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$GaCl_3$-Catalyzed Arylation of Cycloalkanes

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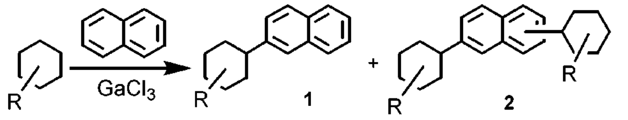
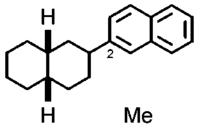
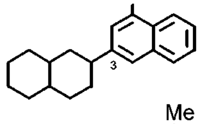
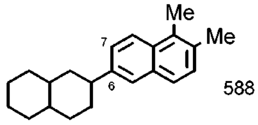
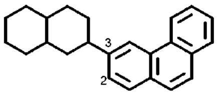
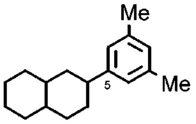
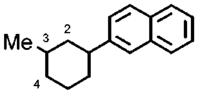
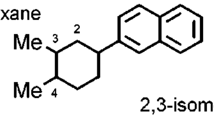
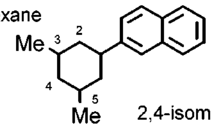
The alkylation of aromatic compounds is generally conducted using alkenes or alkyl halides in the presence of a Lewis acid[1] or a transition-metal complex[2] as the catalyst. The alkylation of arenes with alkanes, which converts an aliphatic C−H bond to a C−Ar bond, is more convenient, if it can be conducted effectively. Such reactions in the presence of sacrificing reagents such as organohalogen compounds or alkenes have been reported.[3] Aromatic alkylation, which proceeds via the C−C bond cleavage of alkane, is known as destructive alkylation.[4] Although a few examples of the direct arylation of the alkane C−H bond, which do not use the sacrificing reagents, have appeared,[5−9] the efficiency of the reaction is low; stoichiometric amounts of the Lewis acid promoter are employed. During our studies on the development of new aromatic C−C bond-formation reactions using $GaCl_3$,[10] we found that the gallium compound catalyzes the direct arylation of cycloalkanes.

Table 1. $GaCl_3$ Catalyzed Arylation of Cycloalkanes



substrate	product[a]	yield[b]/% 1	yield[b]/% 2
bicyclo[4.4.0]decane + naphthalene		590 (30) 819 (41)[c] 7 (0.3)[d]	237 (12) 282 (14)[c] -
bicyclo[4.4.0]decane + 1-methylnaphthalene		464 (23)	231 (12)
bicyclo[4.4.0]decane + 1,2-dimethylnaphthalene	 6-isomer : 7-isomer = 2.1 : 1	588 (29)	57 (3)
bicyclo[4.4.0]decane + phenanthrene	 2-isomer : 3-isomer = 1 : 2.0	689 (34)	193 (10)
bicyclo[4.4.0]decane + *m*-xylene		26 (3)[e]	
methylcyclohexane + naphthalene	 2-isomer : 3-isomer : 4-isomer = **1** : 5 : 4[f]	246 (25)	42 (4)
1,2-dimethylcyclohexane + naphthalene	 2,3-isomer : 3,4-isomer = **1** : 3.6[g]	517 (26) 560 (28)[c] 37 (2)[d]	124 (6) 117 (6)[c] -
1,3-dimethylcyclohexane + naphthalene	 2,4-isome : 3,5-isomer = **1** : 5.4[g]	176 (18)	18 (2)

[a] The structure of the major isomer is shown. [b] The yield is based on $GaCl_3$. Shown in parentheses are yields based on aromatic compounds. [c] *cis*-Cycloalkane was used. [d] *trans*-Cycloalkane was used. [e] The reaction was carried out with irradiation using a high-pressure mercury lamp (400 W). [f] Isomer ratio regarding the methyl position of cycloalkane. [g] Isomer ratio regarding the methyl position of the dehydrogenated compound.

Naphthalene is heated at 70 °C with $GaCl_3$ (5 mol %) in excess bicyclo[4.4.0]decane (a 1:1 mixture of *cis*- and *trans*-decahydronaphthalene) for 40 h. After aqueous workup, the crude product is heated by refluxing in 1-methylnaphthalene in the presence of Pd/C to dehydrogenate the small amounts of 1,2,3,4-tetrahydronaphthalenes formed: For example, ca. 170% (based on $GaCl_3$) of tetrahydronaphthalene is detected in the crude product. 2-(Decahydronaphthalen-3-yl)naphthalenes (590% yield based on $GaCl_3$) and bis(decahydronaphthalen-3-yl)naphthalenes (237% based on $GaCl_3$) are obtained. It should be noted that the turnover number "TON" of the reaction based on $GaCl_3$ is 10.6, if that of dialkylation is calculated to be 2. Some of the hydrogen that is formed from the arene and the cycloalkane may be incorporated in the tetrahydronaphthalene. The structure of the monoalkylated product, being a 1:2.4 mixture of two major isomers by GC, is confirmed by elemental analysis. Treatment of the monoalkylated products with excess dichlorodicyanoquinone (DDQ) by refluxing in toluene for 0.5 h gives 2,2′-binaphthalene as a single product, which indicates that C−C bond formation occurs at the 2-position of naphthalene and at the 3-position of decahydronaphthalene.

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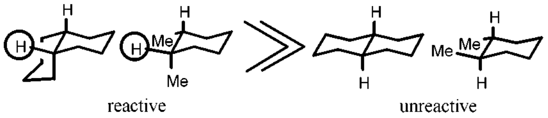
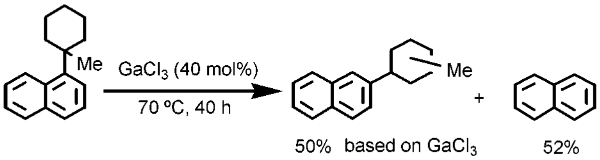
The coupling constants ($J = 10$ Hz) of the benzylic protons show the equatorial configuration of the naphthyl group. The *cis*-stereochemistry of the decahydronaphthalene moiety is determined by comparison with an authentic *trans*-compound. Notably, when *cis*-decahydronaphthalene is used, the monoalkylated product is obtained in 819% yield as a 1:2.4 mixture of two isomers and the dialkylated product in 282% yield.[11] In contrast, the *trans*-isomer gives the alkylated arene only in 7% yield. The *cis*-decahydronaphthalene was found to be the reactive species in this C−C bond-formation reaction.

Arylation of decahydronaphthalene is conducted using methylnaphthalenes, phenanthrene, and *m*-xylene (Table 1). The structures of the products are determined unambiguously by converting them to partially dehydrogenated compounds of single isomers with DDQ. Several authentic samples are prepared by the coupling reaction of 2-bromonaphthalene and arylmagnesium reagents. In all cases, decahydronaphthalene reacts at the 3-position exclusively, and the arenes react at the least hindered positions: 1-Methylnaphthalene reacts at the 3-position predominantly; 1,2-dimethylnaphthalene at the 6- and 7-positions; phenanthrene at the 2- and 3-positions; and *m*-xylene at the 5-position. Monoalkylated products are obtained in more than 400% yield for the bicyclic and tricyclic arenes, while a trace amount of the product is obtained with *m*-xylene. Irradiation with UV light improves the yield of the 1,3-dimethylphenylation to 26% (based on $GaCl_3$). Arylation of methylcyclohexane with naphthalene gives three isomers at the 2-, 3-, and 4-positions in a ratio of 1:5:4, respectively. ^{1}H NMR indicates that the naphthyl group (benzylic H, $J =$ ca. 10 Hz), and probably also the methyl group, occupies the equatorial position. 1,2-Dimethylcyclohexane gives predominantly the 3,4-dimethyl derivative, and 1,3-dimethylcyclohexane, the 3,5-dimethyl derivative. No product derived from the reaction at the tertiary carbon atom is detected. The TONs are higher in the reactions of decahydronaphthalene and 1,2-dimethylcyclohexane than those in methylcyclohexane and 1,3-dimethylcyclohexane. The reaction of cyclohexane and naphthalene gives a very low yield of the naphthylcyclohexane. The importance of the adjacent tertiary carbons with the *cis*-configuration is confirmed again in the reaction of 1,2-dimethylcyclohexane and naphthalene. The *cis*-isomer gives the monoalkylated naphthalene in 560% yield and the dialkylated product in 117%, while from the *trans*-isomer the former compound is obtained only in 37% yield.

Scheme 1



Scheme 2



Contamination of a small amount of cycloalkene in the cycloalkane can be excluded, since the hydrocarbon washed with concentrated sulfuric acid also undergoes the same reaction. The requirement of the tertiary C−H bond in the cycloalkane may be explained by the initial activation of the reactive C−H bonds with $GaCl_3$ to generate the tertiary cations. It appears that the tertiary equatorial protons are preferentially activated by $GaCl_3$ rather than the axial ones (Scheme 1). The formation of the thermodynamically stable alkylated products may be due to the migration of the cycloalkyl group on the aromatic ring under the given reaction conditions. Accordingly, the treatment of 1-(1-methylcyclohexyl)-naphthalene with a catalytic amount of $GaCl_3$ (40 mol %) in cyclohexane for 40 h at 70 °C gives 2-(methylcyclohexyl)-naphthalenes in 50% yield based on $GaCl_3$ as a mixture of three isomers in a 1:3:2 ratio (Scheme 2). The products are identical to those obtained from methylcyclohexane and naphthalene.

To summarize, arylation of cycloalkanes with aromatic hydrocarbons occurs in the presence of $GaCl_3$. This is a novel catalytic reaction that forms a C−C bond between aromatic hydrocarbons and aliphatic hydrocarbons without having to use a sacrificing reagent.

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Supporting Information Available: Experimental procedures and spectral data for all the products are provided (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Under an argon atmosphere, a solution of $GaCl_3$ (1.0 M in *cis*-decahydronaphthalene, 0.25 mL) was added to a solution of naphthalene (640 mg, 5 mmol) in *cis*-decahydronaphthalene (1.25 mL). This mixture was heated to 70 °C and stirred for 40 h at that temperature. After the reaction was quenched by the addition of water, the organic layer was separated, washed with saturated aqueous NH_4Cl and water, and dried over $MgSO_4$. Solvents were removed in vacuo, and the residue was treated with Pd/C (5%, 530 mg) in refluxing 1-methylnaphthalene (0.7 mL) for 4 h. The mixture was diluted with ether, and filtered by passing through Celite. The solvents were removed in vacuo, and the residue was purified by flash column chromatography (silica gel, hexane) and GPC ($CHCl_3$) to give the monoalkylated product (541 mg, 819% based on $GaCl_3$) and the dialkylated product (283 mg, 282% based on $GaCl_3$).