JOC Article

Equatorial Preference in the C−H Activation of Cycloalkanes: $GaCl_3$-Catalyzed Aromatic Alkylation Reaction

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$GaCl_3$ catalyzes the aromatic alkylation of naphthalene or phenanthrene using cycloalkanes. The C−C bond formation predominantly takes place at the least hindered positions of the substrates, and equatorial isomers regarding the cycloalkane moiety are generally obtained. The reaction of bicyclo[4.4.0]decane and naphthalene occurs at the 2-position of naphthalene and at the 2- or 3-carbons of the cycloalkane, and the products possess a trans configuration at the junctures and an equatorial configuration at the naphthyl groups. Notably, *cis*-bicyclo[4.4.0]decane turns out to be much more reactive than the trans isomer, and a turnover number "TON" up to 20 based on $GaCl_3$ is attained. 1,2-Dimethylcyclohexane reacts similarly, and the cis isomer is more reactive than the trans isomer. Monoalkylcycloalkanes react at the secondary carbons provided that the alkyl group is smaller than *tert*-butyl. Adamantanes react at the tertiary 1-position. The alkylation reaction is considered to involve the C−H activation of cycloalkanes with $GaCl_3$ at the tertiary center followed by the migration of carbocations and electrophilic aromatic substitution yielding thermodynamically stable products. The stereochemistry of the reaction reveals that $GaCl_3$ activates the equatorial tertiary C−H bond rather than the axial tertiary C−H bond.

Aromatic hydrocarbons are generally alkylated using alkenes or alkyl halides in the presence of a protic acid, a Lewis acid,[1] or a transition-metal complex[2] as 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 performed effectively. Such reactions in the presence of stoichiometric amounts of sacrificing reagents, organohalogen compounds or alkenes, have been reported.[3] For example, the reaction of benzene, methylcyclohexane, and 1,2-dichloro-2-methylpropane in the presence of a catalytic amount of $AlCl_3$ yields methylphenylcyclohexanes in which the organohalogen compound serves as a hydride acceptor. Aromatic alkylation, which proceeds via the C−C bond cleavage of alkane, is known as "destructive alkylation":[4] 2,2,4-trimethylpentane and benzene react in the presence of a catalytic amount of $AlCl_3$ to yield *tert*-butylbenzene and isobutane. A few examples of the direct arylation of alkanes, which do not use a sacrificing reagent or a "destructive alkylation" methodology, have been reported.[5−9] For example, treating a mixture of benzene and isopentane with $CuCl_2$ and $AlCl_3$ gives pentylbenzenes.[7] Benzene is alkylated with C_1−C_5 alkanes in the presence of anhydrous fluoroantimonic acid ($HF-SbF_5$).[6] The efficiencies of these reactions, however, are not high; more than stoichiometric amounts of a Lewis acid or protic acid promoter are employed. During our studies on the development of novel aromatic C−C bond-forming reactions using $GaCl_3$,[10] we found that the gallium compound catalyzes aromatic alkylation using cycloalkanes.[11] $GaCl_3$ activates the equatorial tertiary C−H bond of cycloalkanes to generate tertiary cations, which after migration undergo electrophilic substitution with aromatic hydrocarbons.

(1) (a) Olah, G. A. *Friedel−Crafts Chemistry*; John Wiley & Sons: New York, 1973. (b) Taylor, R. *Electrophilic Aromatic Substitution*; John Wiley & Sons: New York, 1990.

(2) Recent examples: (a) Matsumoto, T.; Taube, D. J.; Periana, R. A.; Taube, H.; Yoshida, H. *J. Am. Chem. Soc.* **2000**, *122*, 7414−7415. (b) Nishiyama, Y.; Kakushou, F.; Sonoda, N. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2779−2782. (c) Singh, R. P.; Kamble, R. M.; Chandra, K. L.; Saravanan, P.; Singh, V. K. *Tetrahedron* **2001**, *57*, 241−247.

(3) (a) Schmerling, L.; Welch, R. W.; West, J. P. *J. Am. Chem. Soc.* **1956**, *78*, 5406−5409. (b) Schmerling, L.; Welch, R. W.; Luvisi, J. P. *J. Am. Chem. Soc.* **1957**, *79*, 2636−2642. Also see references cited.

(4) (a) Grosse, A. V.; Ipatieff, V. N. *J. Am. Chem. Soc.* **1935**, *57*, 2415−2419. (b) Grosse, A. V.; Ipatieff, V. N. *J. Org. Chem.* **1937**, *2*, 447−458. (c) Grosse, A. V.; Mavity, J. M.; Ipatieff, V. N. *J. Org. Chem.* **1938**, *3*, 137−145. (d) Sugahara, Y.; Hayami, J.; Sera, A.; Goto, R.. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2656−2662.

(5) (a) Miethchen, R.; Kröger, C.-F., *Z. Chem.* **1975**, 135−141. (b) Miethchen, R.; Steege, S.; Kröger, C.-F. *J. Prakt. Chem.* **1983**, *325*, 823−834. Also see references cited therein.

(6) Olah, G. A.; Schilling, P.; Staral, J. S.; Halpern, Y.; Olah. J. A. *J. Am. Chem. Soc.* **1975**, *97*, 6807−6810.

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(9) Koltunov, K. Y.; Subbotina, E. N.; Repinskaya, I. B. *Russ. J. Org. Chem.* **1997**, *33*, 689−693.

(10) (a) Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313−1315. (b) Kido, Y.; Yamaguchi, M. *J. Org. Chem.* **1998**, *63*, 8086−8087. (c) Kido, Y.; Yoshimura, S.; Yamaguchi, M.; Uchimaru, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1445−1458. (d) Yonehara, F.; Kido, Y.; Yamaguchi, M. *Chem. Commun.* **2000**, 1189−1190. (f) Kido, Y.; Yonehara, F.; Yamaguchi, M. *Tetrahedron* **2001**, *57*, 827−833.

(11) Preliminary publication: Yonehara, F.; Kido, Y.; Morita, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2001**, *123*, 11310−11311.

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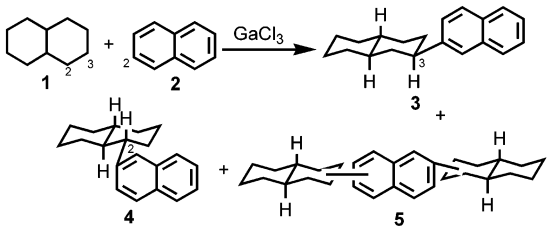
SCHEME 1[a]



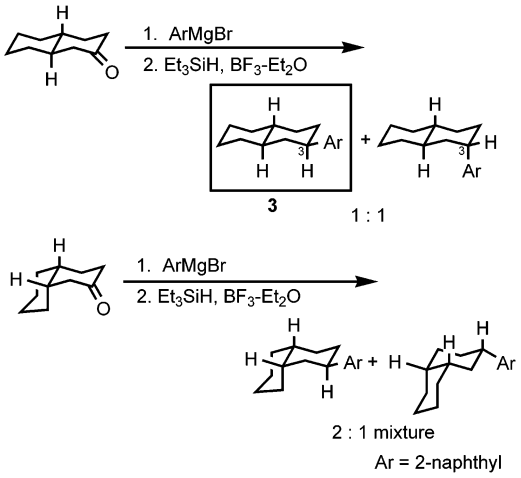
	yield [a]/% monoalkylation	dialkylation	"TON"
cis-**1** + *trans*-**1** (1 : 1)	590 (30) (**3** : **4** = 6 : 1)	237 (12)	10.6[b]
cis-**1**	1188 (30) (**3** : **4** = 4 : 1)	423 (11)	20.3[c]
trans-**1**	11 (0.3) (**3** : **4** = 2 : 1)	-	0.1[c]

[a] Key: (a) The yield is based on $GaCl_3$. The yield based on **2** is shown in parentheses. (b) $GaCl_3$ (5 mol %) was used. (c) $GaCl_3$ (2.5 mol %) was used.

A 2:1 mixture of bicyclo[4.4.0]decane **1** (a 1:1 mixture of *cis*-**1** and *trans*-**1**) and naphthalene **2** was heated at 70 °C with $GaCl_3$ (5 mol % based on **2**) for 40 h. After aqueous workup, the crude product was heated in refluxing 1-methylnaphthalene **6** in the presence of Pd/C in order to dehydrogenate small amounts of tetrahydronaphthalenes formed; for example, ca. 170% (based on $GaCl_3$) of 1,2,3,4-tetrahydronaphthalene was detected in the crude product. (Decahydronaphthyl)naphthalenes **3** and **4** (590% yield based on $GaCl_3$, 30% yield based on **2**) were obtained in a 6:1 ratio and were accompanied by bis(decahydronaphthyl)naphthalenes **5** (237% based on $GaCl_3$, 12% yield based on **2**) (Scheme 1).[12] No product derived from the reaction at the tertiary carbon atom of **1** was detected. It should be noted that the turnover number "TON" of the reaction based on $GaCl_3$ is 10.6, if that of the dialkylation is calculated to be 2. In the following part of this paper, the yield based on $GaCl_3$ and the "TON" are used for discussion. Some part of hydrogen that is formed from **1** and **2** may be incorporated in tetrahydronaphthalene. The contamination of small amounts of cycloalkenes in **1** is excluded, since the hydrocarbon washed with concentrated sulfuric acid also undergoes the same reaction. The molecular formula of the **3/4** mixture was confirmed by elemental analysis. The treatment of the mixture with excess 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing toluene for 3 h yielded 2,2′-binaphthalene (27%) and 1,2′-binaphthalene (12%). This result indicates that C−C bond formation predominantly occurs at the 2-position of **2** and at the 3-position of **1**, which is accompanied by a minor product that reacts at the 2-position of **1**. The coupling constants (tt, J = 12.0, 3.6 Hz) of the benzylic proton of **3** and those (td, J = 11.6, 2.8 Hz) of **4** show the equatorial configurations of the naphthyl groups. The juncture stereochemistry of **3** was determined by comparison with an authentic compound. A mixture of **3** and its 3-epimer was obtained from *trans*-2-decalone[13] and 2-naphthylmagnesium bromide followed by reduction using triethylsilane and boron trifluoride (Scheme 2). The cis isomers were also synthesized for comparison.

When isomerically pure *cis*-**1** was reacted with **2** (molar ratio 2:1) in the presence of $GaCl_3$ (2.5 mol % based on **2**) at 70 °C for 12 h, monoalkylated products **3** and **4** (4:1) were obtained in 1188% yield and dialkylated products in 423% yield, "TON" 20.3 (Scheme 1). In contrast, *trans*-**1** gave **3** and **4** in only 11% yield, "TON" 0.1, which indicates that *cis*-**1** is much more reactive in this C−C bond formation than *trans*-**1**. Despite the different stereochemistries of the starting materials, *cis*-**1** or *trans*-**1**, the same products **3** and **4** with trans configurations at the juncture were obtained. This observation strongly suggests that the initially activated bond is one of the two tertiary C−H bonds in *cis*-**1** and the migration of the resulting carbocations takes place during the reaction. In accordance, *cis*-**1** isomerized to *trans*-**1** in the presence of a catalytic amount of $GaCl_3$.[14] When a solution of $GaCl_3$ (2.5 mol %) in *cis*-**1** was heated at 70 °C for 40 h, a 1.3:1.0 mixture of *cis*-**1** and *trans*-**1** was obtained, and a 1.0:14.2 mixture was obtained after heating for 70 h.

SCHEME 2

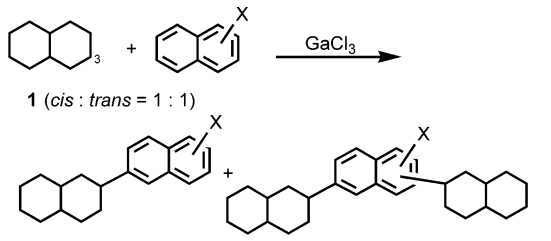


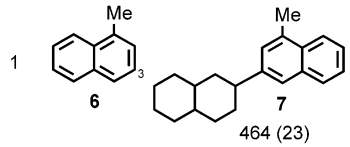
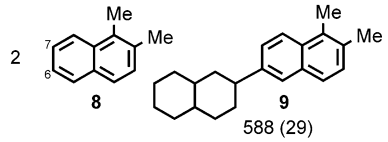
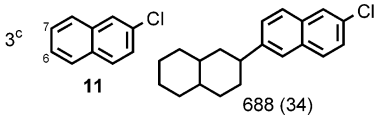
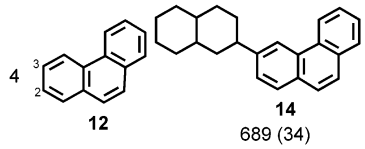
The alkylation of methylnaphthalenes **6** and **8**, 2-chloronaphthalene **11**, and phenanthrene **12** using **1** (cis/trans = 1:1) was also conducted (Table 1). Monoalkylated products were obtained in more than 400% yield, and their "TON" exceeded 7 in all cases. The reactions takes place at the 3-position of **1** preferentially and at the β-positions of naphthalenes giving thermodynamically stable compounds: **6** reacts at the 3-position predominantly giving **7** (entry 1); **8** at the 6- and 7-positions in a 2:1 ratio (entry 2); **12** at the 2- and 3-positions in a 1:2 ratio (entry 4). It was presumed that **11** reacted at the 6- and 7-positions by analogy to the reaction with adamantane (vide infra). The structures of the major products were determined unambiguously by converting the products to partially dehydrogenated compounds of single isomers. For example, the treatment of monoalkylated product **7** derived

(12) We previously reported that the monoalkylated products obtained from **1** and **2** are a 1:2.4 mixture of two isomers and that the major compound was 2-(*cis*-decahydronaphthalen-3-yl)naphthalene **3**.[11] Detailed investigations shown in the present work revealed that the two isomers are **3** and **4**.

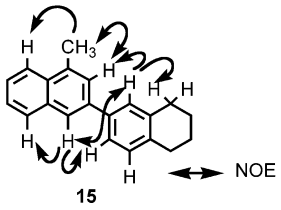
(13) Trimethyl[*trans*-(3,4,4a,5,6,7,8,8a-octahydro-2-naphthalenyl)-oxyl]silane was synthesized by the reported method. Crabtree, S. R.; Mander, L. N.; Sethi, S. P.; *Org. Synth*. **1992**, *70*, 256−264. *trans*-2-Decalone was obtained by the hydrolysis of the silyl enol ether using tetrabutylammonium fluoride in THF and water. *cis*-2-Decalone was synthesized by the hydrogenation of 2-naphthol. Gream, G. E.; Laffer, M. H.; Serelis, A. K. *Aust. J. Chem*. **1978**, *31*, 803−833.

TABLE 1. $GaCl_3$ Catalyzed Arylation of 1 with Substituted Naphthalene



entry	substrate	yield of product [a]/% monoalkylation[b]	dialkylation	"TON"
1	 **6** **7**	464 (23)	231 (12)	9.3
2	 **8** **9**	588 (29)	57 (3)	7.0
	6-isomer **9** : 7-isomer **10** = 2 : 1			
3[c]	 **11**	688 (34)	92 (5)	8.7
4	 **12** **14**	689 (34)	193 (10)	10.8
	2-isomer **13** : 3-isomer **14** = 1 : 2			

[a] The yield is based on $GaCl_3$. The yield based on naphthalene is shown in parentheses. [b] The structure of the major isomer is shown. [c] *cis*-**1** was used.

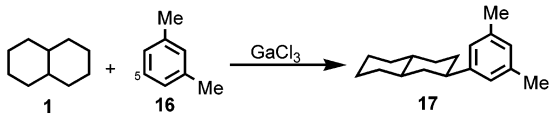


15

from **1** and **6** with DDQ in refluxing toluene for 1 h gave 3-(5,6,7,8-tetrahydro-2-naphthyl)-1-methylnaphthalene **15** as the major product, the structure of which was determined by NOE.

The condensed benzene ring system is required for the effective reaction, and only a trace amount (2%) of monoalkylated product **17** was obtained by the reaction of **1** and *m*-xylene **16** (Scheme 3). **16** reacts at the least hindered 5-position and gives **17** with an equatorial aryl group (benzylic H, tt, J = 12.0, 3.6 Hz). The juncture trans stereochemistry of **17** was determined by comparison with an authentic compound prepared by the method shown in Scheme 2. Irradiation with UV light improves the yield of **17** to 26%, which suggests a partial radical feature of this reaction.

SCHEME 3[a]



1 **16** **17**

cis-**1** + *trans*-**1** (1 : 1) 2% (0.2%)[b]

cis-**1** + *trans*-**1** (1 : 1), *hv* [a] 26% (3%)[b]

[a] Key: (a) The reaction was carried out with irradiation using a high-pressure mercury lamp (400 W). (b) The yield is based on $GaCl_3$. The yield based on **16** is shown in parentheses.

Alkylation using monoalkylcyclohexanes was examined (Table 2). The reaction of methylcyclohexane **18** and **2** (molar ratio 4.7:1.0) gave a mixture of monoalkylated naphthalenes **19**, **20**, and **21** (246%) in a ratio of 1:5:4, which were isomers in terms of the 2-, 3-, and 4-positions of the cycloalkane, respectively. Dialkylated naphthalenes (42%) were also formed, "TON" 3.3 (entry 1). The treatment of the monoalkylated compounds with excess DDQ in refluxing toluene for 0.5 h gave a mixture of 2-(methylphenyl)naphthalenes (*o*/*m*/*p* = 1:3:1), the structures of which were confirmed by comparison with those of the authentic samples prepared from 2-bromonaphthalene and tolylmagnesium bromides. ^{1}H NMR indicated that all the naphthyl groups of **19**, **20**, and **21** occupy the equatorial position (benzylic H, J = ca. 10 Hz). Since previous ^{13}C NMR studies of methylcyclohexanes have revealed that equatorial methyl carbons are generally observed at $>\delta$ 20,[15] the methyl groups of **19**, **20**, and **21** observed at δ 21.0, 22.9, 23.8, respectively, are likely to have the equatorial orientation.

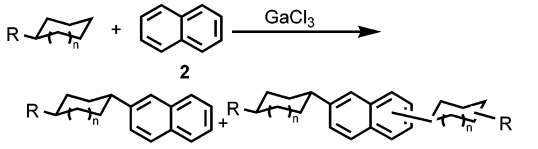
The yield decreases as the alkyl group on the alkylcyclohexane becomes bulky from methyl to isopropyl, and essentially no reaction occurs with *tert*-butylcyclohexane **24** (entries 1−4). The reactivity may be correlated to the amount of axial conformers that possess tertiary equatorial protons (vide infra). Since neopentylcyclohexane **25** is also unreactive (entry 5), the low reactivity of **24** may not be due to the steric hindrances at the vicinity of the tertiary C−H bonds. Methylcyclopentane **26** and methylcycloheptane **27** exhibit reactivity similarly to **18** (entries 6 and 7). In contrast, the reaction of cyclohexane **28** gave a very low yield of naphthylcyclohexane **29**, which confirms that the tertiary C−H bond is necessary for the present reaction.

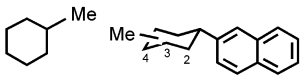
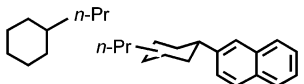
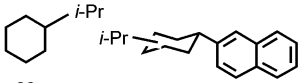
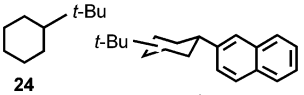
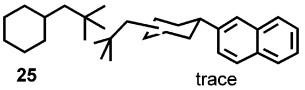
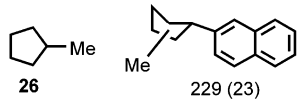
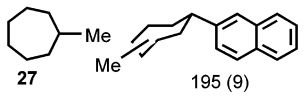
The reaction of acyclic hydrocarbons was examined using 2,3-dimethylbutane, isobutane, and methane (Table 3). The reaction of excess isobutane and **2** gave 2-(*tert*-butyl)naphthalene in 20% yield and bis(*tert*-butyl)naphthalene in 2% yield (entry 1). Addition of oxygen slightly increased the yield of the product (entry 2), which again suggests the partial radical feature of the present reaction. Alkylation of **2** with 2,3-dimethylbutane gave 2,3-dimethyl-2-(2-naphthyl)butane **30** in 28% yield (entry 3). These reactions competed with the oligomerization of **2**. The C−C bond formation occurred at the tertiary carbon

(14) (a) Zelinsky, N.; Turowa-Pollak, M. *Ber*. **1932**, *65B*, 1299−1301. (b) Davies, G. F.; Gilbert, E. C. *J. Am. Chem. Soc*. **1941**, *63*, 1585−1586.

(15) (a) Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc*. **1967**, *89*, 6612−6622. (b) Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*, 3rd completely revised ed.; VCH: Weinheim, 1987. (c) Schneider, H.-J.; Price, R.; Keller, T. *Angew. Chem*. **1971**, *83*, 759−760. (d) Schneider, H.-J.; Hoppen, V. *J. Org. Chem*. **1978**, *43*, 3866−3873.

TABLE 2. Naphthylation of Monoalkylcycloalkenes



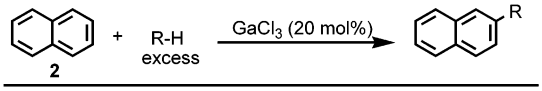
entry	substrate	yield of product [a]/% monoalkylation	dialkylation	"TON"
1[c]	 **18**	246 (25)	42 (4)	3.3
	2-isomer **19** : 3-isomer **20** : 4-isomer **21** = 1 : 5 : 4 [b]			
2[d]	 **22**	120 (6)	2 (0.1)	1.2
	4 isomers (10 : 4 : 2 : 1)			
3[d]	 **23**	169 (8)	7 (0.3)	1.8
	3 isomers (9 : 3 : 1)			
4[d]	 **24**	trace	-	-
5[d]	 **25**	trace	-	-
6[c]	 **26**	229 (23)	38 (4)	3.1
	2 isomers (1 : 1)			
7[d]	 **27**	195 (9)	-	2.0
	6 isomers (3 : 3 : 3 : 1 : 1 : 1)			
8[e]	 **28**	**29** 5 (10)	-	0.05

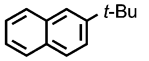
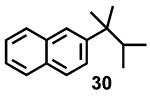
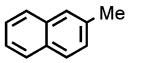
[a] The yield is based on $GaCl_3$. The yield based on naphthalene is shown in parentheses. [b] Isomer ratio regarding the methyl position of cycloalkanes. [c] $GaCl_3$ (10 mol %) was used. [d] $GaCl_3$ (5 mol %) was used. [e] $GaCl_3$ (200 mol %) was used.

in both cases, and no product reacted at the methyl moiety was detected. In terms of "TON", acyclic alkanes are less reactive than cyclic alkanes, even though they both possess tertiary C−H bonds. The presence of not only the tertiary C−H bond but also the configurationally fixed adjacent C−C bond appears to be critical for effective C−H activation. It may be noted that a small amount of 2-methylnaphthalene was detected, when **2** was treated with methane (190 atm) at 180 °C in benzene (entry 4).[16]

To probe the effect of stereochemistry at the tertiary C−H bond of cycloalkanes, the reactions of dialkylcyclo-

TABLE 3. Naphthylation of Acyclic Alkanes



entry	R-H	temp. / °C	time / h	yield of product [a]/%	"TON"
1	$(CH_3)_3CH$	70	12	 20[b]	0.24
2[c]	$(CH_3)_3CH$	70	12	33[b]	0.35
3	$(CH_3)_2CHCH(CH_3)_2$	70	12	 **30** 28	0.28
4[d]	CH_4 (ca. 190 atm)	180	3	 0.1[e]	-

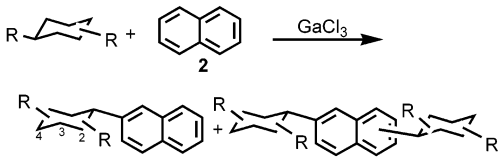
[a] The yield is based on $GaCl_3$. [b] A 1:1 mixture of 2,6- and 2,7-bis(*tert*-butyl)naphthalene was formed in 2%. [c] O_2 (ca 0.3 mol) was added. [d] Benzene was used as solvent. [e] The yield was determined by GC.

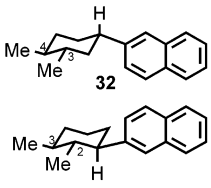
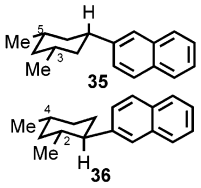
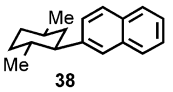
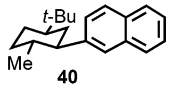
hexanes were examined (Table 4). When **2** and 1,2-dimethylcyclohexane **31** (cis/trans = 1:1) were reacted with $GaCl_3$ (5 mol %), monoalkylated products containing 2-(3,4-dimethylcyclohexyl)naphthalene **32** and 2-(2,3-dimethylcyclohexyl)naphthalene **33** were obtained in 517% yield, which was accompanied by dialkylated products in 124% yield, "TON" 7.7 (entry 1). The monoalkylation products were 4 major isomers in a 5:2:2:1 ratio as determined by GC, namely, **32**, **33**, and their stereoisomers. Their regiochemistry was determined by dehydrogenation to give a mixture of 2-(3,4-dimethylphenyl)naphthalene and 2-(2,3-dimethylphenyl)naphthalene in a 3.6:1 ratio in 48% yield. Their stereostructures were determined by NMR. The benzylic protons of all the four isomers exhibited coupling constants J = ca. 12 Hz, which indicated the equatorial orientation of the naphthyl groups. The methyl groups of the monoalkylated products appeared at δ 20−25 indicating the equatorial configuration, and small peaks at δ 14.3 and 17.7 suggested the presence of axial isomers. Thus, the major isomers should be **32** and **33** with an all equatorial configuration. As in the reaction of **1**, *cis*-**31** gave products with "TON" 7.9 (entry 2), while *trans*-**31** gave monoalkylated products in only 37% yield, "TON" 0.4 (entry 3). GC analysis indicated that the *cis*-**31** and *trans*-**31** gave the same composition of the products.

When 1,3-dimethylcyclohexane **34** (cis/trans = 1:1) and **2** were reacted with $GaCl_3$ (10 mol %), monoalkylated products were obtained in 176% yield, which was accompanied by dialkylated products in 18% yield, "TON" 2.1 (entry 4). The dehydrogenation of monoalkylated naphthalenes provided a mixture of 2-(3,5-dimethylphenyl)naphthalene and 2-(2,4-dimethylphenyl)naphthalene in a 5.4:1 ratio in 31% yield. The monoalkylated product contained six isomers in a ratio of 10:5:2:2:1:1, as determined by GC; the most major isomer was 2-(3,5-

(16) See the following for a related reaction, which is considered to proceed via a radical mechanism. He, S. J. X.; Long, M. A.; Attalla, M. I.; Wilson, M. A. *Energy Fuels* **1992**, *6*, 498−502.

TABLE 4. Naphthylation of Dialkylcycloalkenes



entry	substrate	yield of product [a]/% monoalkylation[b]	dialkylation	"TON"
	 **31**	 **32** **33**		
1[c]	mixture[d]	517 (26)	124 (6)	7.7
2[c]	*cis*-**31**	560 (28)	117 (6)	7.9
3[c]	*trans*-**31**	37 (2)	-	0.4
	 **34**	 **35** **36**		
4[e]	mixture[d]	176 (18)	18 (2)	2.1
5[c]	*cis*-**34**	84 (4)	-	0.8
6[c]	*trans*-**34**	264 (13)	15 (0.7)	2.9
	 **37**	 **38**		
7[e]	mixture[d]	190 (20)	23 (2)	2.4
8[c]	*cis*-**37**	219 (11)	8 (0.4)	2.4
9[c]	*trans*-**37**	143 (7)	5 (0.3)	1.5
	 **39**	 **40**		
10[c]	mixture[d]	188 (9)	3 (0.2)	1.9

[a] The yield is based on $GaCl_3$. The yield based on aromatic compound is shown in parentheses. [b] The structure of the major isomer is shown. [c] $GaCl_3$ (5 mol %) was used. [d] A 1:1 mixture of cis isomer and trans isomer was used. [e] $GaCl_3$ (5 mol %) was used.

dimethylcyclohexyl)naphthalene **35** with an all equatorial configuration, and the second major isomer was 2-(2,4-dimethylcyclohexyl)naphthalene **36**. The benzylic proton of **35** was observed as a tt (J = 12.0, 3.6 Hz) and that of **36** as a td (J = 12.0, 3.6 Hz). ^{13}C NMR indicated that the methyl groups of **35** and **36** occupied equatorial positions: **35** at δ 22.8; **36** at δ 20.9 and 22.9. As for the effect of stereochemistry, *trans*-**34** gave the monoalkylated naphthalenes in 264% yield and the dialkylated naphthalenes in 15%, "TON" 2.9 (entry 6), while *cis*-**34** gave the same monoalkylated naphthalenes in 84% yield, "TON" 0.8 (entry 5). Thus, *trans*-**34** is more reactive than *cis*-**34**, which is contrasted to the higher reactivity of *cis*-**31** than of *trans*-**31**.

The reaction of 1,4-dimethylcyclohexane **37** (cis/trans = 1:1) gave a monoalkylated product **38** in 190% yield as a single isomer and dialkylated products in 23% yield, "TON" 2.4 (entry 7). The ^1H NMR of **38** at the benzylic proton (td, J = 11.2, 3.2 Hz) and the ^{13}C NMR of the 5-methyl δ 22.7 showed that both naphthyl and methyl groups occupied the equatorial positions. *cis*-**37** gave the products at a higher "TON" than *trans*-**37**. Thus, all these experiments using dimethylcyclohexanes reveal that the substrates with an axial methyl group, that is, those with an equatorial tertiary C−H bonds are more reactive.

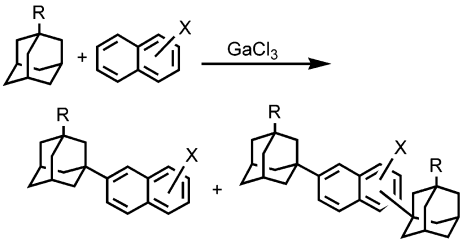
The reaction of 1-(*tert*-butyl)-4-methylcyclohexane **39** (cis/trans = 1:1) and **2** gave a monoalkylated product **40** in 188% yield as a single isomer (entry 10). The C−C bond formation takes place at the less hindered secondary carbon, and the ^1H NMR of the benzylic proton (td, J = 11.2, 3.6 Hz) indicates the equatorial configuration of both methyl and naphthyl groups. Since the *tert*-butyl group should be equatorial, **40** possesses an all equatorial configuration.

The reactivity of adamantane **41** was considered interesting, since all the tertiary C−H bonds of **41** occupy an equatorial position (Table 5). An equimolar amount of **2** and **41** in cyclohexane was reacted in the presence of $GaCl_3$ (5 mol %) at 70 °C for 12 h, and the crude products were heated for 4 h in refluxing 1-methylnaphthalene **6** in the presence of Pd/C for dehydrogenation. 2-(1-Adamanty)naphthalene **42** was obtained in 267% yield, and 2,7-bis(1-adamantly)naphthalene **43** in 11% yield, "TON" 2.9 (entry 1). Since **41** has a relatively high melting point, cyclohexane was used as a solvent, which was inert to the arylation reaction (Table 2, entry 8). C−C bond formation occurred at the 2-position of **2** and at the 1-position of **41**. The structure of **43** was determined by the presence of six aromatic ^{13}C NMR peaks: The 2,6-isomer should exhibit five peaks. Notably, **41** reacts only at the tertiary C−H bond, which is different from the reactions of cycloalkanes at the secondary carbons. The regioselectivity of the reaction may be ascribed to the low tendency of a 1-adamantyl cation to isomerize to a secondary cation.[17] Methyladamantanes **44**, **46**, and **48** react analogously at tertiary centers (entries 2−4). In the reaction of 2-chloronaphthalene **11** and **41**, the crude product was treated with DDQ for dehydrogenation instead of Pd/C in order to avoid hydrogenolysis of the C−Cl bond (entry 5). A 1:1 mixture of 6-chloro and 7-chloro derivatives **50** and **51** was obtained, the structures of which were determined by careful ^1H NMR analysis. The results of the adamantane reactions are consistent with the mechanism that $GaCl_3$ activates the tertiary equatorial C−H bond to generate carbocations.

The reactivity of the substituted cyclohexanes in the present arylation reaction is summarized in Figure 1. The disubstituted cyclohexanes possessing the equatorial C−H bonds exhibit higher "TON"s than the isomers: *cis*-**1** ≫ *trans*-**1**; *cis*-**31** ≫ *trans*-**31**; *trans*-**34** > *cis*-**34**; *cis*-**37** > *trans*-**37**. That the reactivity of monosubstituted cyclohexanes decreases as the bulkiness of the substituent increases is consistent with the explanation. It may

(17) (a) Schleyer, P. v. R.; Lam, L. K. M.; Raber, D. J.; Fry, J. L.; McKervey, M. A.; Alford, J. R.; Cuddy, B. D.; Keizer, V. G.; Geluk, H. W.; Schlatmann, J. L. M. A. *J. Am. Chem. Soc.* **1970**, *92*, 5246−5247. (b) Aubry, C.; Holmes, J. L.; Walton, J. C. *J. Phys. Chem. A* **1998**, *102*, 1389−1393.

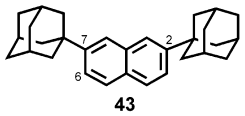
TABLE 5. Naphthylation of Adamantanes



entry	substrate	yield of product [a]/%	"TON"
1	**2** + **41**	**42** 267 (13)[b]	2.9
2	**2** + **44**	**45** 290 (14)	2.9
3	**2** + **46**	**47** 207 (10)	2.0
4	**2** + **48**	**49** 247 (12)	2.5
5	**11** + **41**	**50** 181 (9)	1.8

6-isomer **50** : 7-isomer **51** = 1 : 1

[a] The yield is based on $GaCl_3$. The yield based on **2** is shown in parentheses. [b] 2,7-Bis(1-adamantyl)naphthalene **43** was formed in 11(0.6%) yield.



43

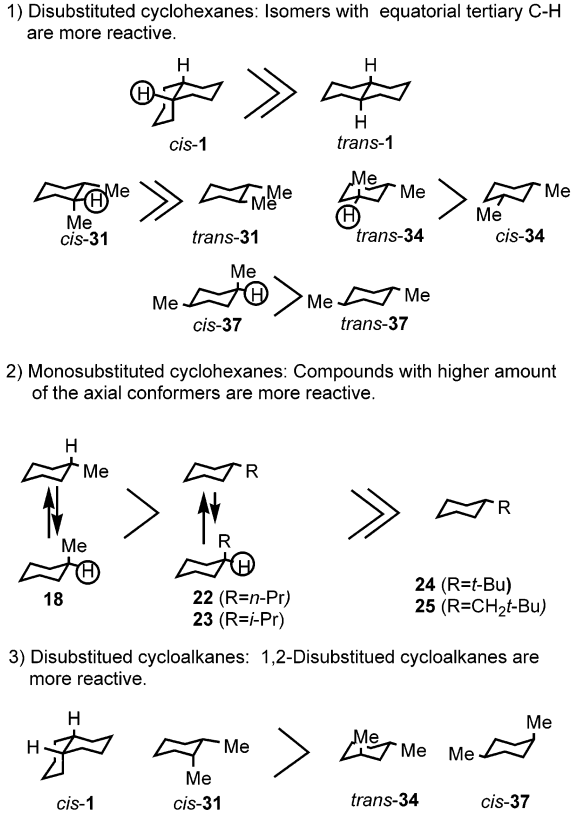
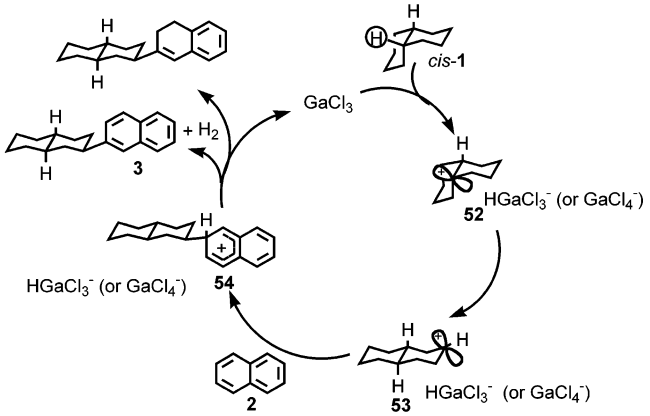


FIGURE 1. Reactivity of substituted cycloalkanes.

SCHEME 4

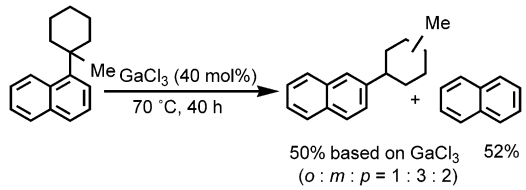


be likely that small amounts of axial conformers with the equatorial C−H are the reactive species in the reactions of **18**, **22**, and **23**. The low reactivity of **24** and **25** can be attributed to the extremely low concentration of axial conformers. It was noted that the presence of adjacent tertiary carbons with the *cis*-configuration enhances reactivity: *cis*-**1** and *cis*-**31** are more reactive than *trans*-**34** and *cis*-**37**. This may be rationalized by cation migration, which readily takes place between adjacent tertiary carbons.[18]

A possible mechanism of the present arylation reaction is shown in Scheme 4. The initial activation of the equatorial tertiary C−H bond of *cis*-**1** with $GaCl_3$ generates the tertiary cation **52** with a counteranion $HGaCl_3^-$. Our previous studies suggest that, in the presence of $GaCl_3$, otherwise unstable carbocations gain a longer lifetime.[10] The interaction of the gallate anion probably stabilized the cation center. Then, **52** isomerizes to the secondary cation **53**, which is attacked by aromatic hydrocarbons to give the arenium cation **54**. $GaCl_3$ is regenerated by the hydride attack of $HGaCl_3^-$ at the acidic proton of **54** giving the aromatized **3** and hydrogen. When the hydride attacks **54** at the aromatic ring, partially hydrogenated products are formed. The cycloalkyl group can also migrate as well as the carbocation under the present conditions: The treatment of 1-(1-methylcyclohexyl)-naphthalene with $GaCl_3$ (40 mol %) in cyclohexane for 40 h at 70 °C gave 2-(methylcyclohexyl)-naphthalenes in 50% yield based on $GaCl_3$ as a mixture of three isomers in a 1:3:2 ratio (Scheme 5). The product

(18) (a) Olah, G. A.; Lukas, J. *J. Am. Chem. Soc.* **1968**, *90*, 933−938. (b) Olah, G. A.; Liang, G.; Westerman, P. W. *J. Org. Chem.* **1974**, *39*, 367−369.

SCHEME 5



ratio and the stereochemistry are identical to those obtained from methylcyclohexane **18** and **2** (Table 2, entry 1). Another C−H activation mechanism involves the protonation of *cis*-**1** via $HGaCl_4$ formed from small amounts of HCl and $GaCl_3$. In this case, the counteranions for **52**, **53**, and **54** should be $GaCl_4^-$.

An interesting aspect of the present reaction is the origin of the selective C−H activation being the equatorial tertiary C−H bond, and several possible explanations are presented (Figure 2). (1) If it can be assumed that $GaCl_3$ (or $HGaCl_4$) gains access to the tertiary C−H bond via a similar trajectory with transition metals,[19] an approach from the side of C−H, the axial C−H may be more hindered by the 1,3-diaxial repulsions than the equatorial C−H. (2) The tertiary cation derived from *cis*-**1** can be more stable because of hyperconjugative stabilization by the adjacent C−C bond, and therefore, the transition state for the hydride abstraction from the equatorial site is preferred.[20] (3) The different reactivities of *cis*- and *trans*-**1** can be attributed to the different stabilities of the carbocation/$HGaCl_3^-$ (or $GaCl_4^-$) ion pairs. Such ion-pair effect was suggested in the solvolysis of *cis*- and *trans*-9-chlorodecalins yielding different products.[21] A preference for the equatorial C−H activation in C−H oxidation has precedents: *cis*-**1** is hydroxylated with *p*-nitroperbenzoic acid 1.5 times faster than *trans*-**1**;[22] *cis*-**1** reacts with methyl(trifluoromethyl)dioxirane twice faster than *trans*-**1**.[23] The equatorial selectivity in the present reaction, however, is much higher.

Although the above cycloalkane activation mechanism appears likely at present, an alternative mechanism is conceivable, which involves the initial activation of arene by $GaCl_3$. $GaCl_3$ is known to interact with aromatic hydrocarbons as indicated by multinuclear NMR, Raman, and UV/vis spectroscopies.[24] We noticed a novel deuteriation reaction of $GaCl_3$-complexed arene. A solution of naphthalene **2** and $GaCl_3$ (molar ratio 1:2) in methylcyclohexane was stirred for 1 h at room temperature, and was then treated with D_2O. **2**-*d* was recovered in 36% yield with 270% deuteriation at both α- and *β*-positions (1:1) as determined by ^{2}H NMR (Scheme 6). Addition of the reaction mixture to 2 M sodium deuterioxide in D_2O also gave **2**-*d* in 48% yield and deuteriation in 228% (α/*β* = 1:1). Accordingly, this deuteriation is not the result of a known aromatic H−D exchange[25] under acidic condition but is likely to be derived from the protiodegallation of the C−Ga bond. Quenching with THF followed by D_2O treatment gave no deuterated naphthalene, which may be consistent with the above explanation. The relatively low yields of **2**-*d* are due to competitive oligomerization.

When the alkaline deuteriation experiment was conducted with **6** in cyclohexane, the yield improved (Table 6). All the aromatic hydrogens on the naphthalene ring were equally deuterated as determined by ^{1}H NMR and ^{2}H NMR spectroscopies employing 1,3,5-trimethylbenzene and dimethyl sulfoxide-d_6 as internal standards, respectively. The methyl group was not deuterated as indicated by ^{2}H NMR. Analogously, the reaction of

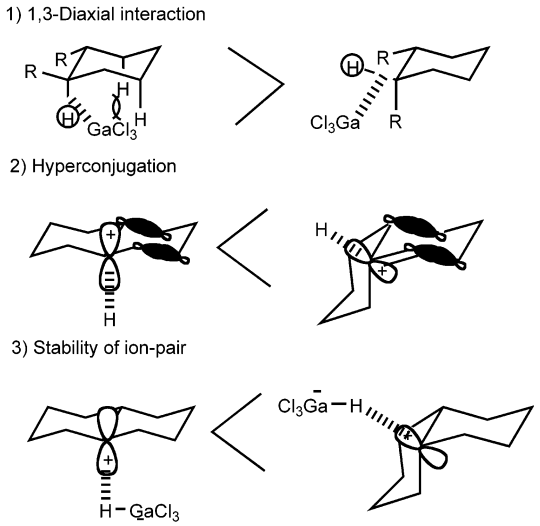


FIGURE 2. Possible explanations of the equatorial selectivity.

SCHEME 6

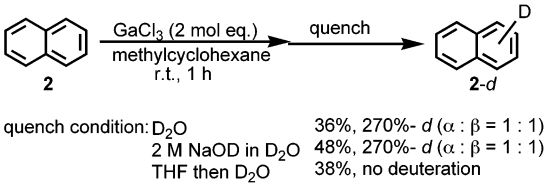
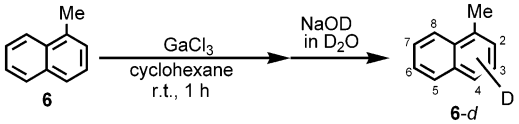


TABLE 6. Deuteration of 1-Methylnaphthalene 6



$GaCl_3$ (equiv)	yield (%)	total deuteration ratio[a]/%	partial deuteration ratio[b] (%)					
			2-H	3-H	4-H	5-H	6,7-H	8-H
1.0	77	156 (135)	22	25	27	22	40	20
3.0	87	218 (202)	30	38	33	32	60	30

[a] Determined by ^{1}H NMR. The ratio obtained by ^{2}H NMR is shown in parentheses. [b] Determined by ^{1}H NMR.

(19) (a) Williams, J. M.; Brown, R. K.; Schultz, A. J.; Stucky, G. D.; Ittel, S. D. *J. Am. Chem. Soc.* **1978**, *100*, 7407−7409. (b) Crabtree, R. H.; Holt, E. M.; Lavin, M.; Morehouse, S. M. *Inorg. Chem.* **1985**, *24*, 1986−1992. Also see references cited therein.

(20) González-Núñez, M. E.; Castellano, G.; Andreu, C.; Royo, J.; Báguena, M.; Mello, R.; Asensio, G. *J. Am. Chem. Soc.* **2001**, *123*, 7487−7491. Also see references cited therein.

(21) (a) Boschung, A. F.; Geisel, M.; Grob, C. A. *Tetrahedron Lett.* **1968**, *50*, 5169−5172. (b) Gream, G. E. *Aust. J. Chem.* **1972**, *25*, 1051−1079.

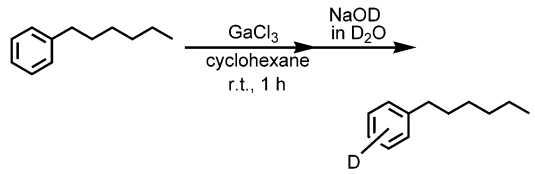
(22) Schneider, H.-J.; Müller, W. *J. Org. Chem.* **1985**, *50*, 4609−4615.

(23) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749−6757.

(24) Ulvenlund, S.; Wheatley. A.; Bengtsson. L. A. *J. Chem. Soc., Dalton Trans.* **1995**, 255−263.

(25) (a) Mackor, E. L.; Smit, P. J.; van der Waals, J. H.; *Trans. Faraday. Soc.* **1957**, *53*, 1309−1316. (b) Lauer, W. M.; Matson, G. W.; Stedman, G. *J. Am. Chem. Soc.* **1958**, *80*, 6433−6437, 6437−6439. Also see ref 1.

TABLE 7. Deuteration of 1-Methylnaphthalene 6



$GaCl_3$ (equiv)	yield (%)	total deuteration ratio[a](%)	partial deuteration ratio[b] (%)		
			ortho[c]	meta[c]	para
1.0	91	123 (103)	25	24	25
3.0	95	248 (226)	50	49	50

[a] Determined by ^{1}H NMR. The ratio obtained by ^{2}H NMR is shown in parentheses. [b] Determined by ^{1}H NMR. [c] Normalized value based on the presence of two protons.

1-phenylhexane resulted in equal extent of deuteriation at the benzene ring, and no deuteriation at the hexyl group (Table 7). The lack of selectivity for aromatic deuteriation suggests the involvement of the protiodegallation of $GaCl_3$−arene complexes. Although it is unclear whether the observation has some relation to the present aromatic alkylation, it is an interesting property of $GaCl_3$-arene complexes.

In summary, the arylation of cycloalkanes with aromatic hydrocarbons occurs in the presence of a catalytic amount of $GaCl_3$. This is a novel catalytic reaction that forms a C−C bond between aromatic and aliphatic hydrocarbons.

Experimental Section

Reaction of Naphthalene 2 and Bicyclo[4.4.0]decane (Decahydronaphthalene) 1. Under an argon atmosphere, a 1.0 M solution of $GaCl_3$ (0.25 mmol) in **1** (cis/trans = 1:1) was added to a solution of **2** (640 mg, 5.0 mmol) in **1** (cis/trans = 1:1) (1.25 mL). The mixture was heated to 70 °C and stirred for 40 h at that temperature. After the reaction was quenched by 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 heated with Pd/C (5%, 530 mg) in refluxing 1-methylnaphthalene **6** (0.7 mL) for 2 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 giving monoalkylated products **3** and **4** (390 mg, 590% based on $GaCl_3$) and dialkylated products **5** (237 mg, 237% based on $GaCl_3$). **3** and **4**:[26] GC analysis indicated the presence of the two isomers in a 6:1 ratio; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76−0.82 (m), 0.99−1.35 (m), 1.47−1.78 (m), 1.81−1.87 (m), 1.94−1.99 (m), 2.35 (td, J = 11.6, 2.8 Hz), 2.74 (tt, J = 12.0, 3.6 Hz), 7.32 (dd, J = 8.4, 1.6 Hz), 7.36−7.45 (m), 7.57 (s), 7.62 (s), 7.75−7.80 (m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 26.77, 26.83, 26.9, 31.4, 34.0, 34.1, 34.37, 34.40, 34.6, 35.9, 41.8, 43.1, 43.4, 43.5, 44.7, 48.0, 51.3, 124.4, 124.8, 124.9, 125.6, 126.1, 127.3, 127.40, 127.44, 127.6, 132.0, 132.1, 133.5, 133.6, 143.8, 145.0; IR (neat) 3053, 2917, 2849, 1633, 1600, 1506, 1446, 852, 815, 742 cm^{-1}; MS (EI, 70 eV) *m*/*z* 264 (100, M$^+$), 154 (71), 142 (26), 128 (20); HRMS (EI, 70 eV) calcd for $C_{20}H_{24}$ 264.1877, found 264.1877 (M$^+$). Anal. Calcd for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.81; H, 9.13. The trans stereochemistry at the ring juncture was determined by comparison with an authentic sample, the synthesis of which is described in the Supporting Information. Dialkylated products **5**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.69−0.83 (m), 0.92−1.36 (m), 1.42−1.88 (m), 1.95 (dq, J = 12.8, 2.4 Hz), 2.31 (br t, J = 10.4 Hz), 2.71 (br t, J = 12.0 Hz), 7.21−7.34 (m), 7.51 (s), 7.57 (s), 7.70 (dd, J = 8.4, 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 26.8, 26.9, 31.4, 34.0, 34.1, 34.39, 34.43, 34.5, 34.6, 35.9, 41.8, 43.1, 43.4, 43.5, 44.6, 44.7, 48.1, 51.3, 51.4, 123.96, 124.04, 124.1, 125.16, 125.23, 125.9, 127.18, 127.23, 127.3, 130.65, 130.71, 132.1, 132.19, 132.24, 133.7, 133.8, 142.86, 142.93, 143.65, 143.70, 144.1, 144.2, 144.89, 144.91; IR (neat) 3050, 2919, 2850, 1634, 1605, 1510, 1455, 1374, 837, 813 cm^{-1}; MS (EI, 70 eV) *m*/*z* 400 (100, M$^+$), 137 (14), 95 (16), 81 (12); HRMS (EI, 70 eV) calcd for $C_{30}H_{40}$ 400.3128, found 400.3136 (M$^+$). Anal. Calcd for $C_{30}H_{40}$: C, 89.93; H, 10.07. Found: C, 89.89; H, 10.33. When isomerically pure *cis*-**1** (19.4 mmol) was reacted with **2** (10 mmol) in the presence of $GaCl_3$ (2.5 mol % based on **2**) at 70 °C for 12 h, the monoalkylated products (**3**/**4** = 4:1) were obtained in 1188% yield and dialkylated products in 423% yield. *trans*-**1** gave the monoalkylated products (**3**/**4** = 2:1) in 11% yield.

1,2′-Binaphthyl and 2,2′-Binaphthyl. Under an argon atmosphere, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (1703 mg, 7.5 mmol) was added to a mixture of 2-(decahydronaphthalenyl)naphthalenes **3** and **4** (79 mg, 0.3 mmol, 4:1) in dry toluene (3 mL), and the mixture was heated at reflux for 3 h. After the mixture was cooled to room temperature, saturated aqueous $NaHCO_3$ was added, and the insoluble materials were removed by passing through Celite. The organic layer was separated, washed with water, and dried over $MgSO_4$. Solvents were removed in vacuo, and the residue was purified by flash column chromatography (silica gel, hexane) giving 2,2′-binaphthyl (21 mg, 27%) and 1,2′-binaphthyl (9 mg, 12%). The structures were confirmed by comparison with the authentic samples, the synthesis of which is described in the Supporting Information.

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Supporting Information Available: Experimental procedures and analytical data, references, and ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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