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Friedel-Crafts Cyclohexylation of Arenes with 1,3-Dicyclohexylcarbodiimide (DCC)

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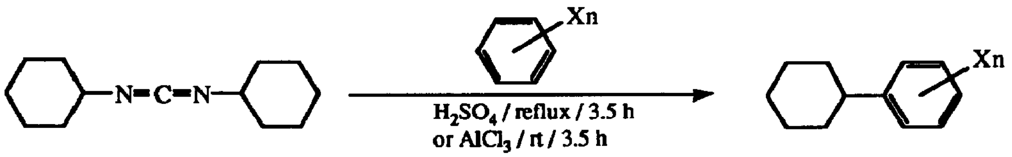
Abstract *: The reaction of arenes with 1,3-dicyclohexylcarbodiimide in the presence of concentrated sulfuric acid or anhydrous aluminum chloride gave the corresponding cyclohexylated arenes in good yields.*

Friedel-Crafts alkylation reactions are important in organic synthesis. These and related reactions have been well studied and reviewed in many reports and monographs.[1] Various electrophile sources could be used in the Friedel-Crafts alkylation reactions including alkyl halides, alkenes, alkynes, alcohols, esters, ethers, alkanes, mercaptans, and thiocyanates.

In our continuing efforts to examine the electrophilic aromatic substitution reactions in the presence of Lewis or Bronstead acid,[2] we found that the reaction of 1,3-dicyclohexylcrbodiimide (DCC) with benzene in the presence of concentrated sulfuric acid afforded cyclohexylbenzene in good yield. DCC is a pivotal and probably the most widely used reagent in chemistry,[3] especially in the peptide-coupling reactions, dehydration reactions, and oxidation reactions. With best of our knowledge, there have no reports that DCC could be used as electrophile in the aromatic electrophilic substitution reaction.[4] Thus we examined the reaction of DCC with various aromatic compounds in the presence of anhydrous aluminum chloride or concentrated sulfuric acid and the results are summarized in **Scheme 1** and **Table 1**.



Scheme 1

As shown in **Table 1**, the reaction of benzene and DCC in the presence of 5 equiv of H_2SO_4 gave cyclohexylbenzene in 98% isolated yield after refluxing the reaction mixture for 3.5 h (entry 1). The use of H_2SO_4 less than 5 equiv decreased the yields of cyclohexylbenzene and the use of H_2SO_4 more than 5 equiv did not improve the yields. When we used $AlCl_3$ instead of H_2SO_4 in the same reaction, cyclohexylbenzene was obtained in good yield at room temperature for 3.5 h by using 2 equiv of $AlCl_3$. In an analogous manner, the corresponding cyclohexylated aromatic compounds were obtained in moderate to good yields in the cases of toluene, *p*-xylene, mesitylene, and naphthalene (entries 5-10 and 12). In the case of chlorobenzene, however, cyclohexylchlorobenzene was obtained in low yield (entry 11). The reaction was performed in an aromatic compound as solvent, thus mono-cyclohexylated product could be obtained as a major product and separated easily from the small amounts of poly-cyclohexylated compounds by distillation. In the reaction of benzene and

DCC in carbon disulfide as solvent, mono-, di-, tri-, and even tetra-cyclohexylated benzenes were detected on the mass spectrum of the crude extracts of the reaction mixtures (entry 3). The reaction of benzene and DCC (3.0 equiv) in carbon disulfide as solvent in the presence of 6.0 equiv of $AlCl_3$ gave 1,3,5-tricyclohexylbenzene in 32% isolated yield (entry 4). The reaction mechanism is uncertain at the present time. The general nature of these observations and the reaction mechanisms are currently under investigation.

Table 1. The Reaction of DCC with Arenes in the Presence of H_2SO_4 or $AlCl_3$.^{a}

Entry	Substrate	Solvent	Catalyst (equiv)	Product^b	Yield(%)^c
1	benzene	benzene	H_2SO_4 (5.0)	cyclohexylbenzene	98 (107)
2	benzene	benzene	$AlCl_3$ (2.0)	cyclohexylbenzene	104 (120)
3	benzene^d	CS_2	$AlCl_3$ (2.0)	mixture(mono-, di-, tri-, tetra-)^e	104
4	benzene^{d,f}	CS_2	$AlCl_3$ (6.0)	tricyclohexylbenzene^e	32
5	toluene	toluene	H_2SO_4 (5.0)	cyclohexyltoluene^g	97 (103)
6	toluene	toluene	$AlCl_3$ (2.0)	cyclohexyltoluene^g	- (104)
7	*p*-xylene	*p*-xylene	H_2SO_4 (5.0)	cyclohexyl-*p*-xylene	103 (116)
8	*p*-xylene	*p*-xylene	$AlCl_3$ (2.0)	cyclohexyl-*p*-xylene	- (94)
9	mesitylene	mesitylene	H_2SO_4 (5.0)	cyclohexylmesitylene	98 (107)
10	mesitylene	mesitylene	$AlCl_3$ (2.0)	cyclohexylmesitylene	- (89)
11	chlorobenzene	chlorobenzene	H_2SO_4 (5.0)	cyclohexylchlorobenzene^g	23 (31)
12	naphthalene^d	CS_2	$AlCl_3$ (2.0)	β-cyclohexylnaphthalene^h	- (70)

a). Reaction conditions: DCC (10 mmol) / H_2SO_4 (50 mmol) or $AlCl_3$ (20 mmol) / solvent (25 ml of arenes or CS_2) /reaction time (3.5 h).

b). Products were identified by ^1H NMR and mass spectra.

c). Isolated yields were determined based on mols of DCC, and the values in parentheses were obtained by GC using 1,3-dichlorobenzene as an external standard. GC analysis was performed with a Helwett-Packard 5890A with a 25 m x 0.2 mm x 0.33 μm fused silica HP-1 capillary column.

d). 10 mmol of substrate was used.

e). Reference 5.

f). Benzene / DCC / $AlCl_3$ = 1 : 3 : 6.

g). A mixture of ortho- and para- isomers.

h). Reference 6.

References and Notes

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