table 1**.



Scheme 1

As shown in **Table 1**, the reaction of benzene with secondary or tertiary alkyl substituted urea derivatives 1 afforded the corresponding alkylbenzenes in moderate to good yields (entries 1-7). Primary alkyl group (entry 4), however, did not participate in the reaction. In the cases of amide derivatives **2** and sulfonamide derivatives **3**, the corresponding alkylbenzenes were also produced in good yields (entries 8-11). It is noteworthy that the reaction of *N*-cyclopropylbenzenesulfonamide and benzene gave a mixture of ring-opened products instead of the expected cyclopropylbenzene.[3] Intramolecular version of this reaction was also examined with 1-phenyl-3-cyclohexylurea (**1e**). Thus the reaction of 1-phenyl-3-cyclohexylurea in carbon disulfide as solvent in the presence of aluminium chloride (2.0 equiv) at room temperature gave *p*-

cyclohexylphenylurea in 7% isolated yield. There has been reported one example by Stamm *et. al.*, in which sulfonamides act as leaving group generating carbocationic species in the Friedel-Crafts alkylation reaction conditions.[4] This and our results suggested that amide bond containing compounds such as ureas, amides, and sulfonamides could be used as alkylating reagents in the Friedel-Crafts alkylation reactions. In these amide bond containing compounds, Lewis basic carbonyl or sulfonyl group could facilitate the departure of the corresponding carbocationic species R_2^+.[5]

Table 1. The Reaction of Benzene and Amide Derivatives **1** - **3** in the Presence of H_2SO_4 or $AlCl_3$.[a]

Entry	Reagent			Catalyst	Product 4[b]	Yield[c]
	1 - 3	R^1	R^2	(equiv)		(%)
1	**1a**	cyclohexyl	cyclohexyl	H_2SO_4 (5.0)	cyclohexylbenzene	68
2	**1a**	cyclohexyl	cyclohexyl	$AlCl_3$ (2.0)	cyclohexylbenzene	106
3	**1b**	isopropyl	isopropyl	$AlCl_3$ (2.0)	isopropylbenzene	100
4	**1c**	*n*-butyl	cyclohexyl	$AlCl_3$ (2.0)	cyclohexylbenzene	70
5	**1d**	H	cyclohexyl	$AlCl_3$ (2.0)	cyclohexylbenzene	76
6	**1e**	phenyl	cyclohexyl	$AlCl_3$ (2.0)	cyclohexylbenzene	80
7	**1f**	phenyl	*tert*-butyl	$AlCl_3$ (2.0)	*tert*-butylbenzene	37
8	**2a**	phenyl	cyclohexyl	$AlCl_3$ (2.0)	cyclohexylbenzene	79
9	**2b**	phenyl	benzyl	$AlCl_3$ (2.0)	diphenylmethane	77
10	**3a**	*p*-tolyl	cyclohexyl	H_2SO_4(5.0)	cyclohexylbenzene	96
11	**3b**	phenyl	cyclopropyl	$AlCl_3$ (2.0)	1,2-dipheylpropane[d]	81

a) Reaction conditions: alkylating reagent (10 mmol) / $AlCl_3$ (20 mmol) or H_2SO_4 (50 mmol) / benzene (25 ml) / reaction time (3.5 h).
b) Products were identified by ^1H NMR and mass spectra.
c) Isolated yields were determined based on mols of the alkylating reagents **1-3**.
d) Product contains a little ammount of 1,3-dipheylpropane, *n*-propylbenzene, and diphenylpropenes by GC/MS and ^1H NMR.

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5. The reaction of cyclohexylamine and benzene in the same reaction conditions did not afford any cyclohexylbenzene.

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