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A Gallium-Catalyzed Cycloisomerization/Friedel−Crafts Tandem

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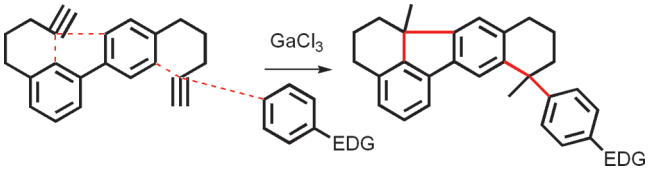

Under noble (Au, Pt, Ru) and group 13 (Ga, In) metals catalysis, 1,6-arenynes rearrange to give 1,2-dihydronaphthalenes in a high yielding, regiocontrolled fashion. When the reaction is carried out in the presence of electron-rich arenes (anisole, phenol, indole derivatives), Friedel−Crafts addition may follow the cycloisomerization step. Only GaX_3 salts proved able to catalyze these two C−C bond formation events. This specificity of gallium has been exploited for the synthesis of valuable polycyclic compounds that would be very difficult to prepare otherwise. For instance, tetrahydroisoquinolines and tetrahydrobenzoazepines have been obtained by selective 6-*exo*-dig or 7-*endo*-dig cyclization of N-tethered 1,6-arenynes. DFT calculations were carried out to shed light on the mechanism and provide a rationale for this regiodivergency. Computations also reveal the fundamental role of the tether in the stabilization of carbocationic species. Differential reactivities of other types of substrates in gallium- and gold-catalyzed cascades are also exposed, showing that the two approaches are complementary. In particular, bimolecular Friedel−Crafts additions are facilitated under gallium catalysis.

1. Introduction

Recent years have witnessed a flurry of activity around the activation of simple alkynes or olefins toward nucleophilic attack with carbophilic π-Lewis acids.[1] The majority of the catalysts used are complexes of noble metals, gold being perhaps one of the most highly regarded nowadays.[2] However, as stated by Fürstner in his critical review on π-acid catalysis,[2e] "conventional Lewis acids may also qualify, provided they are sufficiently polarizable; in fact, CuX, GaX_3, InX_3, BiX_3, and relatives turned out to be attractive and cost efficient alternatives to noble metals in certain conditions." Among these salts, $GaCl_3$ is known as both a powerful σ- and π-Lewis acid.[3−5] In the first category, applications of $GaCl_3$ as catalyst for [4 + 2][6a] or [4 + 1][6b] cycloadditions, Friedel−Crafts and coupling reactions,[6c−g] Mukayama-aldol reactions,[6h] skeletal rearrangements,[6i] and

(1) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410.

(2) (a) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (c) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem., Int. Ed.* **2008**, *47*, 4268. (d) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (e) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208. (f) Lee, S. I.; Chatani, N. *Chem. Commun.* **2009**, 371. (g) Shapiro, D.; Toste, F. D. *Synlett* **2010**, 675.

(3) (a) Amemiya, R.; Yamaguchi, M. In *Acid Catalysis in Modern Organic Synthesis*; Yamamoto, H., Ishihara, K., Eds.; Wiley-VCH: Weinheim, Germany, 2008; Vol. 1, pp 347−375. (b) Nishimura, Y. *Chem. Commun.* **2008**, 35. (c) Amemiya, R.; Yamaguchi, M. *Eur. J. Org. Chem.* **2005**, 5145. (d) Yamaguchi, M.; Shibasaki, M. *e-EROS Encyclopedia of Reagents for Organic Synthesis*, **2005**, Online Posting Date: October 15, 10.1002/047084289X.rn00118u.pub2; (e) Yamaguchi, M. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1, pp 307−322. (f) Barman, D. C. *Synlett* **2003**, 2440.

(4) For the origin of the difference in Lewis acidity between BCl_3, $AlCl_3$, and $GaCl_3$, see: Ogawa, A.; Fujimoto, H. *Inorg. Chem.* **2002**, *41*, 4888.

(5) It becomes a common belief that alkyno- and alkenophilicity are of thermodynamic origin. However, π-Lewis acids are, thermodynamically speaking, often more aza- or oxophilic than carbophilic. For a clarification, see ref 1 and: (a) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817. (b) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395.

(6) For selected examples, see: (a) Hirashita, T.; Kawai, D.; Araki, S. *Tetrahedron Lett.* **2007**, *48*, 5421. (b) Chatani, N.; Oshita, M.; Tobisu, M.; Ishii, Y.; Murai, S. *J. Am. Chem. Soc.* **2003**, *125*, 7812. (c) Kobayashi, S.; Komoto, I.; Matsuo, J.-i. *Adv. Synth. Catal.* **2001**, *343*, 71. (d) Amemiya, R.; Yamaguchi, M. *Adv. Synth. Catal.* **2007**, *349*, 1011. (e) Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002**, *124*, 8528. (f) Yonehara, F.; Kido, Y.; Sugimoto, H.; Morita, S.; Yamaguchi, M. *J. Org. Chem.* **2003**, *68*, 6752. (g) Amemiya, R.; Fujii, A.; Yamaguchi, M. *Tetrahedron Lett.* **2004**, *45*, 4333. (h) Li, H.-J.; Tian, H.-Y.; Wu, Y.-C.; Chen, Y.-J.; Liu, L.; Wang, D.; Li, C.-J. *Adv. Synth. Catal.* **2005**, *347*, 1247. (i) Oshita, M.; Okazaki, T.; Ohe, K.; Chatani, N. *Org. Lett.* **2005**, *7*, 331. (j) Viswanathan, G. S.; Wang, M.; Li, C.-J. *Angew. Chem., Int. Ed.* **2002**, *41*, 2138. (k) Bez, G.; Zhao, C.-G. *Org. Lett.* **2003**, *5*, 4991. (l) Usugi, S.-i.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2004**, *6*, 601.

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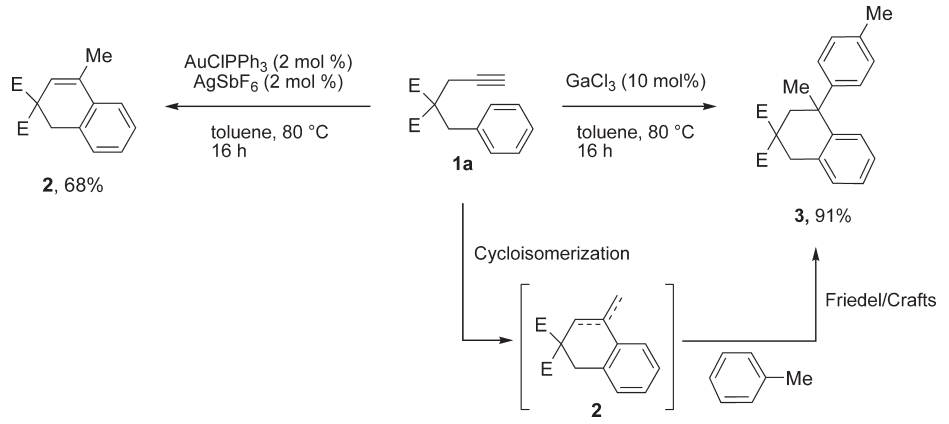
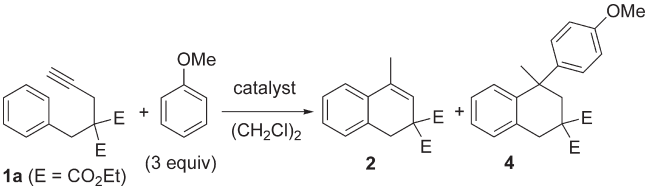
SCHEME 1. Reaction of Arenyne 1a in Toluene under Ga(III)- and Au(I)-Catalysis (E = CO_2Et)



others[6j−l] have been reported. On the other hand, the carbophilicity of $GaCl_3$ has been revealed through a few cycloisomerization reactions involving enynes, allenynes, or arenynes,[7,8] as well as intermolecular dihydroarylations of alkynes.[9] In rare cases, the two types of acidities of $GaCl_3$ have been fruitfully exploited to elaborate complex molecules, showing that this ambivalence is useful in organic synthesis.[10] In this context, it seems clear that gallium salts are not just alternatives to noble metals, for they can also confer specific elements of selectivity. In that respect, we have disclosed that $GaCl_3$ catalyzes the transformation of arenyne **1a** into the bicyclic derivative **3**, presumably after cycloisomerization into **2** and bimolecular Friedel−Crafts type reaction with toluene, used as solvent (Scheme 1).[11] In contrast, with Au(I), the reaction stops at the cycloisomerization step.

TABLE 1. Catalyst Screening



entry	catalyst	mol %	temp (°C)	time (h)	product	yield [%]
1	$AuCl(PPh_3)$/$AgSbF_6$	2/2	rt	6	**2**	80
2	$AuCl_3$	5	rt	6	—[a]	
3	$[RuCl_2(CO)_3]_2$/AgOTf	8/16	80	10	**2**	88
4	$[RuCl_2(CO)_3]_2$	8	80	10	—[a]	
5	$PtCl_2$	5	80	10	—[a]	
6	$PtCl_4$	5	rt	10	**2**	90
7	$PtCl_4$	5	80	10	**2**	71
8	$AlCl_3$	10	80	10	—[b]	0
9	$Ga(OTf)_3$	10	80	10	—[b]	0
10	$GaCl_3$	10	rt	10	**4**	62
11	$GaCl_3$	10	80	10	**4**	88[c]
12	$GaBr_3$	10	80	10	**4**	80
13	$InCl_3$	10	80	10	**2**	89

[a]Complex mixture. [b]No reaction. [c]100% yield with anisole as solvent.

The overall result of the gallium-catalyzed tandem is a bimolecular double hydroarylation of an alkyne.[12] To the best of our knowledge, only intermolecular double hydroarylations of alkynes involving twice the same arene have been reported.[9,12a] Also we are not aware of any precedent of bimolecular or fully intramolecular double hydroarylation reaction. This paper shows how we have exploited the title reaction for synthetic purposes and provides mechanistic insights supported by DFT computations. The differential selectivities induced by gallium and gold catalysts are illustrated throughout the paper.

2. Results and Discussion

2.1. Experimental Results. 2.1.1. Carbon Tethers. To check whether the tandem transformation depicted in Scheme 1 was restricted to the use of $GaCl_3$, various salts of noble and group 13 metals were tested.[13] We began our investigations with arenyne **1a**, anisole as nucleophile, and dichloroethane as solvent (Table 1).

(7) (a) Inoue, H.; Chatani, N.; Murai, S. *J. Org. Chem.* **2002**, *67*, 1414. (b) Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294. (c) Mamane, V.; Hannen, P.; Fürstner, A. *Chem.—Eur. J.* **2004**, *10*, 4556. (d) Lee, S. I.; Sim, S. H.; Kim, S. M.; Kim, K.; Chung, Y. K. *J. Org. Chem.* **2006**, *71*, 7120. (e) Kim, S. M.; Lee, S. I.; Chung, Y. K. *Org. Lett.* **2006**, *8*, 5425. (f) Simmons, E. M.; Sarpong, R. *Org. Lett.* **2006**, *8*, 2883.

(8) InX_3 salts are also effective catalysts, see ref 2c and the references therein.

(9) Ga: (a) Yadav, J. S.; Reddy, B. V. S.; Padmavani, B.; Gupta, M. K. *Tetrahedron Lett.* **2004**, *45*, 7577. In: (b) Tsuchimoto, T.; Hatanaka, K.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2003**, 2454. Au: (c) Li, Z.; Shi, Z.; He, C. *J. Organomet. Chem.* **2005**, *690*, 5049. (d) Hashmi, A. S. K.; Blanco, M. C. *Eur. J. Org. Chem.* **2006**, 4340. (e) Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M. *Chem.—Eur. J.* **2007**, *13*, 1358.

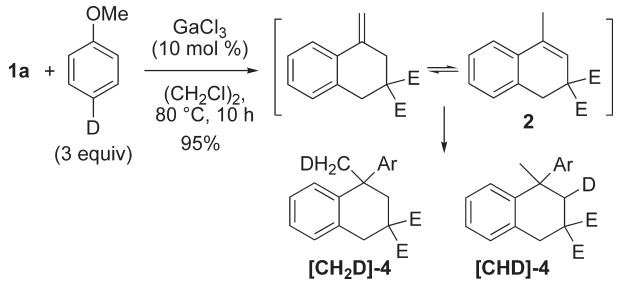
(10) (a) Asao, N.; Asano, T.; Ohishi, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4817. (b) Yadav, J. S.; Reddy, B. V. S.; Biswas, S. K.; Sengupta, S. *Tetrahedron Lett.* **2009**, *50*, 5798.

(11) This transformation is particularly surprising since the $GaCl_3$-catalyzed cycloisomerization of **1a** into **2** was previously described by Murai, also using toluene as solvent, and no double hydroarylation product was mentioned (see ref 7a). The only difference between our experimental conditions and those previously reported lies in the use of a commercially available 0.5 M pentane solution of $GaCl_3$ (Aldrich) in our case, instead of a 1 M methylcyclohexane solution. With the latter, we eventually obtained the reported product **2** in 92% yield. The lower activity of the gallium catalysts might be related to the known interaction between methylcyclohexane and $GaCl_3$ (see ref 6f). Nevertheless, the transformation of **1a** into **3** could be carried out by using various batches of $GaCl_3$ in pentane and proved perfectly reproducible.

(12) For reviews on alkyne hydroarylation, see ref 2d and: (a) Kitamura, T. *Eur. J. Org. Chem.* **2009**, 1111. (b) Nevado, C.; Echavarren, A. M. *Synthesis* **2005**, 167. For illustrative examples, see: (c) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (d) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485. (e) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669. (f) Ferrer, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 1105. (g) Biffis, A.; Gazzola, L.; Gobbo, P.; Buscemi, G.; Tubaro, C.; Basato, M. *Eur. J. Org. Chem.* **2009**, 3189. (h) Menon, R. S.; Findlay, A. D.; Bissember, A. C.; Banwell, M. G. *J. Org. Chem.* **2009**, *74*, 8901.

(13) Use of HCl as catalyst gave rise to an intractable mixture of products.

SCHEME 2. Deuterium Labeling (E = CO_2Et, Ar = 4-MeO-C_6H_5)

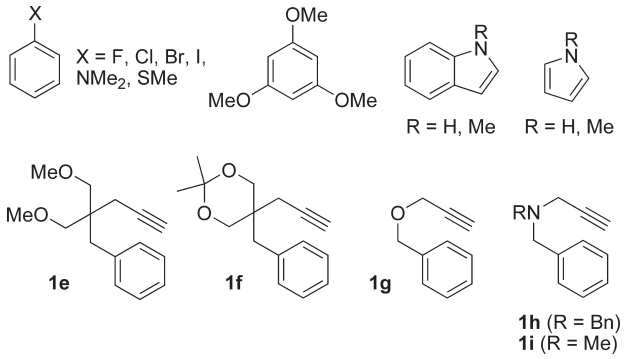


Complex mixtures ensued when using $AuCl_3$, $[RuCl_2(CO)_3]_2$, or $PtCl_2$ (entries 2, 4, and 5). Conversely, the 1,2-dihydronaphthalene derivative **2** could be isolated in good yield employing cationic complexes of gold(I)[14] and Ru(II) (entries 1 and 3, see also Scheme 1), as well as neutral salts of platinum(IV) and indium(III) (entries 6, 7, and 13).[15] Whereas anhydrous $AlCl_3$ and $Ga(OTf)_3$ did not promote any reaction (entries 8 and 9), $GaCl_3$ and $GaBr_3$ furnished the desired 1-aryl-1,2,3,4-tetrahydronaphthalene **4** exclusively (entries 10−12, see also Scheme 1).[16] Although the reaction already took place at room temperature (entry 10), a higher yield was reached at 80 °C (entry 11).

Thus, only Ga(III) halides seem to possess the required Lewis acidity to promote both the cycloisomerization and the bimolecular Friedel−Crafts addition.[17] Arguably, this tandem reaction proceeds first by the cycloisomerization step. Isolated samples of **2** were reacted with anisole in dichloroethane or directly in toluene in the presence of 10 mol % of $GaCl_3$ and transformed in good yields into **4** or **3**, respectively. We also noticed that the exocyclic/endocyclic migration of the methylene fragment of the cycloisomerization product was not completely shifted when the Friedel−Crafts reaction took place, as shown by a deuterium-labeling experiment giving rise to an accidental 1:1 mixture of the two possible adducts (Scheme 2).

The scope of the bimolecular double hydroarylation was investigated next. Unlike halobenzenes, methylphenylsulfane,

CHART 1. Incompatible Substrates



and 1,3,5-trimethoxybenzene which did not react with the cycloisomerization intermediate (Chart 1), electron-rich arenes such as anisole (Table 2, entries 1−3), ortho-substituted anisole derivatives (entries 4−8), and phenols (entries 9−11) could be used successfully. The products were formed regioselectively in high yields. The structures of **9** and **15** were unambiguously confirmed by X-ray analyses (see the Supporting Information). Of relevance is the possibility to generate derivatives of 5-aryl-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene (entry 1) and 5-aryl-5,6,7,8,9,10-hexahydrobenzo[8]annulene (entry 2) by incremental changes in the respective starting materials. Whereas 1,2-dimethoxybenzene and **1a** transformed into the expected product **9** in a very good 90% yield (entry 5), 1,2,3-trimethoxybenzene led to compound **12** in a lower 67% yield (entry 8). Actually two purifications were necessary to get **12** in pure form, the first one providing it admixed with a low amount of **13** arising either from the deprotection of **12** or from the deprotection of 1,2,3-trimethoxybenzene itself, which eventually reacted with **1a**.[18] On the other hand, **13** could be synthesized selectively in good yield with 2,6-dimethoxyphenol (entry 9).

The nitrogen-containing nucleophiles *N*,*N*-dimethylaniline, pyrrole, indole, *N*-methylpyrrole, and *N*-methylindole (Chart 1) prevented any reaction pathway. Nevertheless, 1-(phenylsulfonyl)-1*H*-indole allowed the formation of product **16**, which was isolated in 94% yield (entry 12).

Two other carbon-tethered terminal arenynes were tested (Chart 1, **1e** and **1f**); however, these substrates gave rise to decomposition products, both with gallium and gold, even at room temperature. We next turned our attention to the bishomopropargylic diol **1j**, a case which also turned out to be emblematic of the differential reactivity conferred by gallium and gold catalysts (Scheme 3). In both cases, intramolecular oxacyclization rather than hydroarylation took place, a chemoselectivity which could be explained in terms of alkyne/oxygen chelation control, as described by Yamamoto et al.[10a] Although the intermediate dihydrofuran could not be isolated when using **1j**, the corresponding product **17** resulting from the cycloisomerization of the homopropargyl alcohol **1k** could be separated and fully characterized. In the presence of anisole, a Friedel−Crafts type addition led to tetrahydrofuran **18** as a 1:1 mixture of diastereomers when $GaCl_3$ was used as catalyst. In sharp contrast, as reported by

(14) A few gold-catalyzed bimolecular cycloisomerization/Friedel−Crafts tandem reactions have been described. For selected examples, see: (a) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genêt, J.-P.; Michelet, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 7427. (b) Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698. (c) Chen, Y.; Lu, Y.; Li, G.; Liu, Y. *Org. Lett.* **2009**, *11*, 3838. (d) Leseurre, L.; Chao, C.-M.; Seki, T.; Genin, E.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Tetrahedron* **2009**, *65*, 1911.

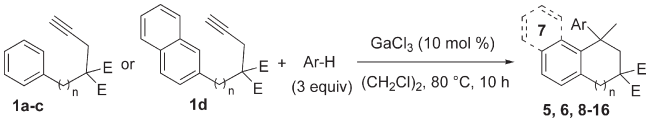
(15) For Ru- and Pt-catalyzed cycloisomerization of arenynes, see: Chatani, N.; Inoue, H.; Ikeda, T.; Murai, S. *J. Org. Chem.* **2000**, *65*, 4913.

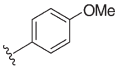
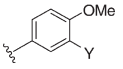
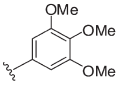
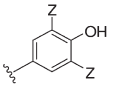
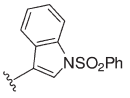
(16) 1-Aryl-1,2,3,4-tetrahydronaphthalene derivatives, their higher homologues, and their heteroanalogues represent important classes of compounds displaying central nervous system activity, notably as dopamine D_1 receptor agonists or antagonists, see inter alia: (a) Zhang, J.; Xiong, B.; Zhen, X.; Zhang, A. *Med. Res. Rev.* **2009**, *29*, 272. (b) Hoffman, B.; Cho, S. J.; Zheng, W.; Wyrick, S.; Nichols, D. E.; Mailman, R. B.; Tropsha, A. *J. Med. Chem.* **1999**, *42*, 3217. (c) Bucholtz, E. C.; Brown, R. L.; Tropsha, A.; Booth, R. G.; Wyrick, S. D. *J. Med. Chem.* **1999**, *42*, 3041. (d) Wyrick, S. D.; Booth, R. G.; Myers, A. M.; Owens, C. E.; Bucholtz, E. C.; Hooper, P. C.; Kula, N. S.; Baldessarini, R. J.; Mailman, R. B. *J. Med. Chem.* **1995**, *38*, 3857. (e) Hussain, R. A.; Dickey, J. K.; Rosser, M. P.; Matson, J. A.; Kozlowski, M. R.; Brittain, R. J.; Webb, M. L; Rose, P. M.; Fernandes, P. *J. Nat. Prod.* **1995**, *58*, 1515. (f) Yous, S.; Durieux-Poissonnier, S.; Lipka-Belloli, E.; Guelzim, H.; Bochu, C.; Audinot, V.; Boutin, J. A.; Delagrange, P.; Bennejean, C.; Renarde, P.; Lesieur, D. *Bioorg. Med. Chem.* **2003**, *11*, 753.

(17) In Friedel−Crafts reactions, it seems that $AlCl_3$ not only generates the electrophile but also activates the aromatic substrate by back-donation from Cl 3p orbital to the arene HOMO. This effect could still exist with $GaCl_3$, but not with $Ga(OTf)_3$. See: (a) Tarakeshwar, P.; Lee, J. Y.; Kim, K. S. *J. Phys. Chem. A* **1998**, *102*, 2253. (b) Tarakeshwar, P.; Kim, K. S. *J. Phys. Chem. A* **1999**, *103*, 9116.

(18) 1,2,3-Trimethoxybenzene is easily demethylated at the most hindered position by using for instance $ZnCl_2$, $AlCl_3$, or BCl_3. See inter alia: Carvalho, C. E.; Russo, A. V.; Sargent, M. V. *Aust. J. Chem.* **1985**, *38*, 777.

TABLE 2. Bimolecular Dihydroarylation of Terminal Alkynes (E = CO_2Et)



Entry	Arenyne	n	Product (Ar)	Yield [%]
				
1	**1b**	2	**5**	81
2	**1c**	3	**6**	72
3	**1d**	1	**7**	78
				
4	**1a**	1	**8** (Y = Me)	90
5	**1a**	1	**9** (Y = OMe)	90
6	**1a**	1	**10** (Y = Cl)	81
7	**1a**	1	**11** (Y = Br)	88
				
8	**1a**	1	**12**	67
				
9	**1a**	1	**13** (Z = OMe)	87
10	**1a**	1	**14** (Z = H)	90
11	**1a**	1	**15** (Z = Me)	89
				
12	**1a**	1	**16**	94

Michelet and Genêt, AuCl, $Ph_3PAuCl/AgSbF_6$, or $AuCl_3$ led to the bicyclic ketal **19**.[19]

A few disubstituted alkynes were tried next, yet the cyclization proved more difficult. Regioselective hydration of the triple bond by adventitious water[20] was the only reaction process that could be monitored with the ester- and phenyl-substituted arenynes **1*l*** and **1m** (Scheme 4). With the brominated alkyne **1n**, although the cycloisomerization product **22B** could be isolated in 20% yield,[21] the main reaction pathway remained the hydrative one, ketone **22A** being obtained in 64% yield. Hydration of alkynes is commonly observed in gold catalysis as well, even when dry solvents and inert atmospheres are employed,[22] and there is a growing interest nowadays for such mercury- and acid-free conditions.[23] However, using the $AuCl(PPh_3)/AgSbF_6$ catalytic system, no transformation of arenynes **1*l*−n** was observed.

Going back to terminal alkynes, we wondered whether substrates bearing two aryl moieties, i.e., diarenynes, could be cyclized. As mentioned in the Introduction, intramolecular dihydroarylations of alkynes have not been reported so far. If successful, such transformations would represent an expedient way to synthesize complex polycyclic molecules from simple precursors. To our delight, arenynes **1o−r** transformed into the expected products **23**, **24**,[24] **25**, and **26** in good to excellent yields (Scheme 5) after double or even triple hydroarylations.[25] Interestingly, although gold catalysts proved unable to catalyze the bimolecular Friedel−Crafts addition step (see Table 1), $Ph_3PAuCl/AgSbF_6$ (2 mol %, dicholoroethane, rt, 10 h) promoted the intramolecular transformation of **1o** into **23** in 87% yield.[26]

The pentacyclic derivative **26** can be considered as the result of a double hydroarylation at one end and a monohydroarylation at the second end of diyne **1r**. A fourth hydroarylation was also attainable by means of an extra intermolecular reaction with anisole, as shown by the formation of **27** under Ga-catalysis (Scheme 6). Although four C−C bonds and three cycles were formed in a single operation, this product was isolated in a good yield nonetheless, further illustrating the synthetic potential of the title reaction. Again, gold catalyzed the skeletal rearrangement of **1r** into **26**, but not the bimolecular Friedel−Crafts addition.

The complementary features of gallium and gold were once more emphasized when using the bis-arenyne **1s**, one carbon homologue of **1r** (Scheme 7). While gold gave rise to compound **28** after hydroarylation of one alkyne terminus and hydration of the second one,[22] inspection of the NMR signals of the reaction product formed under Ga-catalysis

(19) Antoniotti, S.; Genin, E.; Michelet, V.; Genêt, J.-P. *J. Am. Chem. Soc.* **2005**, *127*, 9976.

(20) We can also not exclude the coordination of $GaCl_3$ by the ester groups and alkyne hydration during workup.

(21) The absence of Friedel−Crafts products might be ascribed to the electronegativity of bromine, which prevents the development of a positive charge at the benzylic position.

(22) Under common laboratory conditions, the presence of water cannot be strictly avoided, the more so as very hygroscopic salts are used. For instance, efficient gold-catalyzed hydration of alkynes in dry CH_2Cl_2 has been reported: (a) Davies, P. W.; Detty-Mambo, C. *Org. Biomol. Chem.* **2010**, *8*, 2918. The presence of water was attributed to the use of hygroscopic silver salts for the generation of Au^+. Traces of water can even play a crucial role in transition metal-catalyzed transformations, see inter alia: (b) Baumgarten, S.; Lesage, D.; Gandon, V.; Goddard, J.-P.; Malacria, M.; Tabet, J.-C.; Gimbert, Y.; Fensterbank, L. *ChemCatChem.* **2009**, *1*, 138.

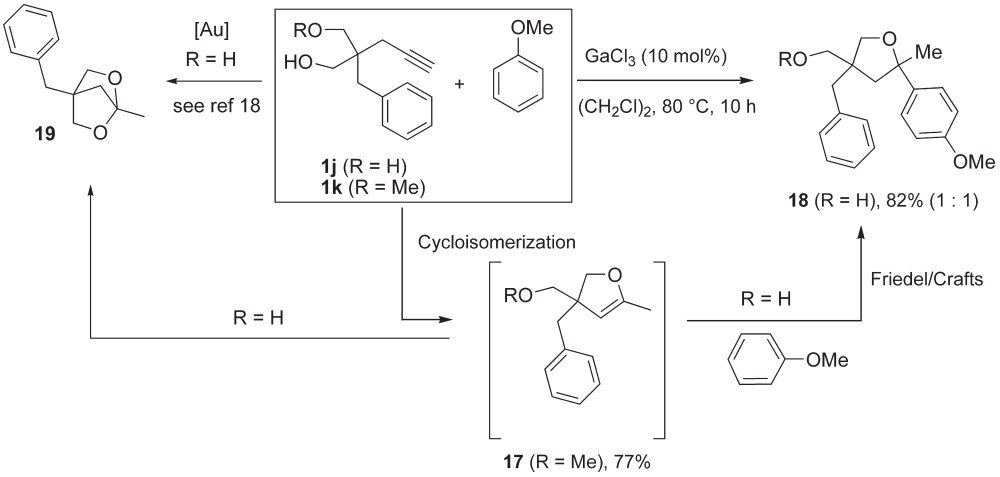
(23) For a seminal paper, see: (a) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415. For a review, see: (b) Hintermann, L.; Labonne, A. *Synthesis* **2007**, 1121. For selected recent examples, see: (c) Marion, N.; Ramón, R. S.; Nolan, S. *J. Am. Chem. Soc.* **2009**, *131*, 448. (d) Layva, A.; Corma, A. *J. Org. Chem.* **2009**, *74*, 2067. (e) Hashmi, A. S. K.; Hengst, T.; Lothschütz, C.; Rominger, F. *Adv. Synth. Catal.* **2010**, *352*, 1315.

(24) A product similar to **24** has been prepared by Pd-catalyzed alkyl to aryl migration and cyclization: Huang, Q.; Fazio, A.; Dai, G.; Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 7460.

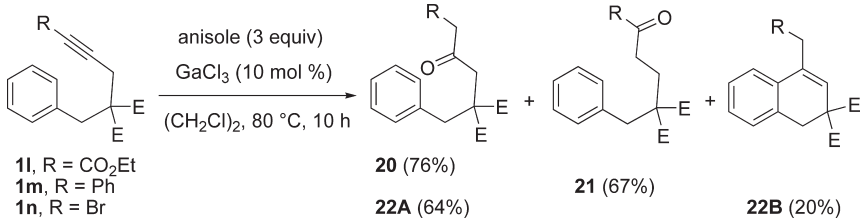
(25) It is worthy of note that the polycyclic frameworks of **23** (5,6,7,12-tetrahydro-6,12-methanodibenzo[a,d]cyclooctene) and **24** (1,2,3,10b-tetrahydrofluoranthene) can be found in natural and/or biologically active compounds, see inter alia: (a) Lee, C.-K.; Yeh, M.-H.; Lee, T.-H.; Chiu, H.-L.; Kuo, Y.-H. *Helv. Chim. Acta* **2009**, *92*, 1983. (b) Bai, H.; Li, S.; Yin, F.; Hu, L. *J. Nat. Prod.* **2005**, *68*, 1159. (c) Chen, C.-L.; Chang, H.-M. *Phytochemistry* **1978**, *17*, 779. (d) Day, B. W.; Sahali, Y.; Hutchins, D. A.; Wildschütte, M.; Pastorelli, R.; Nguyen, T. T.; Naylor, S.; Skipper, P. L.; Wishnok, J. S.; Tannenbaum, S. R. *Chem. Res. Toxicol.* **1992**, *5*, 779.

(26) For gold-catalyzed intramolecular cycloisomerization/Friedel−Crafts tandem reactions, see inter alia: Lemière, G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fenstebank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 7596.

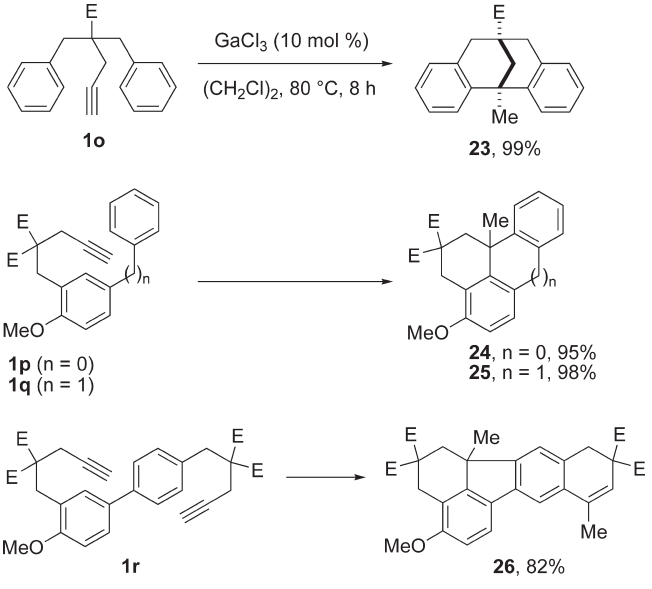
SCHEME 3. Differential Reactivities of Dihydrofurans under Gallium- and Gold-Catalysis



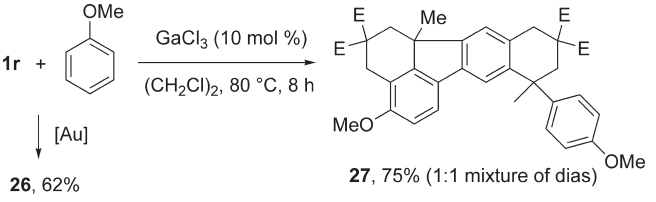
SCHEME 4. Gallium-Catalyzed Hydration of Disubstituted Alkynes (E = CO_2Et)



SCHEME 5. Intramolecular Double and Triple Hydroarylation of Alkynes (E = CO_2Et)



SCHEME 6. Gallium-Catalyzed Quadruple Hydroarylation of Diyne 1r (E = CO_2Et)

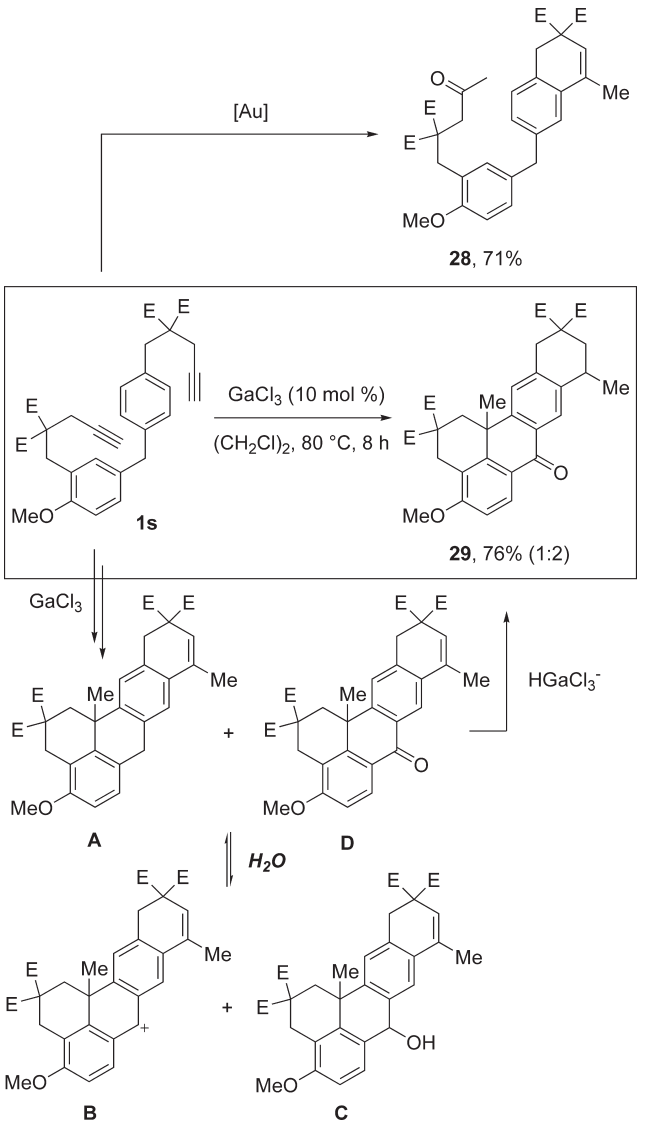


revealed that the expected diphenylmethane moiety was actually oxidized into a ketone and that the expected alkene fragment was hydrogenated. All spectral data converged to the pentacyclic compound **29**, which was isolated as a 1:2 mixture of diastereomers in good yield. We suppose that this product arises from the formation of the dibenzylic **B** from the cycloisomerization product **A**. This cation is then trapped by adventitious water to give the alcohol **C**.[22] **B** and **C** then disproportionate into **A** and the anthracenone **D** as previously described.[27] The equilibrium would be shifted by the double bond Markovnikov hydrogallation promoted by $HGaCl_3^-$. Pertaining to this rationale, $GaCl_3$ is known to generate cations from alkanes, and the resulting hydride $HGaCl_3^-$ can give rise to hydrogallation products.[28] In our case, the possibility of alkene reduction must funnel the reaction since for **25**, also exhibiting a diphenylmethane moiety, no oxidation product was observed.

2.1.2. Oxygen and Nitrogen Tethers. To build heterocycles, we next turned our attention to arenynes displaying oxygen- and nitrogen-tethers. It was already mentioned in the literature that oxygen-tethers were incompatible because of the straightforward cleavage of the carbon−oxygen bond.[7a] Accordingly, a complex mixture of unidentified products ensued after mixing arenyne **1g** (Chart 1) and anisole with $GaCl_3$ or $AuCl(PPh_3)/AgSbF_6$, even at room temperature. On the other hand, the cycloisomerization of arenynes displaying a nitrogen tether was not studied before with

(27) Roberts, R. M.; El-Khawaga, A. M.; Sweeney, K. M.; El-Zohry, M. F. *J. Org. Chem.* **1987**, *52*, 1591.
(28) See ref 6f and: Oshita, M.; Chatani, N. *Org. Lett.* **2004**, *6*, 4323.

SCHEME 7. Hydroarylation of Diyne 1s under Gallium- and Gold-Catalysis (E = CO_2Et)

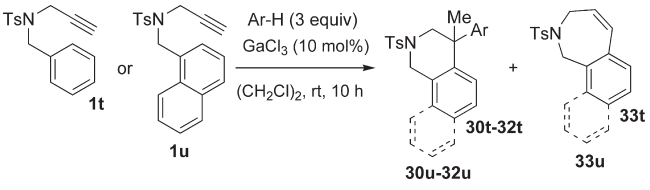


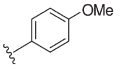
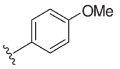
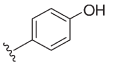
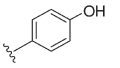
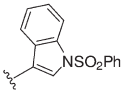
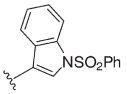
$GaCl_3$. While the NBn- and NMe-tethered substrates **1h** and **1i** proved unreactive (Chart 1),[29] full conversion of the NTs-containing arenynes **1t** and **1u** was reached at room temperature (Table 3). The expected tetrahydroisoquinolines **30t**−**32t** and tetrahydrobenzo[*h*]isoquinolines **30u**−**32u** were isolated as major products (entries 1−6), accompanied by 10−25% of dihydrobenzoazepine **33t** and dihydronaphthoazepine **33u** depending on the nucleophilic arene used. This result prompted us to test the cycloisomerization in the absence of the latter (entries 7 and 8). To our surprise, **33t** and **33u** were obtained as sole products in high yields.

To show the versatility of the process, i.e., the formation of either 6- or 7-membered functionalized heterocycles, isolated samples of dihydroazepines **33t** and **33u** were submitted to gallium-catalyzed hydroarylation at 80 °C (Table 4). Satisfyingly, the corresponding tetrahydroazepines **34t**−**36t** and **37u** could be isolated in high yields as well.

(29) As in the case of indole nucleophiles mentioned above, stronger bases may lead to catalyst deactivation.

TABLE 3. 6-*exo* vs. 7-*endo* Cyclizations of Arenynes 1t and 1u



Entry	Arenyne	Ar-H	Products (Ar)[a]	Yield [%]
1	**1t**	Anisole	 **30t + 33t**	75 + 22[b]
2	**1u**	Anisole	 **30u + 33u**	70 + 21
3	**1t**	Phenol	 **31t + 33t**	81 + 16
4	**1u**	Phenol	 **31u + 33u**	81 + 18
5	**1t**	1-(phenylsulfonyl)-1*H*-indole	 **32t + 33t**	78 + 15
6	**1u**	1-(phenylsulfonyl)-1*H*-indole	 **32u + 33u**	79 + 12
7	**1t**	None	**33t**	90
8	**1u**	None	**33u**	83

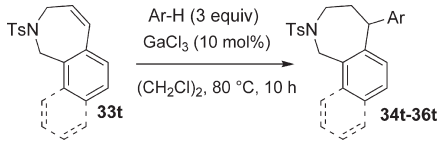
[a]Separated. [b]63 + 22 in anisole as solvent at rt.

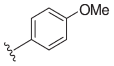
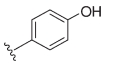
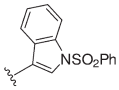
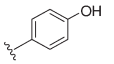
The one-pot procedure proved also possible as follows: a dichloroethane solution of arenyne was stirred at rt in the presence of $GaCl_3$ for 10 h, then the nucleophilic arene was introduced and the mixture was refluxed for 10 h (Scheme 8). This procedure provided **34t** in 57% yield. In contrast, when the reaction was carried out at 80 °C with the reagents and $GaCl_3$ already present, **34t** was obtained in a lower 22% yield.

Thus, it is clearly possible to control the 6-*exo*- and 7-*endo*-dig pathways depending on the reaction conditions. The origin of this intriguing chemoselectivity is discussed in the Theoretical Investigations section (vide infra). Before closing on the N-tethered diynes series, it has to be mentioned that under the same experimental conditions, with or without anisole, $AuCl(PPh_3)/AgSbF_6$ converted **1t** into **33t** in poor yield accompanied by traces of allenamide **38t** (Scheme 9).[30]

(30) Inamoto, K.; Yamamoto, A.; Ohsawa, K.; Hiroya, K.; Sakamoto, T. *Chem. Pharm. Bull.* **2005**, *53*, 1502.

TABLE 4. Gallium-Catalyzed Hydroarylations of Dihydroazepines



Entry	Azepine	Ar-H	Product	Yield [%]
1	**33t**	Anisole	 **34t**	83
2	**33t**	Phenol	 **35t**	87
3	**33t**	1-(phenylsulfonyl)-1*H*-indole	 **36t**	84
4	**33u**	Phenol	 **37u**	82

2.2. Theoretical Investigations. Contrasting with noble metals catalysis, investigations on Ga-catalyzed organic transformations by means of computational chemistry are quite scarce[31] and very few cycloisomerization reactions have been simulated.[31b,d,f] To understand some experimental data, in particular the intriguing selectivities observed with NTs-tethered arenynes, DFT calculations were carried out. The chosen level of theory for the present study was calibrated on the geometry of a recently reported gallium carbene,[32] and on the dissociation energy of Ga_2Cl_6 into $GaCl_3$.[33]

Computational Method. All calculations were performed with the Gaussian series of programs.[34] The geometry optimizations and thermodynamic corrections were carried out with hybrid density functional theory (B3LYP) with the 6-31G(d) (N, H, C, S, O, Cl) and LANL2DZ+ECP basis sets (Ga). Solvation corrections for 1,2-dichloroethane and anisole were computed by the PCM method as implemented in Gaussian 09 with single points at the B3LYP/6-31+G**(LANL2DZ) level. Unless stated otherwise, all relative energies presented in this paper are free energies (ΔG_{DCE}; ΔG_{ani}) in kilocalories per mole.

Because a quasi-substoichiometric amount of $GaCl_3$ is usually used in gallium catalysis, one could argue that $GaCl_3$ is just a precatalyst. However, it is commonly accepted that $GaCl_3$, just like $AlCl_3$ or BCl_3, actually is the active species, but because of its hygroscopic character, a larger amount is necessary to ensure the presence of active material.

Geometry optimization of the $\mathbf{A_1}$ system, comprising a model arenyne and Ga_2Cl_6, a well-known dimer of $GaCl_3$ that exists both in the solid state and in solution, was implemented (Scheme 10). It yielded three distinct minima in which $GaCl_3$ is coordinated to the triple bond. In $\mathbf{B_1}$, the metal center is bound unsymmetrically to the alkyne fragment. This complex is much more stable than the Cl-stabilized cation $\mathbf{B'_1}$ or the ion-paired cationic intermediate $\mathbf{B''_1}$ which have been postulated as potential intermediates in Ga-promoted linear trimerization of silylacetylenes.[35]

The *exo* and *endo* cyclizations could be modeled from monogallium species of type **B** only (Scheme 11). In the *gem*-diester series, using 1,2-dichloroethane solvation corrections, the 6-*exo*-dig cyclization transition state was located 13.59 kcal/mol above $\mathbf{B_1}$ and led directly to the alkene−gallium complex $\mathbf{D_1}$ (see Figure 1 in the Supporting Information for the geometries). This transformation, which involves simultaneous cyclization and 1,3-proton shift, is appreciably exergonic by 43.72 kcal/mol. The migration of gallium from the C−C double bond to one oxygen atom of the ester moiety to give $\mathbf{E_1}$ also proved exergonic and kinetically facile. The final dissociation of $GaCl_3$ giving $\mathbf{F_1}$ was found slightly endergonic by less than 1 kcal/mol.

In the N-tether series (X = NTs), the *exo* cyclization proceeds in two steps. The first one, leading to the Wheland intermediate $\mathbf{C_2}$, requires an activation free energy of 10.46 kcal/mol and is endergonic by 3.35 kcal/mol. Interestingly, the 6-membered ring of $\mathbf{C_2}$ is strongly folded (see Figure 1 in the Supporting Information), as the result of the electron donation from the nitrogen atom to the cationic center.[36] Due to this stabilization, and in contrast with the carbon-tether series, complex $\mathbf{C_2}$ does not collapse. Moreover, the activation energy barrier to reach the 1,3-proton shift transition state is quite high (12.10 kcal/mol from $\mathbf{C_2}$), as it requires to unfold the 6-membered ring. From $\mathbf{D_2}$, gallium migration to one oxygen atom of the tosyl group to give $\mathbf{E_2}$ and regeneration of the catalyst follow an exergonic pathway.

The study of the 7-*endo*-dig cyclization pathway also showed the crucial role of the tethers on the stabilization of cationic intermediates. Again, in the NTs series, an N-stabilized Wheland intermediate was located ($\mathbf{G_2}$). On the other hand, in the *gem*-diester series, the corresponding species converged as the nonclassical cation $\mathbf{G_1}$. Although both barriers to cyclization are similar, the formation of the latter is much more endergonic than that of the former (6.80 vs 3.10 kcal/mol).[37] Rearomatization then follows through 1,2-proton shift transition states connecting $\mathbf{G_{1/2}}$ to the O-stabilized

(31) See ref 6i and: (a) Yamabe, S.; Minato, T. *J. Org. Chem.* **2000**, *65*, 1830. (b) Xu, K.; Wu, Y.; Xie, D.; Yan, G. *Chin. Sci. Bull.* **2004**, *49*, 9883. (c) Wu, Y.; Xu, K.; Xie, D. *Tetrahedron* **2005**, *61*, 507. (d) Soriano, E.; Marco-Contelles, J. *Organometallics* **2006**, *25*, 4542. (e) Wong, C. T.; Wong, M. W. *J. Org. Chem.* **2007**, *72*, 1425. (f) Zhu, Y.; Guo, Y.; Xie, D. *J. Phys. Chem. A* **2007**, *111*, 9387.

(32) Species **3** of: Marion, N.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Stevens, E. D.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Organometallics* **2007**, *26*, 3256 (RMSD 0.0942).

(33) $\Delta H_{298\ exp} = 21.0\ kcal \cdot mol^{-1}$; $\Delta H_{298\ comp} = 19.04\ kcal \cdot mol^{-1}$, see: Shäfer, H.; Binnewies, M. *Z. Anorg. Allg. Chem.* **1974**, *410*, 251.

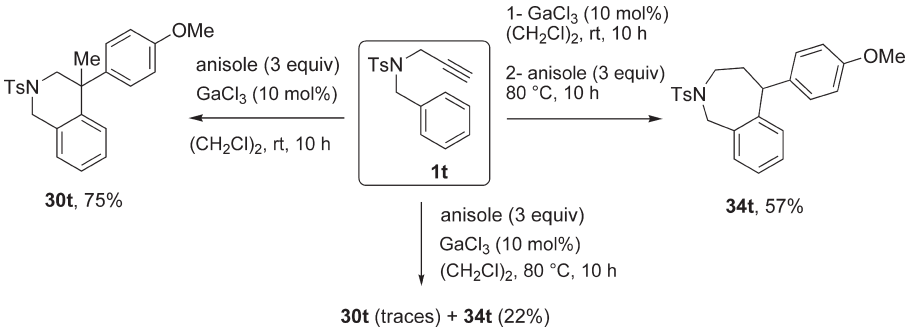
(34) Frisch, M. J.; et al. *Gaussian 09*, Revision A.1; Gaussian, Inc., Wallingford, CT, 2009.

(35) (a) Kido, Y.; Yoshimura, S.; Yamaguchi, M.; Uchimaru, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1445. (b) Kido, Y.; Yamaguchi, M. *J. Org. Chem.* **1998**, *63*, 8086.

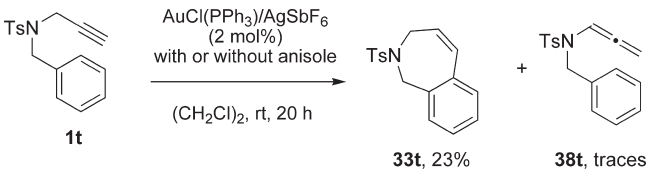
(36) Efforts to optimize a corresponding O-stabilized cation $\mathbf{C_1}$ using the esters functionalities failed.

(37) It is worthy of note that in the NTs series, it was possible to model both species $\mathbf{G_1}$ and $\mathbf{G_2}$. The former is less stable by 4.70 kcal/mol than the latter. A transition state connecting these complexes lies 5.53 kcal/mol above $\mathbf{G_2}$. Again, in the *gem*-diester series, it was not possible to stabilize the Wheland intermediate with the oxygen atoms.

SCHEME 8. Concomitant vs Stepwise Addition of Reagents and Catalyst



SCHEME 9. Gold-Catalyzed Cycloisomerization of Arenyne 1t



carbocations $\mathbf{H_{1/2}}$, lying approximately 20 kcal/mol below $\mathbf{B_{1/2}}$. The comparison of all barrier heights displayed in Scheme 11 shows that, although *exo* and *endo* pathways are close-lying trajectories, the experimental trend is respected. In the *gem*-diester series, *endo* cyclization is the lowest kinetically attainable pathway. However this step in reversible, as it is endergonic and followed by a second barrier that is higher than the *exo* one (14.53 vs 13.59 kcal/mol). Thus, *exo* cyclization is expected to prevail, as observed experimentally. In the NTs series, although both pathways have reversible first steps, the second one is more accessible for the *endo* mode (15.45 vs 13.43 kcal/mol). Consequently, the preferential formation of 7-membered ring products can be presumed, in agreement with the experimental data.

The rest of the *endo* pathway relies on a 1,2-hydride shift giving the η^2 alkene complex $\mathbf{I_2}$ (Scheme 12, see also Figure 2 in the Supporting Information for geometries). Also in line with the experimental results, the $\mathbf{H_2} \rightarrow \mathbf{I_2}$ transformation is kinetically favored over that of enamine $\mathbf{I'_2}$. The formation of the latter requires first the formation of the unstabilized cation $\mathbf{L_2}$ to allow the passing of the hydride. Thus, the tether also plays a role on the control of the regioselectivity.

The preference for the *endo* cyclization pathway in the NTs series seems at odds with the experimental results which were obtained in the presence of nucleophilic arenes. Indeed, the major compounds arising from the cycloisomerization/Friedel−Crafts tandem were systematically 6-membered ring products (see Table 3). We envisaged that in the presence of the nucleophile, the active species could be modified. Attempts to use $GaCl_3 \cdot$anisole failed because of the systematic expulsion of the arene ligand during optimization. Conversely, with $GaCl_3 \cdot H_2O$, water stuck to gallium; however its presence resulted in, at least, doubling the barrier heights, making them virtually impassable.

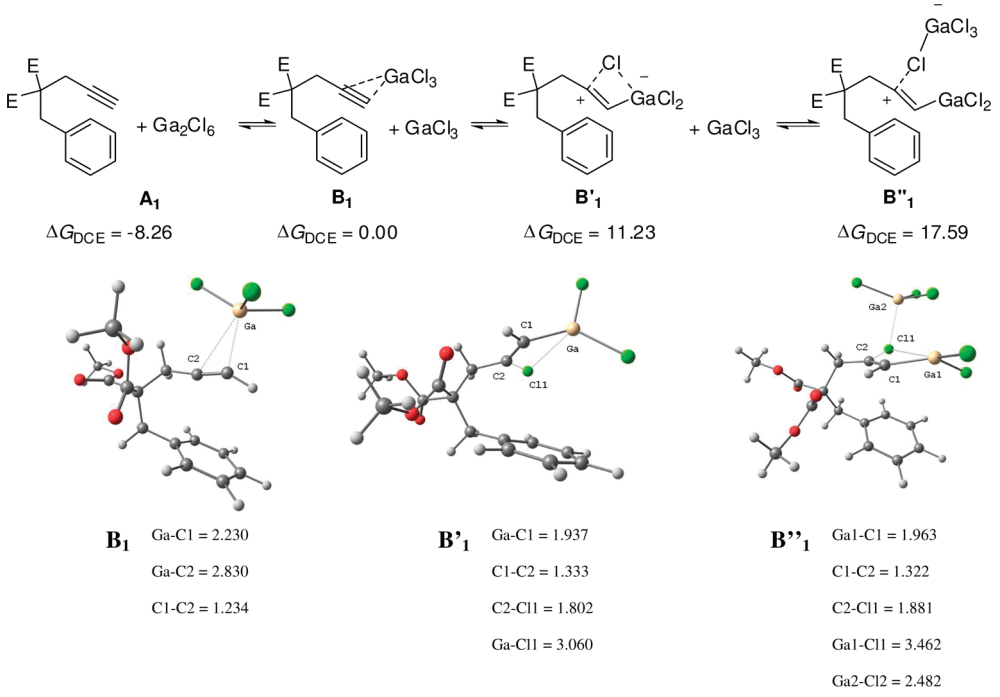
We wondered whether an escape lane could be modeled from 7- to 6-membered ring products, i.e., by ring contraction of $\mathbf{H_2}$. Indeed, the transformation of the latter into the nonclassical carbocation $\mathbf{M_2}$ displaying a nascent piperidine framework could be modeled. Although moderately endergonic, this step is realized through the most accessible transition state lying 11.25 kcal/mol below $\mathbf{B_2}$. However, the next step, which leads to complex $\mathbf{D_2}$, has a higher activation energy barrier than that of the irreversible $\mathbf{H_2} \rightarrow \mathbf{I_2}$ transformation.

Because an excess of nucleophile and high concentration of the reagents in 1,2-dichloroethane were used experimentally, we next envisaged that the changes in the *exo*/*endo* scenario could stem from the actual polarity of the reaction medium. As reported in Table 3, anisole could be used as solvent, still leading to the six-membered ring product as the major component of the mixture. Besides, the ratio between 6- and 7-membered ring products proved dependent on the nucleophile used. In the calculations, replacing 1,2-dichloroethane by anisole as solvent increased the relative energy of most of the transition states (see Schemes 11 and 12). This result is consistent with the lower polarity of anisole compared to 1,2-dichloroethane, which limits the stabilization effects of the solvent on species with strong charge separation ($C^+ \cdots Ga^-$). On the other hand, the moderately charged product-like $\mathbf{M_2} \rightarrow \mathbf{D_2}$ transition state gets a powerful stabilization from anisole compared to 1,2-dichloroethane. As a result, and in agreement with the observations depicted in Scheme 8, the $\mathbf{H_2} \rightarrow \mathbf{M_2} \rightarrow \mathbf{D_2}$ transformation becomes kinetically favored over $\mathbf{H_2} \rightarrow \mathbf{I_2}$, leading to a 6-membered ring product rather than a 7-membered one. Thus, the way nucleophiles modify the 6-*exo*- vs 7-*endo*-dig could be due to the modification of the overall polarity of the reaction medium, switching close-lying trajectories.

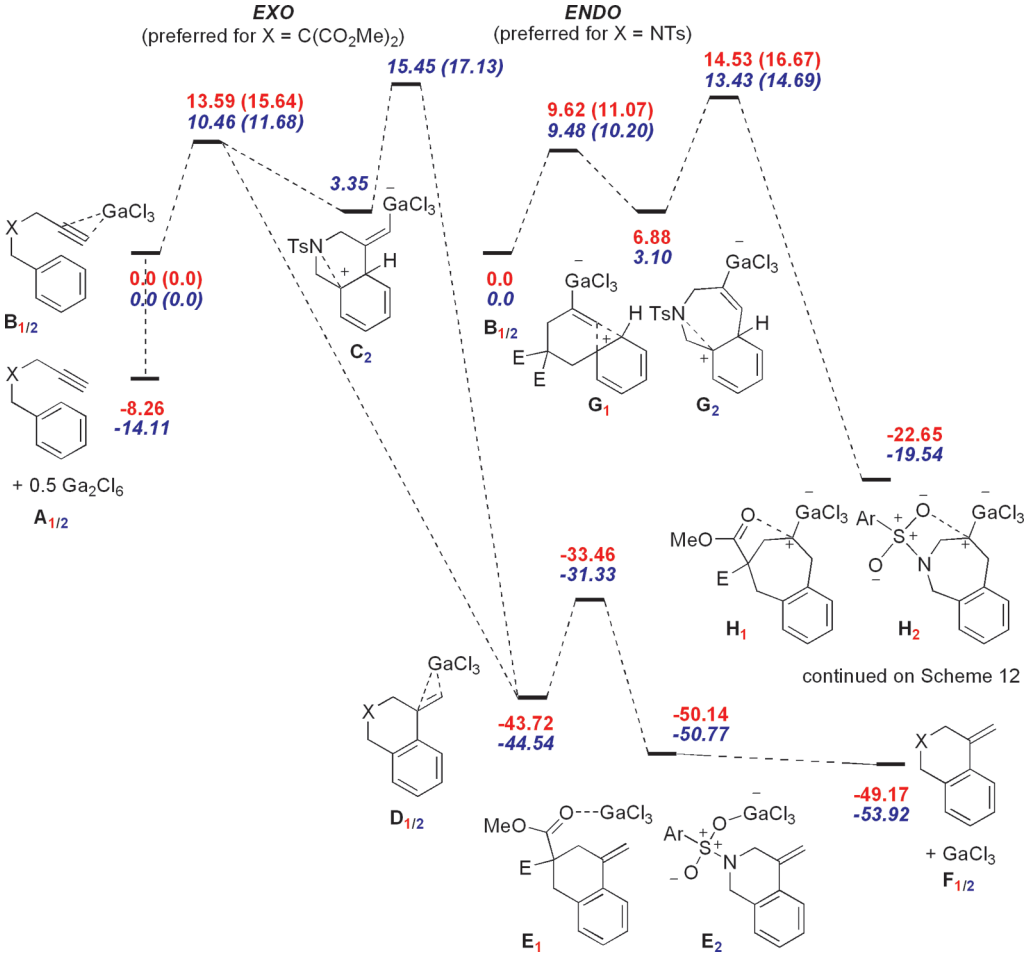
3. Conclusion

We have developed an elusive polyhydroarylation protocol based on the finding that $GaCl_3$ not only catalyzes the cycloisomerization of arenynes but also traps the intermediates by electron-rich arenes, even in an intermolecular fashion. In a recent review on π-acid catalysis,[2e] Fürstner stated: "*a priori*, there is no need to tie the two reaction partners together, thus making intermolecular transformations feasible, even though the number of successful cases still remains somewhat limited." In that sense, our study shows that gallium is not just an alternative to gold or other noble metals, as it allows us to go one step beyond. DFT computations have shed light on peculiar cyclization selectivities. They rationalized the crucial role played by the tether of arenynes on the stabilization of cationic intermediates and the regiodivergency between *exo* and *endo* cyclizations. Lastly, some unexpected transformations were uncovered, in particular a new type of oxidative hydride transfer from

SCHEME 10. **Alkyne Complexes of $GaCl_3$ (E = CO_2Me, Selected Distances in Å)**

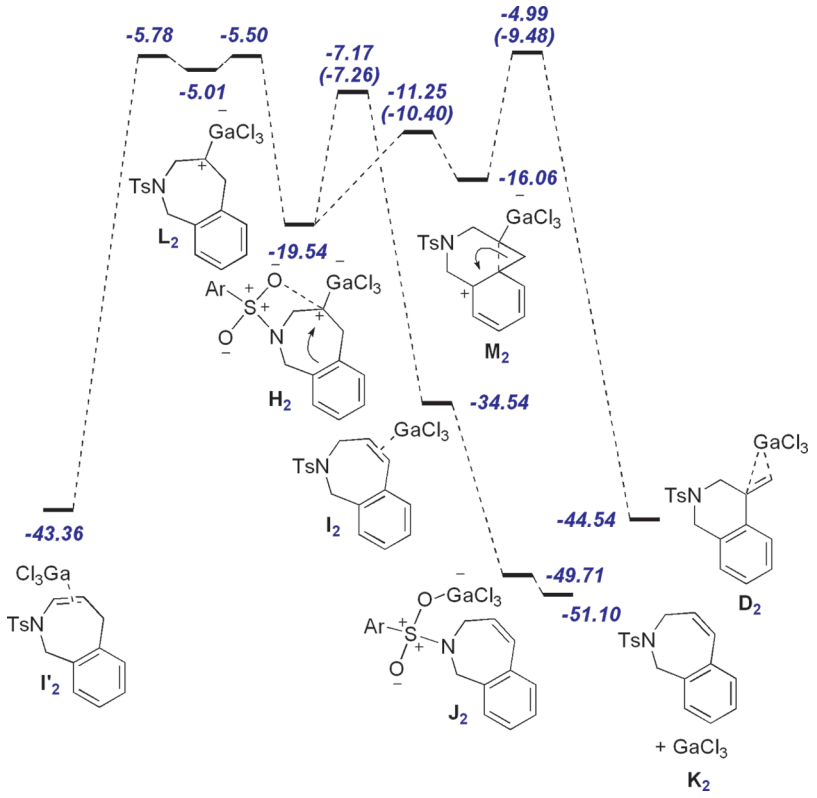


SCHEME 11. **Free Energy Progress Profile (ΔG_{DCE} in kcal/mol) for the 6-*exo* and 7-*endo* Cyclizations (ΔG_{ani} Is Indicated in Parentheses)**[a]



[a]In red, A_1–H_1: X = CE_2, E = CO_2Me. In blue A_2–H_2: X = NTs, Ar = *p*-Tol

SCHEME 12. Free Energy Progress Profiles (ΔG_{DCE} in kcal/mol) of Intermediate H_2 Relatively to B_2 (ΔG_{ani} Is Indicated in Parentheses)



diphenylmethane to alkene moieties. Work on the enantioselective version of the title reaction is in progress in our laboratory, as well as the valorization of the side issues that were revealed during our study.

4. Experimental Section

General methods, solvent purification procedures, and details on NMR spectroscopy are described in the Supporting Information. $GaCl_3$ (0.5 M in pentane) was obtained from Aldrich. All J values are given in hertz.

Reaction of Arenyne 1a in Toluene under Ga(III)- and Au(I)-Catalysis. To a solution of substrate **1a** (72.1 mg, 0.25 mmol) in toluene (1 mL) at 80 °C was added $AuClPPh_3$ (2.5 mg, 0.005 mmol) and $AgSbF_6$ (1.7 mg, 0.005 mmol) in one portion. The mixture was stirred at 80 °C for 16 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compound **2**[7] (49.0 mg) in 68% yield. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19−7.12 (m, 4H), 5.90 (s, 1H), 4.15−4.03 (m, 4H), 3.29 (s, 2H), 2.07 (s, 3H), 1.14 (t, J = 7.2, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 134.9, 133.5, 132.8, 127.8, 127.7, 126.9, 123.4, 121.4, 61.6, 54.8, 34.6, 19.4, 14.0; FTIR (film) 2983, 1732, 1449, 1365, 1266, 1225, 1133, 1049, 1015, 762 cm^{-1}. HRMS (TOF-QII) m/z calcd for $C_{17}H_{20}NaO_4$ $[M + Na]^+$ 311.1254, found 311.1251.

To a solution of substrate **1a** (72.1 mg, 0.25 mmol) in toluene (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compound **3** (86.6 mg) in 91% yield. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.13 (m, 4H), 7.02 (d, J = 8.1, 2H), 6.94 (d, J = 8.1, 2H), 4.17 (q, J = 7.2, 1H), 4.16 (q, J = 7.2, 1H), 3.83 (dq, J = 10.8, 7.2, 1H), 3.47 (dq, J = 10.8, 7.2, 1H), 3.31 (d, J = 15.9, 1H), 3.14 (d, J = 15.9, 1H), 2.91 (d, J = 14.4, 1H), 2.51 (d, J = 14.4, 1H), 2.29 (s, 3H), 1.71 (s, 3H), 1.23 (t, J = 7.2, 3H), 1.04 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 170.6, 146.2, 142.0, 135.1, 134.2, 128.7, 128.3, 128.2, 127.3, 126.3, 126.2, 61.3, 61.0, 52.5, 43.4, 42.0, 35.0, 31.9, 20.7, 13.9, 13.6; FTIR (film) 2975, 2930, 1713, 1582, 1511, 1493, 1446, 1369, 1335, 1213, 1184, 1115, 1091, 1046, 910, 861, 818, 767, 732, 701 cm^{-1}. HRMS (TOF-QII) m/z calcd for $C_{24}H_{28}O_4Na$ $[M + Na]^+$ 403.1886, found 403.1820.

Typical Procedure for Bimolecular Dihydroarylations. To a solution of substrates **1** (0.25 mmol) and possibly arenes (0.75 mmol) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford products **4**−**18**.

Compound 4: colorless oil; 88% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.15 (m, 4H), 6.96 (d, J = 9.0, 2H), 6.75 (d, J = 9.0, 2H), 4.17 (q, J = 7.2, 1H), 4.16 (q, J = 7.2, 1H), 3.84 (dq, J = 10.8, 7.2, 1H), 3.75 (s, 3H), 3.48 (dq, J = 10.8, 7.2, 1H), 3.33 (d, J = 16.2, 1H), 3.13 (d, J = 16.2, 1H), 2.90 (d, J = 14.4, 1H), 2.49 (d, J = 14.4, 1H), 1.70 (s, 3H), 1.23 (t, J = 7.2, 3H), 1.04 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 170.5, 157.4, 141.8, 141.1, 134.1, 128.7, 128.4, 128.0, 126.3, 126.2, 112.8, 61.3,

61.0, 55.0, 52.3, 43.3, 41.5, 34.9, 32.0, 13.8, 13.6; FTIR (film) 2976, 2934, 2835, 1730, 1607, 1580, 1508, 1462, 1444, 1366, 1332, 1247, 1215, 1127, 1091, 1030, 860, 810, 830, 768, 732 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{24}H_{28}O_5Na$ $[M + Na]^+$ 419.1835, found 419.1820.

Compound 5: colorless oil; 81% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26−7.15 (m, 2H), 7.03 (d, J = 9.0, 2H), 6.99−6.78 (m, 2H), 6.75 (d, J = 9.0, 2H), 4.16−4.06 (m, 4H), 3.78 (s, 3H), 3.24 (d, J = 13.8, 1H), 3.18 (d, J = 13.8, 1H), 2.51 (dt, J = 12.9, 4.2, 1H), 1.93 (dt, J = 12.9, 4.2, 1H), 1.68 (dt, J = 13.8, 4.5, 1H), 1.61 (s, 3H), 1.52 (dt, J = 13.8, 4.5, 1H), 1.21 (t, J = 7.2, 3H), 1.18 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 171.2, 157.9, 142.8, 136.8, 136.1, 129.9, 128.0, 127.7, 126.8, 120.4, 112.9, 61.1, 61.0, 58.8, 55.3, 44.2, 37.6, 33.2, 27.1, 26.9, 14.1, 14.0; FTIR (film) 2977, 2936, 1729, 1606, 1510, 1490, 1455, 1368, 1286, 1243, 1219, 1180, 1094, 1032, 914, 862, 829, 740, 702, 623 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{25}H_{31}O_5$ $[M + H]^+$ 411.2166, found 411.2151.

Compound 6: colorless oil; 72% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26−7.17 (m, 2H), 7.02 (d, J = 8.7, 2H), 7.00−6.77 (m, 2H), 6.75 (d, J = 8.7, 2H), 4.14−4.05 (m, 4H), 3.77 (s, 3H), 3.14 (d, J = 13.8, 1H), 3.09 (d, J = 13.8, 1H), 2.38 (dt, J = 12.0, 4.5, 1H), 1.92 (dt, J = 12.0, 4.5, 1H), 1.74−1.68 (m, 2H), 1.59 (s, 3H), 1.16 (t, J = 7.2, 3H), 1.15 (t, J = 7.2, 3H), 1.09−0.95 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 171.2, 156.9, 142.9, 137.2, 136.2, 129.8, 128.1, 127.5, 126.9, 120.3, 112.8, 61.1, 61.0, 58.8, 55.4, 44.5, 39.8, 37.7, 32.2, 27.0, 19.5, 14.0 (2C); FTIR (film) 2960, 1730, 1597, 1510, 1489, 1462, 1369, 1294, 1244, 1213, 1181, 1096, 1032, 925, 830, 701, 618 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{26}H_{33}O_5$ $[M + H]^+$ 425.2323, found 425.2303.

Compound 7: colorless oil; 78% yield; ^1H NMR (300 MHz, $CDCl_3$, 2:1 mixture of conformers (see below)); **major conformer**: δ 7.83−7.32 (m, 4H), 7.13 (dd, J = 6.9, 1.5, 1H), 7.10 (dd, J = 6.9, 1.5, 1H), 6.98 (d, J = 8.7, 2H), 6.73 (d, J = 8.7, 2H), 4.18 (q, J = 7.2, 2H), 3.93 (dq, J = 10.8, 7.2, 1H), 3.75 (s, 3H), 3.65 (dq, J = 10.8, 7.2, 1H), 3.45 (s, 2H), 2.70 (d, J = 14.4, 1H), 2.61 (d, J = 14.4, 1H), 1.90 (s, 3H), 1.24 (t, J = 7.2, 3H), 1.05 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 170.7, 157.4, 142.3, 136.2, 134.0, 132.5, 131.3, 128.8, 128.1, 128.0, 127.9, 127.8, 124.6, 124.2, 113.4, 61.4, 61.3, 55.2, 51.5, 48.3, 42.3, 36.9, 29.7, 14.0, 13.7; **minor conformer**: δ 7.83−7.32 (m, 4H), 7.30 (dd, J = 7.8, 1.0, 1H), 7.27 (dd, J = 7.8, 1.0, 1H), 7.13−7.02 (m, 2H), 6.79−6.74 (m, 2H), 4.10 (q, J = 7.2, 2H), 4.05−3.76 (m, 2H), 3.73 (s, 3H), 3.26 (br s, 2H), 3.13 (d, J = 14.7, 1H), 2.51 (d, J = 14.7, 1H), 1.78 (s, 3H), 1.18 (t, J = 7.2, 3H), 1.14 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 171.2, 157.7, 133.4, 132.6, 132.4, 127.8, 127.1, 127.0, 125.7, 125.6, 125.3, 113.2, 61.5, 53.4, 42.6, 42.5, 13.9 (8 C hidden or accidentally isochronous with major conformer); FTIR (film) 2979, 2339, 1731, 1607, 1509, 1463, 1367, 1296, 1248, 1182, 1102, 1034, 832, 732 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{28}H_{30}O_5Na$ $[M + Na]^+$ 469.1985, found 469.1979.

Compound 8: colorless oil; 90% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23−7.13 (m, 4H), 6.90 (d, J = 2.1, 1H), 6.71 (dd, J = 8.7, 2.1, 1H), 6.62 (d, J = 8.7, 1H), 4.17 (q, J = 7.0, 1H), 4.16 (q, J = 7.0, 1H), 3.84 (dq, J = 10.8, 7.2, 1H), 3.77 (s, 3H), 3.48 (dq, J = 10.8, 7.2, 1H), 3.31 (d, J = 16.2, 1H), 3.13 (d, J = 16.2, 1H), 2.88 (d, J = 14.4, 1H), 2.48 (d, J = 14.4, 1H), 2.15 (s, 3H), 1.68 (s, 3H), 1.22 (t, J = 7.2, 3H), 1.04 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 170.7, 155.7, 142.1, 140.8, 134.1, 129.6, 128.7, 128.2, 126.3, 126.2, 125.9, 125.5, 108.8, 61.4, 61.1, 55.2, 52.5, 43.4, 41.6, 35.0, 32.0, 16.3, 13.9, 13.6; FTIR (film) 2976, 2934, 2834, 1730, 1608, 1504, 1463, 1444, 1366, 1332, 1296, 1245, 1227, 1191, 1167, 1125, 1095, 1051, 1031, 945, 891, 861, 811, 766, 749, 702, 616 cm^{-1}; HRMS (TOF MS ES$^+$) *m/z* calcd for $C_{25}H_{30}O_5Na$ $[M + Na]^+$ 433.1991, found 433.1996.

Compound 9: white crystals; 90% yield; mp 108 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.20−7.15 (m, 4H), 6.67 (d, J = 8.4, 1H), 6.58 (d, J = 2.4, 1H), 6.50 (dd, J = 8.4, 2.4, 1H), 4.07 (q, J = 7.2, 1H), 4.06 (q, J = 7.2, 1H), 3.76 (dq, J = 10.8, 7.2, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.38 (dq, J = 10.8, 7.2, 1H), 3.28 (d, J = 16.2, 1H), 3.09 (d, J = 16.2, 1H), 2.90 (d, J = 14.1, 1H), 2.45 (d, J = 14.1, 1H), 1.69 (s, 3H), 1.20 (t, J = 7.2, 3H), 1.00 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 170.6, 148.0, 146.9, 141.8, 141.7, 134.2, 128.7, 128.0, 126.4, 126.2, 119.7, 111.3, 110.2, 61.3, 61.0, 55.7, 55.6, 52.4, 43.2, 41.9, 34.9, 32.0, 13.9, 13.8; FTIR (film) 2975, 2934, 2834, 1729, 1604, 1588, 1511, 1463, 1444, 1408, 1366, 1332, 1251, 1236, 1211, 1183, 1165, 1146, 1124, 1093, 1051, 1026, 947, 912, 858, 808, 768, 730, 650 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{25}H_{30}O_6Na$ $[M + Na]^+$ 449.1940, found 449.1928.

Compound 10: 81% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23−7.11 (m, 5H), 6.76 (dd, J = 8.7, 2.1, 1H), 6.71 (d, J = 8.7, 1H), 4.16 (q, J = 7.2, 1H), 4.15 (q, J = 7.2, 1H), 3.86 (dq, J = 10.8, 7.2, 1H), 3.83 (s, 3H), 3.50 (dq, J = 10.8, 7.2, 1H), 3.29 (d, J = 16.2, 1H), 3.11 (d, J = 16.2, 1H), 2.84 (d, J = 14.4, 1H), 2.47 (d, J = 14.4, 1H), 1.67 (s, 3H), 1.21 (t, J = 7.2, 3H), 1.05 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 170.5, 152.9, 142.4, 141.2, 134.1, 129.1, 128.9, 128.0, 127.0, 126.7, 126.5, 121.7, 111.0, 61.5, 61.2, 56.0, 52.4, 43.2, 41.7, 34.9, 31.9, 13.9, 13.6; FTIR (film) 2977, 1782, 1729, 1602, 1497, 1462, 1443, 1393, 1366, 1332, 1292, 1254, 1220, 1182, 1126, 1095, 1066, 1023, 862, 813, 769, 725, 708, 621 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{24}H_{27}ClO_5Na$ $[M + Na]^+$ 453.1445, found 453.1420.

Compound 11: colorless oil; 88% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, J = 2.4, 1H), 7.23−7.10 (m, 4H), 6.78 (dd, J = 8.7, 2.4, 1H), 6.68 (d, J = 8.7, 1H), 4.16 (q, J = 7.2, 1H), 4.15 (q, J = 7.2, 1H), 3.90 (dq, J = 10.8, 7.2, 1H), 3.82 (s, 3H), 3.52 (dq, J = 10.8, 7.2, 1H), 3.30 (d, J = 16.2, 1H), 3.10 (d, J = 16.2, 1H), 2.83 (d, J = 14.4, 1H), 2.47 (d, J = 14.4, 1H), 1.66 (s, 3H), 1.21 (t, J = 7.2, 3H), 1.05 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 170.5, 153.8, 142.9, 141.2, 134.1, 132.1, 129.0, 128.0, 127.9, 126.7, 126.5, 111.0, 110.9, 61.5, 61.3, 56.2, 52.4, 43.3, 41.6, 34.9, 32.0, 13.9, 13.7; FTIR (film) 2977, 1730, 1600, 1493, 1462, 1443, 1390, 1366, 1332, 1256, 1220, 1182, 1126, 1095, 1054, 1020, 861, 812, 768 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{24}H_{27}BrO_5Na$ $[M + Na]^+$ 497.0940, found 497.0934.

Compound 12: colorless oil; 67% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23−7.18 (m, 4H), 6.22 (s, 2H), 4.15 (q, J = 7.2, 1H), 4.14 (q, J = 7.2, 1H), 3.89−3.81 (m, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.43 (dq, J = 10.8, 7.2, 1H), 3.30 (d, J = 16.2, 1H), 3.07 (d, J = 16.2, 1H), 2.90 (dd, J = 14.4, 1.2, 1H), 2.43 (d, J = 14.4, 1H), 1.71 (s, 3H), 1.21 (t, J = 7.2, 3H), 1.00 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 170.6, 152.2, 144.9, 141.5, 135.8, 134.3, 128.9, 128.2, 126.6, 126.3, 105.2, 61.5, 61.2, 60.6, 55.9, 52.4, 43.2, 42.5, 35.0, 32.0, 14.0, 13.7; FTIR (film) 2983, 1731, 1587, 1508, 1456, 1413, 1256, 1126, 1010, 748, 620 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{26}H_{32}O_7Na$ $[M + Na]^+$ 479.2040, found 479.2045.

Compound 13: colorless oil; 87% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22−7.19 (m, 4H), 6.23 (s, 2H), 5.34 (br s, 1H, OH), 4.15 (q, J = 7.2, 1H), 4.14 (q, J = 7.2, 1H), 3.89−3.82 (m, 1H), 3.73 (s, 6H), 3.49 (dq, J = 10.8, 7.2, 1H), 3.27 (d, J = 15.9, 1H), 3.08 (d, J = 15.9, 1H), 2.91 (d, J = 14.4, 1H), 2.42 (d, J = 14.4, 1H), 1.69 (s, 3H), 1.21 (t, J = 7.2, 3H), 1.00 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 170.7, 146.1, 141.8, 140.3, 134.3, 132.7, 128.8, 128.0, 126.6, 126.3, 104.8, 61.5, 61.2, 56.1, 52.5, 43.3, 42.4, 34.9, 32.0, 13.9, 13.6; FTIR (film) 2967, 2934, 1730, 1612, 1519, 1452, 1420, 1366, 1332, 1317, 1243, 1217, 1169, 1113, 1029, 859, 799, 664, 625 cm^{-1}; HRMS (TOF-QII) *m/z* calcd for $C_{25}H_{30}O_7Na$ $[M + Na]^+$ 465.1884, found 465.1867.

Compound 14: colorless oil; 90% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.20−7.16 (m, 4H), 6.85 (d, J = 6.6, 2H), 6.61 (d, J = 6.6, 2H), 5.39 (br s, 1H, OH), 4.16 (q, J = 7.2, 1H), 4.15 (q, J = 7.2, 1H), 3.81 (dq, J = 10.8, 7.2, 1H), 3.45 (dq, J = 10.8, 7.2, 1H), 3.31 (d, J = 16.2, 1H), 3.09 (d, J = 16.2, 1H), 2.86 (d, J = 14.1,

1H), 2.46 (d, J = 14.1, 1H), 1.66 (s, 3H), 1.21 (t, J = 7.2, 3H), 1.03 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 170.9, 153.7, 141.9, 141.0, 134.1, 128.8, 128.7, 128.2, 126.4, 126.3, 114.4, 61.5, 61.3, 52.5, 43.4, 41.6, 35.0, 32.1, 13.9, 13.6; FTIR (film) 3432, 2978, 1729, 1713, 1612, 1511, 1492, 1462, 1444, 1367, 1333, 1262, 1220, 1180, 1127, 1092, 1052, 834, 773 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{23}H_{26}O_5Na$ [M + Na]$^+$ 405.1678, found 405.1665.

Compound 15: white crystals; 89% yield; mp 156 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.12 (m, 4H), 6.63 (s, 2H), 4.67 (br s, 1H, OH), 4.16 (q, J = 7.2, 2H), 3.86 (dq, J = 10.8, 7.2, 1H), 3.55 (dq, J = 10.8, 7.2, 1H), 3.28 (d, J = 16.2, 1H), 3.14 (d, J = 16.2, 1H), 2.85 (d, J = 14.4, 1H), 2.46 (d, J = 14.4, 1H), 2.14 (s, 6H), 1.65 (s, 3H), 1.22 (t, J = 7.2, 3H), 1.05 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 170.8, 150.1, 142.3, 140.7, 134.0, 128.7, 128.2, 127.6, 126.9, 126.2, 122.0, 61.4, 61.1, 52.6, 43.5, 41.6, 35.0, 31.9, 16.0, 13.9, 13.6; FTIR (film) 3501, 2976, 2930, 1721, 1602, 1488, 1445, 1366, 1331, 1295, 1256, 1241, 1207, 1193, 1164, 1125, 1096, 1052, 1028, 949, 911, 862, 764, 731, 645, 632 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{25}H_{30}O_5Na$ [M + Na]$^+$ 433.1991, found 433.1974.

Compound 16: pale yellow foam; 94% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.89 (m, 3H), 7.48−7.35 (m, 3H), 7.18−6.98 (m, 7H), 6.85 (s, 1H), 4.08 (q, J = 7.2, 2H), 3.40−3.30 (m, 1H), 3.29 (d, J = 16.5, 1H), 3.18 (d, J = 16.5, 1H), 2.99 (d, J = 14.4, 1H), 2.81−2.70 (m, 1H), 2.36 (d, J = 14.4, 1H), 1.66 (s, 3H), 1.13 (t, J = 7.2, 3H), 0.57 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 170.5, 140.2, 138.0, 135.7, 133.7, 133.1, 130.3, 129.2, 129.0, 128.8, 127.8, 127.0, 126.9, 126.6, 124.7, 124.2, 122.8, 121.5, 113.6, 61.4, 60.6, 52.0, 39.5, 38.0, 34.7, 30.1, 13.9, 13.2; FTIR (film) 2982, 1728, 1446, 1368, 1257, 1221, 1174, 1135, 1090, 1071, 1053, 1024, 964, 909, 861, 805, 725, 685, 648, 624 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{31}H_{31}NO_6SNa$ [M + Na]$^+$ 568.1764, found 568.1765.

Compound 17: colorless oil; 77% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.16 (m, 5H), 5.53 (s, 1H), 3.65 (d, J = 6.6 Hz, 1H), 3.54 (d, J = 6.6 Hz, 1H), 3.39−3.33 (m, 5H), 2.84 (s, 2H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.7, 134.2, 128.4, 127.3, 126.6, 123.1, 78.0, 68.3, 59.5, 40.7, 33.4, 19.5; FTIR (film) 2926, 1275, 1260, 764, 750, 723, 700 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{14}H_{19}O_2$ [M + H]$^+$ 219.1380, found 219.1397; calcd for $C_{14}H_{18}NaO_2$ [M + Na]$^+$ 241.1199, found 241.1185.

Compound 18: 82% yield. **18a/18b** = (1/1 mixture of diastereomers). **18a**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−6.81 (m, 8H), 3.90−3.77 (m, 2H), 3.78 (s, 3H), 3.27−3.19 (m, 2H), 2.96 (d, J = 13.5 Hz, 1H), 2.83 (d, J = 13.5 Hz, 1H), 2.08 (s, 2H), 1.50 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 140.7, 138.4, 130.2, 128.3, 126.4, 125.5, 113.5, 84.4, 73.6, 65.3, 55.2, 50.5, 47.5, 40.8, 31.6; FTIR (film) 3424, 2935, 1610, 1510, 1452, 1370, 1298, 1245, 1178, 1108, 1032, 832, 705, 660, 612 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{20}H_{25}O_3$ [M + H]$^+$ 313.1798, found 313.1781; calcd for $C_{20}H_{24}O_3Na$ [M + Na]$^+$ 335.1618, found 335.1625. **18b**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−6.89 (m, 8H), 3.88−3.67 (m, 2H), 3.83 (s, 3H), 3.58−3.47 (m, 2H), 2.69 (d, J = 13.2 Hz, 1H), 2.55 (d, J = 13.2 Hz, 1H), 2.33 (d, J = 13.2 Hz, 1H), 1.89 (d, J = 13.2 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 140.6, 138.3, 129.9, 128.2, 126.3, 125.8, 113.7, 84.6, 74.2, 66.2, 55.2, 50.5, 47.2, 40.0, 32.0; FTIR (film) 3457, 2926, 2339, 1728, 1611, 1510, 1297, 1246, 1032, 833, 704 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{20}H_{25}O_3$ [M + H]$^+$ 313.1798, found 313.1793; calcd for $C_{20}H_{24}O_3Na$ [M + Na]$^+$ 335.1618, found 335.1637.

Gallium-Catalyzed Hydrations. To a solution of substrate **1*l*−n** (0.25 mmol) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compounds **20**−**22**.

Compound 20: colorless oil; 76% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.00 (m, 5H), 4.24−4.14 (m, 6H), 3.43 (s, 2H), 3.38 (s, 2H), 3.06 (s, 2H), 1.28−1.23 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.9, 169.9, 166.6, 136.1, 129.9, 128.5, 127.2, 61.8, 61.4, 56.4, 49.5, 44.8, 38.4, 14.1, 13.9; FTIR (film) 2980, 2340, 1733, 1449, 1366, 1238, 1183, 1057, 1030, 863, 704 cm^{-1}; MS (ESI Q1MS) m/z calcd for $C_{20}H_{27}O_7$ [M + H]$^+$ 379.18, found 379.22; calcd for $C_{20}H_{26}NaO_7$ [M + Na]$^+$ 401.16, found 401.22.

Compound 21: colorless oil; 67% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.12 (m, 10H), 4.18 (q, J = 7.2 Hz, 4H), 3.32 (s, 2H), 3.05 (q, J = 7.8 Hz, 2H), 2.26 (q, J = 7.8 Hz, 2H), 1.23 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 171.0, 135.8, 133.1, 130.0, 128.6, 128.3, 128.02, 127.99, 127.1, 61.4, 58.2, 39.7, 34.0, 27.1, 14.0; FTIR (film) 2981, 2354, 1728, 1686, 1599, 1448, 1367, 1243, 1179, 1091, 1032, 862, 733, 701, 622 cm^{-1}; MS (ESI Q1MS) m/z calcd for $C_{23}H_{27}O_5$ [M + H]$^+$ 383.19, found 383.25; calcd for $C_{23}H_{26}NaO_5$ [M + Na]$^+$ 405.17, found 405.24.

Compound 22A: colorless oil; 64% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.02 (m, 5H), 4.25 (q, J = 7.2 Hz, 1H), 3.86 (s, 2H), 3.45 (s, 2H), 3.14 (s, 2H), 1.29 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 169.9, 135.9, 129.9, 128.5, 127.3, 61.9, 56.7, 42.0, 38.7, 34.1, 13.9; FTIR (film) 2980, 1733, 1730, 1456, 1275, 1188, 1048, 764, 750, 704 cm^{-1}. HRMS (TOF-QII) m/z calcd for $C_{17}H_{21}BrO_5Na$ [M + Na]$^+$ 407.0465, found 407.0465.

Compound 22B: colorless oil; 20% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.18 (m, 4H), 6.29 (s, 1H), 4.21−4.15 (m, 4H), 3.33 (s, 2H), 3.03 (s, 2H), 1.23 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 135.1, 134.8, 128.7, 128.2, 127.7, 125.5, 101.5, 61.8, 54.5, 39.5, 35.0, 14.1; FTIR (film) 2972, 1732, 1681, 1454, 1251, 1192, 1159, 1106, 1079, 1054, 1018, 928, 857, 749, 703 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{17}H_{19}BrO_4Na$ [M + Na]$^+$ 389.0359, found 389.0359.

Typical Procedure for Intramolecular Double and Triple Hydroarylations. To a solution of substrates **1o**−**r** (0.25 mmol, see text, Scheme 5) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 8 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compounds **23**−**26** in high yields.

Compound 23: colorless oil; 99% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 4.5, 2H), 7.16−7.06 (m, 6H), 4.29 (q, J = 4.2, 2H), 3.48 (d, J = 10.2, 2H), 2.99 (d, J = 10.2, 2H), 2.22 (s, 2H), 1.89 (s, 3H), 1.36 (t, J = 4.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 144.2, 134.1, 129.1, 126.3, 125.6, 124.3, 60.8, 41.3, 40.5, 39.9, 38.3, 25.7, 11.2; FTIR (film) 2934, 2197, 1725, 1574, 1489, 1450, 1367, 1293, 1240, 1210, 1158, 1124, 1083, 1041, 863, 818, 781, 727, 618 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{21}H_{23}O_2$ [M + H]$^+$ 307.1693, found 307.1690.

Compound 24: pasty solid; 95% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 4.5, 1H), 7.51 (d, J = 4.5, 1H), 7.48 (d, J = 4.5, 1H), 7.32 (t, J = 4.5, 1H), 7.25 (t, J = 4.5, 1H), 6.86 (d, J = 4.5, 1H), 4.36−4.31 (m, 2H), 4.04−3.97 (m, 2H), 3.95 (s, 3H), 3.93 (d, J = 7.8, 1H), 3.14 (d, J = 7.8, 1H), 3.13 (d, J = 8.4, 1H), 1.91 (d, J = 8.4, 1H), 1.38 (s, 3H), 1.35 (t, J = 4.2, 3H), 1.09 (t, J = 4.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 171.9, 156.2, 153.8, 151.1, 139.9, 130.7, 127.2, 126.0, 123.0, 120.6, 119.9, 118.9, 109.6, 61.7, 61.4, 56.0, 55.7, 45.9, 38.2, 26.3, 24.3, 14.1, 13.7; FTIR (film) 2979, 2933, 1728, 1622, 1494, 1458, 1440, 1387, 1355, 1311, 1246, 1190, 1097, 1066, 1046, 1021, 931, 903,

858, 811, 782, 748, 699 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{24}H_{26}NaO_5$ $[M + Na]^+$ 417.1672, found 417.1657.

Compound 25: pasty solid; 98% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.7, 1.5 Hz), 7.32−7.24 (m, 2H), 7.18 (dt, J = 8.7, 1.2 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 4.31−4.06 (m, 5H), 3.88−3.80 (m, 5H), 3.20 (dd, J = 13.8, 1.5 Hz, 1H), 2.74 (d, J = 11.1 Hz, 1H), 2.69 (d, J = 11.1 Hz, 1H), 1.283 (t, J = 6.9 Hz, 3H), 1.280 (t, J = 6.9 Hz, 3H), 1.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.3, 155.6, 146.2, 139.1, 136.0, 128.7, 127.7, 126.4, 125.83, 125.78, 123.5, 121.1, 107.7, 61.6, 61.4, 55.6, 38.6, 37.9, 35.5, 27.9, 27.1, 14.0, 13.9; FTIR (film) 2972, 1731, 1592, 1456, 1260, 764 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{25}H_{28}O_5Na$ $[M + Na]^+$ 431.1829, found 431.1825.

Compound 26: pasty solid; 82% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.47 (d, J = 8.4, 1H), 7.28 (s, 1H), 6.82 (d, J = 8.4, 1H), 5.98 (s, 1H), 4.35−3.90 (m, 8H), 3.89 (s, 3H), 3.83 (d, J = 2.4, 1H), 3.40 (d, J = 1.5, 2H), 3.11−3.04 (m, 2H), 2.21 (t, J = 1.5, 3H), 1.85 (d, J = 13.2, 1H), 1.35−1.19 (m, 12H), 1.07 (t, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 171.9, 170.6, 170.5, 156.1, 153.4, 151.1, 138.7, 135.2, 132.8, 131.1, 130.7, 122.6, 121.1, 120.6, 118.5, 115.1, 109.6, 61.8, 61.6, 61.4, 56.0, 55.0, 45.9, 42.0, 38.2, 35.1, 26.3, 24.3, 19.8, 14.1, 14.0, 13.9 (2C), 13.8; FTIR (film) 2979, 1732, 1651, 1636, 1508, 1472, 1258, 749, 652, 620 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{35}H_{40}NaO_9$ $[M + Na]^+$ 627.2565, found 627.2547.

Gallium-Catalyzed Quadruple Hydroarylation of Diyne 1r. To a solution of substrate **1r** (151.2 mg, 0.25 mmol) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) and anisole (81.1 mg, 0.75 mmol) in one portion. The mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compound **27** (133.7 mg) in 75% yield. Colorless oil; 1:1 mixture of 2 diastereomers; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.33 (m, 4 H, 2 dias), 7.28 (br, s, 2 H, 2 dias), 7.03 (d, J = 9.0, 2 H, 1 dias), 6.96 (d, J = 9.0, 2 H, 1 dias), 6.78 (d, J = 9.0, 1 H, 1 dias), 6.77 (d, J = 9.0, 1 H, 1 dias), 6.76 (d, J = 9.0, 2 H, 1 dias), 6.72 (d, J = 9.0, 2 H, 1 dias), 4.36−4.27 (m, 4 H, 2 dias), 4.20−4.10 (m, 4 H, 2 dias), 3.89 (s, 3 H, 1 dias), 3.88 (s, 3 H, 1 dias), 3.92−3.78 (m, 4 H, 2 dias), 3.75 (s, 3 H, 1 dias), 3.74 (s, 3 H, 1 dias), 4.06−3.90 (m, 4 H, 2 dias), 3.50−3.39 (m, 2 H, 2 dias), 3.38 (d, J = 11.1, 2 H, 2 dias), 3.18−3.07 (m, 4 H, 2 dias), 3.07 (d, J = 11.1, 2 H, 2 dias), 2.90 (d, J = 14.1, 1 H, 1 dias), 2.89 (d, J = 14.1, 1 H, 1 dias), 2.51 (d, J = 14.1, 1 H, 1 dias), 2.48 (d, J = 14.1, 1 H, 1 dias), 1.90 (d, J = 13.5, 1 H, 1 dias), 1.86 (d, J = 13.5, 1 H, 1 dias), 1.77 (s, 3 H, 1 dias), 1.73 (s, 3 H, 1 dias), 1.40 (s, 3 H, 1 dias), 1.35 (s, 3 H, 1 dias), 1.36−0.98 (m, 24 H, 2 dias); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9 (C═O, 1 dias), 172.8 (C═O, 1 dias), 172.1 (C═O, 1 dias), 172.0 (C═O, 1 dias), 171.9 (2 C═O, 2 dias), 170.7 (C═O, 1 dias), 170.6 (C═O, 1 dias), 157.6 (C, 1 dias), 157.4 (C, 1 dias), 156.1 (2 C, 2 dias), 152.1 (C, 1 dias), 152.0 (C, 1 dias), 152.0 (C, 1 dias), 151.2 (2 C, 2 dias), 141.4 (C, 1dias), 141.3 (C, 1 dias), 140.9 (C, 1 dias), 140.8 (C, 1dias), 138.3 (2 C, 2 dias), 132.2 (C, 1dias), 132.1 (C, 1dias), 130.9 (2 C, 2dias), 128.7 (4 CH, 2 dias), 123.4 (2 C, 2 dias), 120.6 (2 CH, 2 dias), 119.4 (2 CH, 2 dias), 118.7 (2 CH, 2 dias), 112.9 (4 CH, 2 dias), 109.6 (CH, 1 dias), 109.5 (CH, 1 dias), 61.7 (3 CH_2, 2 dias), 61.5 (CH_2, 1 dias), 61.4 (3 CH_2, 2 dias), 61.1 (CH_2, 1 dias), 56.1 (2 C, 2 dias), 56.0 (2 C, 2 dias), 55.8 (C, 1 dias), 55.7 (C, 1 dias), 55.2 (2 CH_3, 2 dias), 52.6 (2 CH_3, 2 dias), 45.6 (2 CH_2, 2 dias), 43.6 (C, 1 dias), 43.4 (C, 1 dias), 41.9 (2 CH_2, 2 dias), 38.4 (CH_2, 1 dias), 38.3 (CH_2, 1 dias), 35.5 (CH_2, 1 dias), 35.4 (CH_2, 1 dias), 32.4 (CH_3, 1 dias), 26.3 (CH_3, 1 dias), 24.4 (CH_3, 1 dias), 24.2 (CH_3, 1 dias), 14.1 (2 CH_3, 2 dias), 14.0 (2 CH_3, 2 dias), 13.9 (CH_3, 1 dias), 13.8 (CH_3, 1 dias), 13.7 (2 CH_3, 2 dias); FTIR (film) 2978, 1729, 1608, 1508, 1465, 1365, 1249, 1181, 1094, 1054, 913, 832, 732, 651 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{42}H_{48}NaO_{10}$ $[M + Na]^+$ 735.3140, found 735.3145.

Gold-Catalyzed Hydroarylation of Diyne 1s. To a solution of substrate **1s** (154.7 mg, 0.25 mmol) in DCE (1 mL) at room temperature was added $AuClPPh_3$ (2.5 mg, 0.005 mmol) and $AgSbF_6$ (1.7 mg, 0.005 mmol) in one portion. The mixture was stirred at room temperature for 8 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compound **28** (118.4 mg) in 71% yield. Colorless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.10−6.70 (m, 6 H), 5.95 (q, J = 1.5, 1 H), 4.21−4.01 (m, 8 H), 3.80 (s, 2 H), 3.69 (s, 3 H), 3.39 (s, 2 H), 3.30 (s, 2 H), 2.91 (s, 2 H), 2.10 (d, J = 1.5, 3 H), 1.95 (s, 3 H), 1.24−1.16 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.1, 170.5, 170.4, 156.4, 139.9, 134.9, 133.5, 133.1, 132.1, 130.5, 128.7, 128.2 127.7, 125.1, 124.0, 121.5, 110.6, 61.6, 61.3, 55.7, 55.3, 54.8, 45.1, 40.9, 34.2, 32.0, 29.5, 19.4, 14.0, 13.9; FTIR (film) 2981, 1733 (br), 1611, 1503, 1465, 1445, 1366, 1269, 1236, 1210, 1186, 1127, 1096, 1078, 1046, 1032, 863, 815, 733, 647 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{36}H_{45}O_{10}$ $[M + H]^+$ 637.3007, found 637.3011.

Gallium-Catalyzed Hydroarylation of Diyne 1s. To a solution of substrate **1s** (154.7 mg, 0.25 mmol) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 8 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford compound **29** (120.6 mg) in 76% yield. Colorless oil; 1:2 mixture of 2 diastereomers; ^1H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, J = 8.7, 1 H), 8.18 (s, 1 H), 7.44 (s, 1 H), 6.96 (d, J = 8.7, 1 H), 4.35−4.00 (m, 8 H), 3.95 (s, 3 H), 3.76 (d, J = 17.1, 1 H), 3.51 (d, J = 17.1, 1 H), 3.28−3.12 (m, 3 H), 3.03−2.88 (m, 1 H), 2.68−2.56 (m, 2 H), 1.92−1.80 (m, 1 H), 1.48−1.05 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$, major) δ 183.12, 172.48, 171.67, 171.63, 170.76, 160.47, 148.47, 146.48, 139.72, 138.77, 128.68, 128.25, 125.58, 125.51, 123.61, 121.39, 108.97, 61.96, 61.63 (d), 61.47, 55.79, 53.74, 53.04, 39.16, 37.10, 37.03, 35.77, 34.53, 29.83, 25.93, 21.02, 14.08, 14.05, 13.97, 13.83; ^{13}C NMR (75 MHz, $CDCl_3$, minor) δ 183.18, 172.41, 171.63, 171.58, 170.70, 160.47, 148.51, 146.58, 139.75, 138.77, 128.71, 128.25, 125.73, 125.68, 123.68, 121.39, 108.97, 61.96, 61.63 (d), 61.44, 55.79, 53.77, 53.15, 39.44, 37.10, 37.03, 35.95, 34.80, 29.81, 25.93, 21.39, 14.08, 14.05, 13.97, 13.83; FTIR (film) 2970, 1731 (br), 1656, 1608, 1590, 1464, 13685, 1300, 1263, 1244, 1188, 1138, 1095, 1050 cm^{-1}; HRMS (TOF-QII) *m*/*z* calcd for $C_{36}H_{43}O_{10}$ $[M + H]^+$ 635.2851, found 635.2858.

Gallium-Catalyzed 6-*exo* Cyclizations of Arenynes 1t and 1u. To a solution of substrate **1** (**1t** or **1u**, 0.25 mmol) and possibly arenes (0.75 mmol) in DCE (1 mL) was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at room temperature for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford the corresponding products.

Compound 30t: pasty solid; 75% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.4, 2H), 7.29 (d, J = 8.4, 2H), 7.18−7.05 (m, 5H), 6.88 (dd, J = 7.5, 1.2, 1H), 6.79 (d, J = 9.0, 2H), 4.58 (d, J = 14.7, 1H), 4.03 (d, J = 14.7, 1H), 3.79 (s, 3H), 3.48 (dd, J = 11.7, 1.2, 1H), 3.02 (d, J = 11.7, 1H), 2.41 (s, 3H), 1.78

(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 143.6, 142.6, 138.3, 133.3, 131.2, 129.7, 128.8, 128.7, 127.7, 127.1, 126.3, 126.2, 113.4, 57.4, 55.2, 48.3, 43.5, 27.3, 21.5; FTIR (film) 1652, 1509, 1457, 1340, 1248, 1164, 1091, 1031, 832, 768, 660 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{24}H_{25}NO_3Na$ $[M + Na]^+$ 430.1447, found 430.1434.

Compound 31t: pasty solid; 81% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1, 2H), 7.32 (d, J = 8.1, 2H), 7.18−6.90 (m, 6H), 6.74 (d, J = 8.4, 2H), 5.44 (s, br, 1H), 4.57 (d, J = 14.7, 1H), 4.07 (d, J = 14.7, 1H), 3.48 (d, J = 11.7, 1H), 3.07 (d, J = 11.7, 1H), 2.43 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 143.7, 142.5, 138.2, 133.1, 131.0, 129.7, 128.9, 128.6, 127.7, 127.1, 126.3, 126.1, 114.9, 57.4, 48.2, 43.4, 27.2, 21.5; FTIR (film) 3414, 2973, 1612, 1596, 1512, 1491, 1448, 1333, 1264, 1215, 1155, 1089, 1028, 976, 959, 834, 813, 760, 734, 706, 661 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{23}H_{23}NO_3SNa$ $[M + Na]^+$ 416.1291, found 416.1284.

Compound 32t: pasty solid; 78% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2, 2H), 7.79−7.13 (m, 15H), 6.75 (d, J = 8.1, 2H), 4.77 (d, J = 15.3, 1H), 4.01 (d, J = 15.3, 1H), 3.60 (d, J = 12.0, 1H), 3.11 (d, J = 12.0, 1H), 2.38 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 140.0, 138.1, 133.9, 130.5, 129.8, 129.4, 129.2, 128.0, 127.5, 127.4, 126.84,126.81, 126.6, 126.3, 124.7, 124.4, 122.8, 121.3, 119.6, 117.2, 113.8, 54.3, 48.1, 40.1, 27.9, 21.5; FTIR (film) 2925, 1447, 1353, 1276, 1260, 1168, 1136, 1092, 820, 764, 750, 724, 684 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{31}H_{28}N_2O_4S_2Na$ $[M + Na]^+$ 579.1383, found 579.1394.

Compound 30u: pasty solid; 70% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dt, J = 9.0, 1.2, 2H), 7.73 (d, J = 8.1, 2H), 7.61−7.46 (m, 3H), 7.32 (d, J = 8.1, 2H), 7.08 (d, J = 8.7, 2H), 6.96 (d, J = 8.7, 1H), 6.79 (d, J = 9.0, 1H), 5.09 (d, J = 15.3, 1H), 4.40 (d, J = 15.3, 1H), 3.79 (s, 3H), 3.62 (dd, J = 11.7, 0.9, 1H), 3.08 (d, J = 11.7, 1H), 2.42 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 143.6, 139.9, 138.1, 133.4, 131.8, 129.8, 129.7, 128.9, 128.6, 127.7, 127.3, 126.7, 126.4, 125.9, 125.8, 122.0, 113.5, 57.2, 55.2, 46.0, 43.9, 26.5, 21.5; FTIR (film) 2963, 1608, 1509, 1461, 1341, 1310, 1251, 1183, 1165, 1090, 1030, 981, 834, 814, 750, 726, 661 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{28}H_{28}NO_3S$ $[M + H]^+$ 458.1784, found 458.1778; calcd for $C_{28}H_{27}NO_3SNa$ $[M + H]^+$ 480.1604, found 480.1597.

Compound 31u: pasty solid; 81% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (t, J = 8.7, 2H), 7.62 (d, J = 8.1, 2H), 7.50−7.35 (m, 3H), 7.22 (d, J = 8.1, 2H), 6.91−6.84 (m, 3H), 6.62 (d, J = 8.7, 2H), 5.45 (s, br, 1H), 4.97 (d, J = 15.0, 1H), 4.32 (d, J = 15.0, 1H), 3.49 (d, J = 11.4, 1H), 2.99 (d, J = 11.4, 1H), 2.31 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 143.8, 139.8, 137.9, 133.2, 131.8, 129.8, 129.7, 129.0, 128.6, 127.7, 127.3, 126.7, 126.4, 125.8, 125.7, 121.9, 115.0, 57.2, 46.0, 43.8, 26.5, 21.5; FTIR (film) 3429, 2972, 1614, 1586, 1514, 1456, 1335, 1261, 1160, 1091, 817, 764, 747, 678, 664 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{27}H_{25}NO_3SNa$ $[M + Na]^+$ 466.1447, found 466.1445.

Compound 32u: pasty solid; 78% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95−7.50 (m, 16H), 7.15 (t, J = 7.5, 1H), 6.86 (d, J = 8.5, 1H), 6.75 (t, J = 8.0, 1H), 6.33 (d, J = 8.0, 1H), 5.30 (d, J = 15.0, 1H), 4.34 (d, J = 15.0, 1H), 3.70 (d, J = 11.5, 1H), 3.70 (d, J = 11.5, 1H), 2.39 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 138.1, 137.6, 135.8, 134.0, 133.6, 132.1, 129.9, 129.7, 129.4, 128.7, 127.8, 127.6, 127.4, 127.3, 126.9, 126.8, 125.9, 125.4, 124.8, 124.4, 122.8, 122.1, 121.2, 113.7, 53.8, 45.8, 40.5, 27.3, 21.5; FTIR (film) 3433, 2970, 1455, 1270, 1159, 1091, 820, 665 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{35}H_{30}N_2O_4S_2Na$ $[M + H]^+$ 629.1539, found 629.1542.

Compound 33t:[38] white solid; mp 98−100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.1, 2H), 7.18−7.06 (m, 3H), 6.95 (d, J = 8.1, 2H), 6.87−6.83 (m, 1H), 6.20 (d, J = 12.6, 1H), 5.55 (dt, J = 12.6, 3.6, 1H), 4.36 (s, 2H), 4.15 (d, J = 3.6, 2H), 2.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.6, 136.3, 135.8, 135.2, 130.7, 130.0, 129.0, 128.6, 127.8, 127.6, 127.3, 127.0, 52.7, 51.2, 21.3; FTIR (film) 3024, 2922, 1597, 1493, 1439, 1333, 1184, 1155, 1112, 1090, 1066, 899. 827, 813, 784, 750, 734, 710, 685, 654 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{17}H_{17}NO_2SNa$ $[M + Na]^+$ 322.0872, found 322.0872.

Compound 33u: white solid; mp 127−129 °C; 1:1 mixture of conformers; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77−7.16 (m, 10 H), 7.01 (d, J = 8.7, 0.5 H), 5.27−5.17 (m, 1 H), 4.35−4.22 (m, 1 H), 4.06 (d, J = 10.2, 0.5 H), 3.52 (d, J = 10.5, 0.5 H), 2.96 (d, J = 10.5, 0.5 H), 2.52−2.42 (m, 2 H), 2.33 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 143.9, 143.6, 142.5, 139.3, 134.1, 133.9, 133.0, 132.1, 130.0, 129.87, 129.83, 129.7, 129.0, 128.7, 127.8, 127.6, 127.4, 127.2, 127.04, 127.00, 126.5, 126.2, 126.05, 125.96, 125.6, 125.3, 124.1, 123.9, 121.8, 121.7, 53.1, 52.2, 43.7, 42.1, 27.3, 21.5; HRMS (TOF-QII) m/z calcd for $C_{21}H_{19}NO_2SNa$ $[M + Na]^+$ 372.1029, found 372.1022.

Gallium-Catalyzed Hydroarylations of Dihydroazepines 33t and 33u. To a solution of substrates **32** (**32t** or **32u**, 0.25 mmol) and possibly arenes (0.75 mmol) in DCE (1 mL) at 80 °C was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford the corresponding products.

Compound 34t: pasty solid; 83% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 8.5 Hz, 2H), 7.31−7.12 (m, 5H), 6.98−6.69 (m, 5H) 4.49−4.38 (m, 2H), 4.22 (d, J = 7.5 Hz, 1H), 3.80 (s, 3H), 3.68−3.61 (m, 1H), 3.50−3.43 (m, 1H), 2.39 (m, 1H), 2.21−2.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 143.7, 143.0, 136.6, 134.5, 129.9, 129.5, 129.2, 129.1, 128.1, 127.2, 126.6, 114.0, 55.2, 52.9, 48.6, 47.6, 33.1, 21.5; FTIR (film) 3301, 2924, 1616, 1540, 1507, 1457, 1337, 1305, 1250, 1178, 1158, 1091, 1032, 888, 797, 764, 714 657 cm^{-1}. HRMS (TOF-QII) m/z calcd for $C_{24}H_{25}NO_3SNa$ $[M + Na]^+$ 430.1447, found 430.1438.

Compound 35t: pasty solid; 87% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.1 Hz, 2H), 7,22 (dd, J = 7.2, 1.5 Hz, 1H), 7.13 (d, J = 8.1 Hz, 2H), 7.10−7.02 (m, 2H), 6.82(d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 6.63 (d, J = 6.9 Hz, 1H), 5.31 (s, br, 1H), 4.39 (d, J = 15.0 Hz, 1H), 4.31 (d, J = 15.0 Hz, 1H), 4.12 (dd, J = 8.4, 3.3 Hz, 1H), 3.59−3.33 (m, 2H), 2.31 (s, 3H), 2.13−2.00 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 143.7, 143.1, 136.5, 136.4, 134.4, 129.8, 129.5, 128.1, 127.2, 126.6, 115.5, 52.8, 48.5, 47.5, 33.0, 21.4; FTIR (film) 3411, 2923, 1614, 1596, 1513, 1450, 1327, 1305, 1264, 1214, 1151, 1089, 1015, 948, 889, 834, 814, 764, 736, 714, 654 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{23}H_{23}NO_3SNa$ $[M + Na]^+$ 416.1291, found 416.1286.

Compound 36t: pasty solid; 84% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 1H), 7.87 (d, J = 8.7 Hz, 2H), 7.61−7.03 (m, 14H), 6.60 (d, J = 7.5 Hz, 1H), 4.63 (d, J = 15.0 Hz, 1H), 4.52 (d, J = 15.0 Hz, 1H), 4.45−4.41 (m, 2H), 3.63−3.45 (m, 2H), 2.40 (s, 3H), 2.24−2.14 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 141.3, 137.9, 136.4, 135.8, 135.6, 133.8, 129.9, 129.8, 129.5, 129.2, 128.2, 128.1, 127.1, 127.0, 126.6, 124.9, 124.6, 124.1, 123.2, 120.4, 113.9, 52.8, 48.3, 39.9, 32.2, 21.4; FTIR (film) 2922, 1599, 1447, 1367, 1333, 1266, 1173, 1155, 1122, 1089, 1020, 980, 908, 884, 814, 725, 685, 653 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{31}H_{28}N_2O_4S_2Na$ $[M + Na]^+$ 579.1383, found 579.1388.

(38) Bradshaw, B.; Evans, P.; Fletcher, J.; Lee, A. T. L.; Mwashimba, P. G.; Oehlrich, D.; Thomas, E. J.; Davies, R. H.; Allen, B. C. P.; Broadley, K. J.; Hamrouni, A.; Escargueil, C. *Org. Biomol. Chem.* **2008**, *6*, 2138.

Compound 37u: pasty solid; 82% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.16 (m, 13H), 6.92 (d, J = 8.7 Hz, 2H), 5.58 (s, br, 1H), 4.38 (d, J = 15.0 Hz, 1H), 3.87 (d, J = 15.0 Hz, 1H), 3.22 (d, J = 7.5 Hz, 2H), 3.07 (d, J = 15.0 Hz, 1H), 2.78 (dd, J = 11.7, 1.5 Hz, 1H), 2.42 (s, 3H), 2.20 (d, J = 11.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 139.7, 133.84, 13.75, 130.0, 129.6, 128.7, 128.0, 127.7, 127.4, 127.2, 126.9, 126.01, 125.96, 125.9, 125.7, 123.8, 121.9, 52.3, 50.0, 47.1, 28.1, 21.5; FTIR (film) 3734, 2925, 1456, 1339, 1274, 1161, 1091, 812, 764, 751 cm^{-1}; HRMS (TOF-QII) m/z calcd for $C_{27}H_{25}NO_3SNa$ $[M + Na]^+$ 466.1447, found 466.1442.

One-Pot Procedure for the Synthesis of Compound 34t. To a solution of substrate **1t** (74.8 mg, 0.25 mmol) in DCE (1 mL) was added $GaCl_3$ (0.5 M in pentane, 0.05 mL, 0.025 mmol) in one portion. The mixture was stirred at room temperature for 10 h and added to anisole (81.1 mg, 0.75 mmol). The resulting mixture was stirred at 80 °C for 10 h, then sat. aq $NaHCO_3$ (1 mL) was added at 0 °C. The two layers were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to flash column chromatography on silica gel to afford product **34t** (58.0 mg) in 57% overall yield.

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Supporting Information Available: Detailed experimental procedures for the starting materials, deuterium-labeling experiments, X-ray data for **9** and **15** (CIF), computational details, and copies of ^{1}H and ^{13}C NMR spectra of the reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.