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Substitution of Hydroxybiaryls via Directed *ortho*-Lithiation of *N*-Silylated *O*-Aryl *N*-Isopropylcarbamates

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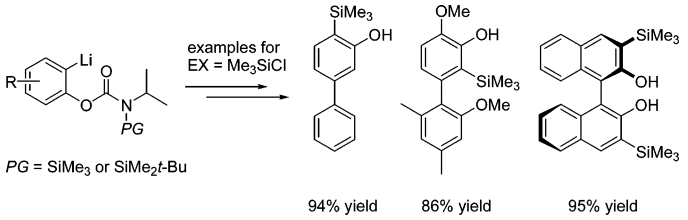

Herein we report regioselective substitution reactions of a series of 2- and 3-hydroxybiaryls including BINOL via a new directed *ortho*-metalation procedure. *O*-Aryl *N*-isopropylcarbamates, conveniently prepared from phenols and isopropyl isocyanate, are temporarily and in situ *N*-protected by means of silyl triflates to form stable intermediates for low temperature lithiation reactions using butyllithium/TMEDA in diethyl ether. The resulting aryllithiums are efficiently substituted by a wide range of electrophilic reagents to afford functionalized biaryls in high yields. *N*-Desilylation already occurs during aqueous workup. The following deprotection of the urethanes to the corresponding phenols proceeds rapidly and in quantitative yields. Even sensitive substituents (e.g., CO_2Me, CHO, $SiMe_3$, I) in the products are preserved under mild alkaline conditions which have been established for carbamate ester cleavage. Furthermore, applications of *ortho*-substituted products in common cross-coupling reactions for further C−C bond formations are demonstrated.

Introduction

The Directed *ortho*-Metalation (DoM reaction) allows the efficient introduction of substituents into aromatic and heteroaromatic substrates adjacent to a Lewis-basic substituent via preceding coordination and regioselective deprotonation.[1] For phenols, besides the weakly directing methoxy group[2] and the modest but synthetically useful methoxymethoxy group (MOM),[3] the very powerful *N*,*N*-diethyl *O*-carbamoyl-directed metalation group (DMG) was introduced in 1983 by Sibi and Snieckus (Scheme 1).[4] Frequently, migration of the carbamoyl group in the *ortho*-lithiated intermediate ("anionic *ortho*-Fries rearrangement")[4] complicates efficient quench with electrophiles,[5] although the migration reaction is useful in its own right.[1b,6] In addition, harsh conditions which are required for liberating the free hydroxyl group under basic conditions have to be taken into account.[7] To

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(1) For reviews, see: (a) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879−933. (b) Hartung, C. G.; Snieckus, V. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinheim, Germany, 2002; pp 330−367. (c) Clayden, J. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, U.K., 2004; pp 495−646. For mechanistic aspects, especially related to the influence of the Complex Induced Proximity Effect (CIPE), see: (d) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2206−2225.

(2) For tabulated lists, see: (a) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1−360. (b) Schlosser, M. In *Organometallics in Synthesis*, 2nd ed.; Schlosser, M., Ed.; Wiley: Chichester, U.K., 2002; pp 1−352. See also ref 1c.

(3) Christensen, H. *Synth. Commun.* **1975**, *5*, 65−78. For further examples, see ref 2.

(4) Sibi, M. P.; Snieckus, V. *J. Org. Chem.* **1983**, *48*, 1935−1937.

(5) Side product formation by this rearrangement may be avoided in certain cases by using lower reaction temperatures; for an example, see: (a) Wang, W.; Snieckus, V. *J. Org. Chem.* **1992**, *57*, 424−426. (b) van Doorn, A. R.; Bos, M.; Harkema, S.; van Eerden, J.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1991**, *56*, 2371−2380.

(6) For synthetic applications of the anionic *ortho*-Fries rearrangement and other O → C carbamoyl transfer reactions, see ref 5a and: (a) Kalinin, A. V.; Miah, M. A. J.; Chattopadhyay, S.; Tsukazaki, M.; Wicki, M.; Nguen, T.; Coelho, A. L.; Kerr, M.; Snieckus, V. *Synlett* **1997**, 839−841. (b) Mohri, S.-i.; Stefinovic, M.; Snieckus, V. *J. Org. Chem.* **1997**, *62*, 7072−7073. (c) Kalinin, A. V.; da Silva, A. J. M.; Lopes, C. C.; Lopes, R. S. C.; Snieckus, V. *Tetrahedron Lett.* **1998**, *39*, 4995−4998. (d) Kalinin, A. V.; Snieckus, V. *Tetrahedron Lett.* **1998**, *39*, 4999−5002. (e) Chauder, B. A.; Kalinin, A. V.; Taylor, N. J.; Snieckus, V. *Angew. Chem., Int. Ed.* **1999**, *38*, 1435−1438. (f) Reed, M. A.; Chang, M. T.; Snieckus, V. *Org. Lett.* **2004**, *6*, 2297−2300.

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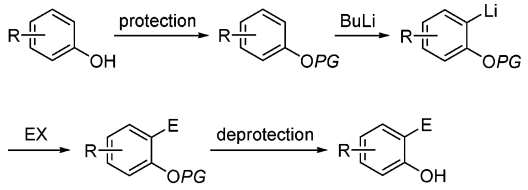
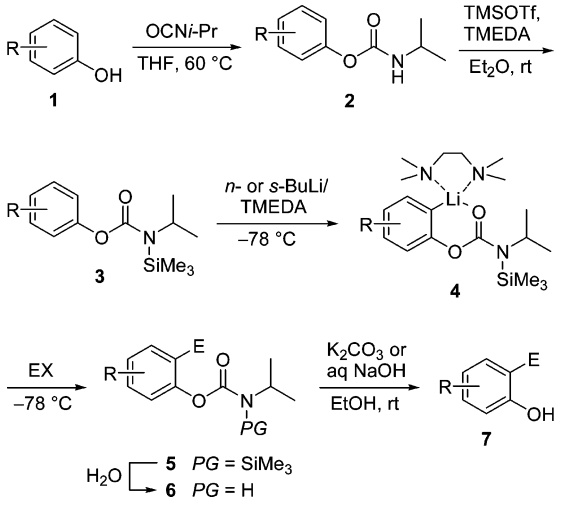
SCHEME 1. Substitution of Phenols by the Directed *ortho*-Lithiation



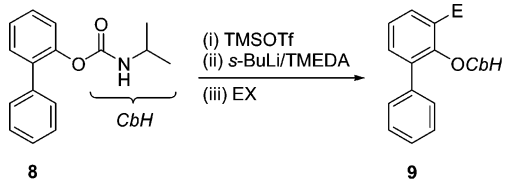
SCHEME 2. Directed *ortho*-Lithiation of in Situ *N*-Silylated *O*-Aryl *N*-Isopropylcarbamates



overcome this deficiency, Snieckus introduced the *N*-cumyl-*N*-methyl *O*-carbamoyl group, which can be removed under mild acidic conditions.[8]

Kauch and Hoppe found[9] that the *N*-isopropyl-*N*-trimethylsilylcarbamoyl DMG[10] provides the following advantages (Scheme 2): the *O*-aryl *N*-isopropylcarbamate **2** is conveniently produced from phenol **1** by treatment with isopropyl isocyanate.[11] Furthermore, steps **2** → **6** of the standard sequence are carried out in a one-flask operation, beginning with the reaction of **2** with trimethylsilyl triflate in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) in diethyl ether to form the *N*-silyl derivative **3**. Although the isolation and characterization of similar *N*-benzyl carbamates has been

SCHEME 3. Directed *ortho*-Lithiation of *O*-2-Biphenylyl Carbamate 8



reported,[12] in this case, the solution of **3** is directly treated with 2 equivalents of *n*- or *s*-butyllithium/ TMEDA,[13] and the lithium chelate **4** is subsequently trapped by suitable electrophiles EX. During the aqueous workup, the silyl group in the initial product **5** is lost and in most cases, the crystalline urethane **6** is isolated in high yield.

The removal of the carbamoyl group for the formation of phenol **7** proceeds smoothly and quantitatively by treatment with aqueous NaOH or solid K_2CO_3 in ethanol at room temperature. Herein we report the utilization of this new method for the regioselective synthesis of substituted hydroxybiaryls.

Results and Discussion

***O*-2- and *O*-3-Biphenylyl *N*-Isopropylcarbamates.** The directed *ortho*-lithiation of **8** and subsequent substitution by some carbo- and hetero-electrophiles have been reported[9] previously to proceed smoothly in high yield (Scheme 3). In continuation of this study, we find that reactions with allyl and benzyl bromide proceed only slowly (Table 1, entries 1 and 2) and require large excess of the alkylation agent in order to achieve good yields of **9a** and **9b**. Formation of ketones or esters by use of acid chlorides (entries 3 and 4) may be followed by further attack by the aryllithium on the incipient carbonyl group; hence, use of excess reagent was found to be advantageous. The same was also found in formylation by means of DMF (entry 5). In this reaction, aldehyde-carbamate cyclization during workup was observed.[14] Boronation by means of triisopropyl borate proceeded smoothly, but for facile purification by liquid chromatography, re-esterification of the crude arylboronic acid with pinacol to form the more hydrolytically stable 1,3,2-dioxaborolane **9f** was carried out.[15]

In contrast to observations of the analogous *N*,*N*-diethyl carbamate,[5] in all reactions of **8** with electro-

(7) The hydrolysis of tertiary *N*,*N*-diethyl *O*-aryl carbamates to phenols normally requires vigorous basic conditions utilizing NaOH (MeOH/H_2O or ethylene glycol, reflux; see ref 4), LAH (THF, reflux; see ref 4), or MeLi (Et_2O, rt; see ref 24a). Recently, a new method using $Cp_2Zr(H)Cl$ has been developed: Morin, J.; Snieckus, V. Unpublished results.

(8) Metallinos, C.; Nerdinger, S.; Snieckus, V. *Org. Lett.* **1999**, *1*, 1183−1186.

(9) Kauch, M.; Hoppe, D. *Can. J. Chem.* **2001**, *79*, 1736−1746.

(10) Direct *N*,*C*-dilithiation of *O*-aryl *N*-monoalkylcarbamates cannot be achieved due to an irreversible cleavage reaction of the initial formed *N*-lithiated intermediate (see ref 9). In contrast to this observation, the analogues *O*-allyl and *S*-allyl carbamates can be converted to the dianionic species, see: (a) Hanko, R.; Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 127−128. (b) Marr, F.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **1999**, *1*, 2081−2083. (c) Marr, F.; Fröhlich, R.; Wibbeling, B.; Diedrich, C.; Hoppe, D. *Eur. J. Org. Chem.* **2002**, 2970−2988.

(11) (a) Petersen, S. In *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed.; Müller, E., Ed.; Thieme: Stuttgart, Germany, 1956; Vol. VIII, pp 137−149. The *N*-monoalkylcarbamoyl group has been used as protecting group for phenols of tyrosine derivatives: (b) Jäger, G.; Geiger, R.; Siedel, W. *Chem. Ber.* **1968**, *101*, 2762−2770.

(12) (a) Roby, J.; Voyer, N. *Tetrahedron Lett.* **1997**, *38*, 191−194. (b) Barberis, C.; Voyer, N. *Synlett* **1999**, 1106−1108. (c) Barberis, C.; Voyer, N.; Roby, J.; Chénard, S.; Tremblay, M.; Labrie, P. *Tetrahedron* **2001**, *57*, 2965−2972.

(13) Normally, the salt TMEDA·HOTf precipitates as an oil, which solidifies on cooling to −78 °C. Due to its consistency, it undergoes reaction more slowly than **3** with the alkyllithium reagent. As a result, even when applying only 1.1 equiv of butyllithium, high yields of **6** are achieved (see ref 9).

(14) The oxazinone byproduct **10** reacted under deprotection conditions C (see Table 2, entry 3) as well as carbamate **9e** to the corresponding salicylic aldehyde **15c**, so that a high overall yield was obtained.

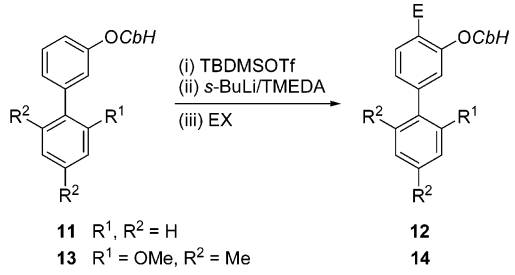
(15) The purification and analysis of organoboronic acids are generally difficult due to their spontaneous condensation to various degrees to boroxines; for a discussion of possibilities for their derivatization and isolation, see: (a) Miyaura, N. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004; pp 41−123. See also ref 26c. For a general review on organoboronic acids and their esters, see: (b) Köster, R. In *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed.; Köster, R., Ed.; Thieme: Stuttgart, Germany, 1982; Vol. 13/3a, pp 489−852.

TABLE 1. Directed *ortho*-Lithiation and Substitution of *O*-Biphenylyl *N*-Isopropylcarbamates 8, 11, and 13

entry	substrate	electrophile EX (equiv)	reaction time	product	E	yield (%)
1	**8**	CH_2=$CHCH_2Br$ (10)	6 h	**9a**	CH_2CH=CH_2	85[a]
2	**8**	$PhCH_2Br$ (10)	6 h	**9b**	CH_2Ph	80[b]
3	**8**	*t*-BuC(O)Cl (6)	1 h	**9c**	C(O)*t*-Bu	90[c]
4	**8**	MeOC(O)Cl (6)	1 h	**9d**	C(O)OMe	82
5	**8**	DMF (10)	1 h	**9e**	CHO	77[d,e]
6	**8**	$B(Oi\text{-}Pr)_3$ (4)	2 h	**9f**		66[f]
7	**11**	Me_3SiCl (2.5)	1 h	**12a**	$SiMe_3$	96[g] (64)[h]
8	**11**	Bu_3SnCl (2.5)	1 h	**12b**	$SnBu_3$	90[g] (70)[h]
9	**11**	ICH_2CH_2I (2.5)	1 h	**12c**	I	89[g] (64)[h]
10	**11**	C_2Cl_6 (2.5)	1 h	**12d**	Cl	85[g]
11	**11**	PhSSPh (2.5)	1 h	**12e**	SPh	95[g]
12	**11**	MeI (2.5)	1 h	**12f**	Me	92[g] (78)[h]
13	**11**	PhCHO (2.5)	1 h	**12g**	CH(OH)Ph	88[g] (74)[h]
14	**11**	Ph_2CO (2.5)	1 h	**12h**	$C(OH)Ph_2$	94[g] (67)[h]
15	**13**	Me_3SiCl (2.5)	1 h	**14a**	$SiMe_3$	97[g]
16	**13**	C_2Cl_6 (2.5)	1 h	**14b**	Cl	94[g]
17	**13**	MeSSMe (2.5)	1 h	**14c**	SMe	93[g]

[a] 2.5 equiv of allyl bromide, 1 h: 63%; see ref 9. [b] 2.5 equiv of benzyl bromide, 2 h: 75%; see ref 9. [c] 2.5 equiv of acid chloride, 2 h: 48%. [d] 11% of 3,4-dihydro-4-hydroxy-3-isopropyl-8-phenylbenzo[*e*]-[1,3]-oxazin-2-one (**10**) was also isolated. [e] 2.5 equiv of DMF: 35% of **9e** and 31% of **10** were isolated. [f] After re-esterification with pinacol. [g] TBDMSOTf and *s*-BuLi/TMEDA were used. [h] TMSOTf and *n*-BuLi/TMEDA were used.

SCHEME 4. Directed *ortho*-Lithiation of *O*-3-Biphenylyl Carbamates 11 and 13



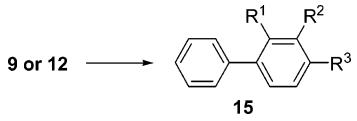
11 R^1, R^2 = H **12**
13 R^1 = OMe, R^2 = Me **14**

philes, the carboxamide, which may be formed by competing anionic Fries rearrangement, was not detected; such products were observed only at elevated temperatures.[9]

3-Hydroxybiphenyl (**11**, H for *CbH*) was prepared by Suzuki-Miyaura coupling of 3-bromophenol with phenylboronic acid,[16] and converted into the urethane **11** with isopropyl isocyanate in 96% yield. Application of the standard sequence (TMSOTf and *n*-BuLi/TMEDA) in diethyl ether provided, after trapping with different electrophiles, the 4-substituted products **12** (Scheme 4, Table 1, entries 7−14). Although no 2-substituted regioisomers were isolated, the yields (64−78%) were unusually low. Since 3-hydroxybiphenyl was found along with recovered starting material **11**, we suspected that, to some extent, attack of *n*-BuLi at the carbamoyl group was a competitive reaction. Indeed, after having exchanged TMSOTf for the bulkier TBDMSOTf and *n*-BuLi for *s*-BuLi, the usual high yields of **12** (85−96%) were achieved.

Equally smoothly proceeded the 4-lithio-deprotonation of the 2′,4′,6′-trisubstituted *O*-3-biphenylyl carbamate **13** by application of the TBDMS method (Table 1, entries 15−17).[17] From these results, we conclude that the 4-H in 3-hydroxybiphenyls is much more readily removed than the 2-H, presumably due to steric shielding and that

TABLE 2. Deprotection of *O*-Isopropylcarbamoyl-Substituted Hydroxybiaryls 9 and 12[a]



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entry	substrate	method	product	R^1	R^2	R^3	yield (%)
1	**9b**	A	**15a**[b]	OH	CH_2Ph	H	98
2	**9d**	B	**15b**	OH	CO_2Me	H	96
3	**9e**	C	**15c**[b]	OH	CHO	H	89[c]
4	**12a**	D	**15d**	H	OH	$SiMe_3$	98
5	**12c**	D	**15e**	H	OH	I	99
6	**12d**	C	**15f**	H	OH	Cl	98
7	**12e**	C	**15g**	H	OH	SPh	97
8	**12f**	C	**15h**[b]	H	OH	Me	99

[a] Conditions A: cyclohexylamine (10 equiv), THF, reflux, 6 h. Conditions B: Bu_4NF (1.5 equiv), THF, rt, 2 h. Conditions C: 2 M NaOH (4 equiv), EtOH, rt, 2 h. Conditions D: K_2CO_3 (10 equiv), EtOH, rt, 12 h. [b] Known compounds, see: refs 18 (for **15a**), 5b and 19 (for **15c**), and 20 (for **15h**). [c] Crude **9e** was used, yield based on **8**.

the other aryl substituent does not play a contributing DMG role.

As we have shown previously,[9] cleavage of the *N*-isopropylcarbamates to form the corresponding phenols is a very facile process under basic conditions (Scheme 2, Table 2). Surprisingly, the silicophilic tetrabutylammonium fluoride is a suitable reagent for decarbamoylation, leaving the methoxycarbonyl group in ester **9d** untouched.

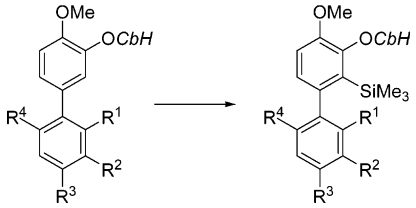
(16) Bumagin, N. A.; Bykov, V. V. *J. Gen. Chem. USSR* **1996**, *66*, 1925−1938.

(17) Carbamate **13** was prepared via Suzuki-Miyaura coupling of 1-bromo-3-isopropoxybenzene with (2-methoxy-2,4-dimethylphenyl)-boronic acid pinacol ester (95%) and subsequent *O*-deisopropylation with $AlCl_3$ (94%) and treatment of the resulting phenol with isopropyl isocyanate (95%). The exact procedure will be published elsewhere, see ref 22.

(18) Factor, A.; Finkbeiner, H.; Jerussi, R. A.; White, D. M. *J. Org. Chem.* **1970**, *35*, 57−62.

(19) (a) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502−12508. (b) Antonisse, M. M. G.; Snellink-Ruël, B. H. M.; Ion, A. C.; Engbersen, J. F. J.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1211−1218.

TABLE 3. C_2-Lithiation and Silylation of *O*-4-Methoxy-3-biphenylyl *N*-Isopropylcarbamates[a]



entry	substrate	R^1	R^2	R^3	R^4	silane	yield (%)
1[b]	**16**	H	H	H	H	**17**	80
2	**18**	OMe	H	Me	Me	**19**	90
3	**20**	OMe	Me	H	*i*-Pr	**21**	85
4	**22**	OMe	H	*t*-Bu	*t*-Bu	**23**	91

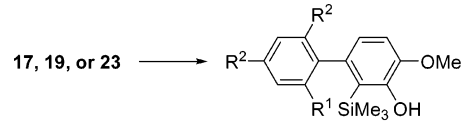
[a] Conditions: (i) TBDMSOTf, TMEDA, Et_2O; (ii) *s*-BuLi/TMEDA (4.0 equiv), −60 °C, 4 h; (iii) TMSCl. [b] Reaction time: 2 h.

***O*-4-Methoxy-3-biphenylyl *N*-Isopropylcarbamates.** To achieve 2-deprotonation of *O*-3-biphenylyl carbamates, blocking of the 4-position is necessary. Synthesis of 3-hydroxy-4-methoxybiphenyl (**16**, H for *CbH*) was accomplished in 81−90% yield by *ortho*-deprotonation of commercially available 4-methoxybiphenyl by means of *s*-BuLi/TMEDA, boronation with trimethyl borate, followed by oxidative workup with H_2O_2.[21] The carbamate **16** was then prepared in 96% yield by the usual treatment with isopropyl isocyanate. The higher substituted biphenylols, corresponding to carbamates **18** (95%), **20** (85%), and **22** (96%), were prepared by carefully optimized Suzuki-Miyaura protocols.[22] By applying the standard method (TMSOTf and 2 equiv of *s*-BuLi/TMEDA, Et_2O, −78 °C, 1 h; EX = Me_3SiCl), none or only trace amounts of the expected silanes **17**, **19**, **21**, or **23** (Table 3) were detected, indicating low reactivity of these substrates.

However, by applying TBDMSOTf as the *N*-silylating reagent, *s*-BuLi/TMEDA in large excess (4.0 equiv), and higher reaction temperatures (−60 °C), the resulting 2-silylated biphenyls were isolated in good yields (80−91%). The urethanes **17**, **19**, and **23** were cleaved by aqueous NaOH in ethanol to give the free phenols **24a**−**c** in nearly quantitative yields (Table 4).

1,1′-Binaphthyl-2,2′-diyl Dicarbamates. 3,3′-Disubstituted 2,2′-dihydroxy-1,1′-binaphthyls are frequently used as chiral ligands in enantioselective catalysis.[23] The possible access, starting from BINOL (**25**), via dideprotonation of the bis(*N*,*N*-diethyl *O*-carbamate), has already been demonstrated by Snieckus[24] and their deprotection to the corresponding BINOL derivatives was described for the 3,3′-dimethylated product (10 equiv of MeLi, Et_2O, rt). In the present work, the dicarbamate (*R*)-**26** was deprotonated after conversion into the *N*,*N*′-bis(trimethylsilyl)diurethane under standard conditions and then excess trimethylsilyl chloride was added to form (*R*)-**27** in essentially quantitative yield (Scheme 5). Carbamate cleavage using aqueous NaOH gave the bis-silylated BINOL derivative (*R*)-**28**[25] in 99% yield. As expected from lithiation-electrophile quench reactions of the MOM-BINOL series,[24a] all three steps proceeded without racemization of the chiral axis.[26] The same sequence, carbamoylation (93%), bis-silylation (97%), and deprotection (99%), was performed on racemic material to furnish *rac*-**28** with comparable high yield. It is quite likely that, in view of the mild conditions, other electrophiles may also be introduced into (*R*)- or (*S*)-**25** with similar efficiency without racemization.

TABLE 4. Deprotection of Carbamates 17, 19 and 23[a]



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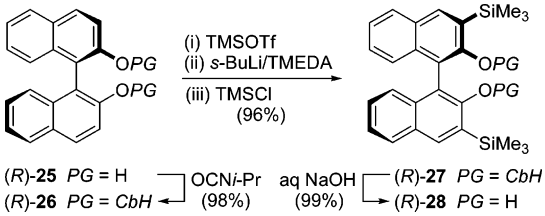
entry	substrate	R^1	R^2	product	yield (%)
1	**17**	H	H	**24a**	97
2	**19**	OMe	Me	**24b**	96
3	**23**	OMe	*t*-Bu	**24c**	98

[a] Conditions: 2 M NaOH (4 equiv), EtOH, rt, 2 h.

SCHEME 5. Bis-silylation of BINOL by Directed *ortho*-Lithiation



Pd-catalyzed Cross-coupling Reactions of *O*-Haloaryl *N*-Isopropylcarbamates. The combination of directed *ortho*-lithiation and cross-coupling reactions provides a useful synthetic tool for introduction of further aryl, vinyl, or alkynyl substituents.[27] The *ortho*-metalated *N*-isopropylurethanes produced by the method described above are suitable substrates for Pd-catalyzed coupling reactions. For instance, the intermediate lithium compound **29** (Scheme 6), after addition of $ZnCl_2$, underwent smooth Negishi coupling[28] with iodobenzene to form *m*-terphenyl-2′-yl *N*-isopropylcarbamate (**30**). The same compound is accessible by Stille coupling[29] of stannane **9g**.[9] Furthermore, *o*-iodoaryl carbamates, as exemplified

(20) Wessely, F.; Holzer, L.; Vilcsek, H. *Monatsh. Chem.* **1952**, *83*, 1253−1273.

(21) (a) Ainley, A. D.; Challenger, F. *J. Chem. Soc.* **1930**, 2171−2180. For illustration of the boronation-oxidation of aryllithiums to introduce an OH^+ synthon, see: (b) Brandsma, L. In *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed.; Hanack, M., Ed.; Thieme: Stuttgart, Germany, 1993; Vol. E19d, pp 369−447. See also ref 1a.

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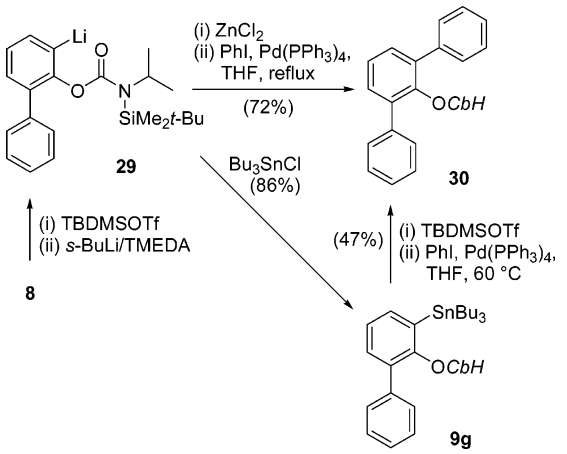
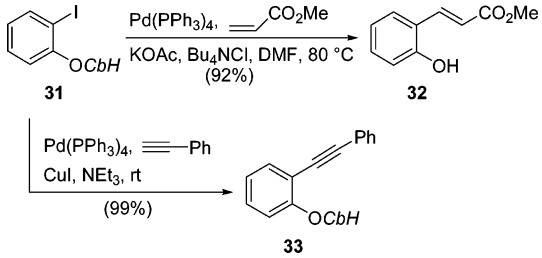
SCHEME 6. Negishi and Stille Couplings of Carbamate 8



SCHEME 7. Heck and Sonogashira Couplings of Carbamate 31



for the parent compound **31** (Scheme 7), behave well in Heck[30] and Sonogashira[31] reactions.

Conclusions

Directed *ortho*-lithiation of simple *O*-2-biaryl *N*-isopropylcarbamate **8** proceeds smoothly after in situ *N*-silylation by means of TMSOTf with *n*- or *s*-BuLi/TMEDA at −78 °C to give **9** in good to excellent yields. *O*-3-Biaryl carbamates **11** and **13** are metalated with complete regioselectivity at the 4-position to afford products **12** and **14**. For the removal of the 2-proton in biaryl substrates **16**, **18**, **20**, or **22**, higher temperatures (−60 °C) and excess *s*-BuLi are required; here *N*-protection with the more robust TBDMS-group is essential to obtain good yields (∼90%) of substituted products **17**, **19**, **21**, and **23**. A wide range of electrophiles may be introduced by these methods. *N*-Desilylation already occurs during aqueous workup. Liberation of the free phenols may be accomplished quantitatively under mild basic conditions. Even highly substituted biphenylols and binaphthols may be further readily functionalized.

Experimental Section

All reactions were run in flame-dried glassware under an atmosphere of dry argon using syringe-septum cap techniques. Et_2O was dried extensively over sodium/benzophenone ketyl and then distilled prior to use. Pentane and TMEDA were refluxed and distilled from CaH_2 before use. The commercial solution of *s*-BuLi (1.3 M in cyclohexane/hexane, 92:8) was filtered using Celite and titrated against diphenylacetic acid; *n*-BuLi (1.6 M in hexane), TMSOTf, and TBDMSOTf were used without further purification. NMR spectra were recorded in $CDCl_3$ with TMS as the internal reference. Melting points are uncorrected. For TLC, Merck precoated plates (silica gel 60 F_{254}) were used. Flash column chromatography (FCC) was performed on Merck silica gel 60 (0.040−0.063 mm) using Et_2O/PET mixtures; PET = light petroleum ether, bp 36−46 °C.

Directed *ortho*-Lithiation and Substitution of Carbamate 8. General Procedure A: *O*-3-Allylbiphenyl-2-yl *N*-Isopropylcarbamate (9a).[9] A solution of carbamate **8** (0.255 g, 1.0 mmol) in 10 mL of Et_2O at room temperature under Ar was sequentially treated with TMEDA (0.128 g, 1.1 mmol) and dropwise with TMSOTf (1.05 mmol, 1.1−1.4 M solution in pentane), and the reaction mixture was stirred for 30 min. The resulting mixture was cooled to −78 °C and TMEDA (0.233 g, 2.0 mmol) and *s*-BuLi (2.0 mmol) were added consecutively. The yellow solution was stirred for 1 h and treated with allyl bromide (0.87 mL, 10.0 mmol). After an additional stirring for 6 h, 0.1 mL of MeOH and 5 mL of 2 M HCl were added, and the mixture was allowed to warm to room temperature. The aqueous phase was extracted with Et_2O and the combined organic extracts were washed with saturated $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated in vacuo. The crude residue was purified by FCC (Et_2O/PET, 1:10 to 1:5) to yield **9a** (0.252 g, 0.853 mmol, 85%) as a colorless solid.

***O*-3-Benzylbiphenyl-2-yl *N*-Isopropylcarbamate (9b).**[9] According to General Procedure A, reaction of **8** (0.255 g, 1.0 mmol) with TMEDA, TMSOTf, *s*-BuLi/TMEDA, and benzyl bromide (1.19 mL, 10.0 mmol, 6 h), and purification of the crude product (FCC, Et_2O/PET, 1:10 to 1:5) gave **9b** (0.277 g, 0.802 mmol, 80%) as a colorless solid.

***O*-3-(2,2-Dimethylpropionyl)biphenyl-2-yl *N*-Isopropylcarbamate (9c).** Following the General Procedure A, reaction of **8** (0.255 g, 1.0 mmol) with TMEDA, TMSOTf, *s*-BuLi/TMEDA, and pivaloyl chloride (0.74 mL, 6.0 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 1:2) gave **9c** (0.305 g, 0.899 mmol, 90%) as a colorless solid: mp 118−119 °C; IR (KBr) ν 3333, 3054, 2972, 2931, 1722, 1699, 1533, 1202, 1171, 1029, 974, 940, 783, 763, 706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (d, J = 6.5 Hz, 6H), 1.28 (s, 9H), 3.57 (m, 1H), 4.61 (br d, 1H, NH), 7.19−7.45 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5 (CH_3), 27.4 (CH_3), 43.2 (CH), 44.9 (C), 125.0 (CH), 125.3 (CH), 127.4 (CH), 128.2 (CH), 128.9 (CH), 131.4 (CH), 135.4 (C), 136.8 (C), 137.6 (C), 143.9 (C), 152.3 (C), 211.0 (C) ppm; TLC R_f = 0.33 (Et_2O/PET, 1:2). Anal. Calcd for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.21; H, 7.46; N, 4.10.

2-(Isopropylcarbamoyloxy)biphenyl-3-carboxylic Acid Methyl Ester (9d). Following the General Procedure A, reaction of **8** (0.255 g, 1.0 mmol) with TMEDA, TMSOTf, *s*-BuLi/TMEDA, and methyl chloroformate (0.92 mL, 10.0 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 1:2) afforded **9d** (0.256 g, 0.817 mmol, 82%) as a colorless solid: mp 107−108 °C; IR (KBr) ν 3397, 3058, 2973, 1740, 1531, 1429, 1309, 1286, 1206, 1022, 935, 788, 749, 707

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cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (d, J = 6.4 Hz, 6H), 3.76 (m, 1H), 3.87 (s, 3H), 4.77 (br s, 1H, NH), 7.21−7.46 (m, 6H), 7.53 (dd, J = 7.6, 1.7 Hz, 1H), 7.96 (dd, J = 7.8, 1.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7 (CH_3), 43.4 (CH), 52.1 (CH_3), 124.9 (C), 125.4 (CH), 127.5 (CH), 128.1 (CH), 129.1 (CH), 130.7 (CH), 134.9 (CH), 137.2 (C), 137.3 (C); 147.6 (C), 153.3 (C), 165.5 (C) ppm; TLC R_f = 0.38 (Et_2O/PET, 1:2). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 69.34; H, 6.25; N, 4.34.

***O*-3-Formylbiphenyl-2-yl *N*-Isopropylcarbamate (9e).** According to General Procedure A, reaction of **8** (0.255 g, 1.0 mmol) with TMEDA, TMSOTf, *s*-BuLi/ TMEDA, and DMF (0.77 mL, 10.0 mmol, 1 h), and purification of the crude residue (FCC, Et_2O/PET, 1:5 to 1:1) gave oxazinone **10** (0.032 g, 0.113 mmol, 11%) as a colorless solid and aldehyde **9e** (0.217 g, 0.766 mmol, 77%) as a colorless solid: mp 118−119 °C; IR (KBr) ν 3334, 3067, 2973, 2877, 1716, 1686, 1531, 1254, 1209, 1082, 1023, 791, 761, 704 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 6H), 3.70 (m, 1H), 4.86 (br d, 1H, NH), 7.32−7.45 (m, 6H), 7.60 (dd, J = 7.5, 1.8 Hz, 1H), 7.88 (dd, J = 7.6, 1.8 Hz, 1H), 10.20 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6 (CH_3), 43.5 (CH), 126.1 (CH), 127.8 (CH), 128.3 (CH), 128.7 (CH), 129.0 (CH), 129.9 (C), 136.5 (CH), 136.6 (C), 137.1 (C), 149.7 (C), 153.0 (C), 188.9 (C) ppm; TLC R_f = 0.19 (Et_2O/PET, 1:5). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.09; H, 6.15; N, 4.92.

3,4-Dihydro-4-hydroxy-3-isopropyl-8-phenylbenzo[*e*]-[1,3]-oxazin-2-one (10): mp 160−161 °C; IR (KBr) ν 3323, 3027, 2986, 1698, 1432, 1216, 798, 756, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40/1.45 (d, J = 6.8 Hz, 6H), 2.00 (s, 1H, OH), 4.32 (septet, J = 6.8 Hz, 1H), 5.86 (s, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.32−7.38 (m, 2H), 7.38−7.46 (m, 3H), 7.52−7.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9/21.3 (CH_3), 50.3 (CH), 76.5 (CH), 121.6 (C), 124.4 (CH), 125.9 (CH), 127.7 (CH), 128.3 (CH), 129.3 (CH), 129.5 (C), 131.3 (CH), 135.9 (C), 145.7 (C), 149.5 (C) ppm; TLC R_f = 0.09 (Et_2O/PET, 1:2). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.01; H, 5.98; N, 4.78.

***O*-3-(4,4,5,5-Tetramethyl-[1,3,2]-dioxaborolan-2-yl)biphenyl-2-yl *N*-Isopropylcarbamate (9f).** Following the General Procedure A, reaction of **8** (0.255 g, 1.0 mmol) with TMEDA, TMSOTf, *s*-BuLi/TMEDA, and triisopropyl borate (0.92 mL, 4.0 mmol, 2 h) yielded the crude product, which was stirred with pinacol (0.591 g, 5.0 mmol) and $MgSO_4$ (0.5 g) in 5 mL of CH_2Cl_2 for 18 h. The reaction mixture was subjected to filtration, the filtrate was concentrated and the residue was purified by FCC (Et_2O/PET, 1:5 to 1:2) to afford **9f** (0.251 g, 0.658 mmol, 66%) as a colorless solid: mp 130−131 °C; IR (KBr) ν 3296, 3056, 2984, 1705, 1543, 1365, 1210, 1135, 862, 793, 762, 707 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09 (d, J = 6.5 Hz, 6H), 1.32 (s, 12H), 3.77 (m, 1H), 4.65 (br s, 1H, NH), 7.24−7.47 (m, 7H), 7.77 (dd, J = 7.3, 1.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0 (CH_3), 24.8 (CH_3), 43.1 (CH), 83.6 (C), 125.3 (CH), 127.0 (CH), 128.0 (CH), 129.1 (CH), 133.6 (CH), 135.5 (CH), 135.4 (C), 138.2 (C), 137.9 (C), 152.2 (C), 154.1 (C) ppm; TLC R_f = 0.23 (Et_2O/PET, 1:2). Anal. Calcd for $C_{22}H_{28}BNO_4$: C, 69.30; H, 7.40; N, 3.67. Found: C, 69.39; H, 7.38; N, 3.60.

Directed *ortho*-Lithiation and Substitution of Carbamates 11, 13, 16, 18, 20, and 22. General Procedure B: *O*-4-(Trimethylsilyl)biphenyl-3-yl *N*-Isopropylcarbamate (12a). The General Procedure A described above was used, but the protecting reagent TMSOTf was exchanged for TBDMSOTf. Reaction of carbamate **11** (0.255 g, 1.0 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and trimethylsilyl chloride (0.32 mL, 2.5 mmol, 1 h), and purification of the crude product by FCC (Et_2O/PET, 1:5 to 1:2) gave **12a** (0.315 g, 0.962 mmol, 96%) as a colorless solid: mp 137.5−138.5 °C; IR (KBr) ν 3332, 3063, 2963, 1712, 1607, 1526, 1244, 1086, 886, 837, 751, 704 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.31 (s, 9H), 1.25 (d, J = 6.5 Hz, 6H), 3.94 (m, 1H), 4.80 (br s, 1H, NH), 7.29−7.46 (m, 5H), 7.51 (d, J = 7.7 Hz, 1H), 7.56−7.62 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.8 (CH_3), 23.0 (CH_3), 43.5 (CH), 121.0 (CH), 123.8 (CH), 127.2 (CH), 127.5 (CH), 128.7 (CH), 130.3 (C), 135.2 (CH), 140.3 (C), 143.6 (C), 153.8 (C), 156.1 (C) ppm; TLC R_f = 0.35 (Et_2O/PET, 1:5). Anal. Calcd for $C_{19}H_{25}NO_2Si$: C, 69.68; H, 7.69; N, 4.28. Found: C, 69.45; H, 7.64; N, 4.11.

***O*-4-(Tributylstannyl)biphenyl-3-yl *N*-Isopropylcarbamate (12b).** According to General Procedure B, reaction of **11** (0.128 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/ TMEDA, and tributyltin chloride (0.41 mL, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:20 to 1:10) afforded **12b** (0.246 g, 0.452 mmol, 90%) as a colorless solid: mp 76−77 °C; IR (KBr) ν 3316, 3061, 2959, 1705, 1594, 1526, 1467, 1240, 1065, 1167, 881, 827, 761, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.3 Hz, 9H), 1.04−1.14 (m, 6H), 1.25 (d, J = 6.5 Hz, 6H), 1.28−1.41 (m, 6H), 1.49−1.62 (m, 6H), 3.93 (m, 1H), 4.70 (br s, 1H, NH), 7.28−7.35 (m, 1H), 7.36−7.44 (m, 4H), 7.47 (d, 1H), 7.56−7.62 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.9 (CH_2), 13.6 (CH_3), 23.0 (CH_3), 27.4 (CH_2), 29.1 (CH_2), 43.4 (CH), 120.2 (CH), 123.9 (CH), 127.2 (CH), 127.4 (CH), 128.6 (CH), 132.4 (C), 137.2 (CH), 140.6 (C), 142.7 (C), 153.8 (C), 156.6 (C) ppm; TLC R_f = 0.43 (Et_2O/PET, 1:5). Anal. Calcd for $C_{28}H_{43}NO_2Sn$: C, 61.78; H, 7.96; N, 2.57. Found: C, 61.83; H, 7.79; N, 2.47.

***O*-4-Iodobiphenyl-3-yl *N*-Isopropylcarbamate (12c).** According to General Procedure B, reaction of **11** (0.255 g, 1.0 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and 1,2-diiodoethane (0.705 g in 3 mL of Et_2O, 2.5 mmol, 1 h), and purification of the residue (FCC, Et_2O/PET, 1:5 to 1:2) yielded **12c** (0.328 g, 0.887 mmol, 89%) as a colorless solid: mp 116−117 °C; IR (KBr) ν 3314, 3049, 2974, 1710, 1535, 1254, 1021, 1057, 890, 819, 760, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (d, J = 6.5 Hz, 6H), 3.93 (m, 1H), 5.01 (br s, 1H, NH), 7.16 (dd, J = 8.2, 2.1 Hz, 1H), 7.31−7.46 (m, 4H), 7.51−7.57 (m, 2H), 7.83 (d, J = 8.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.9 (CH_3), 43.7 (CH), 89.4 (C), 122.0 (CH), 125.8 (CH), 127.0 (CH), 127.9 (CH), 128.8 (CH), 129.8 (CH), 139.3 (C), 142.9 (C), 151.5 (C), 152.6 (C) ppm; TLC R_f = 0.22 (Et_2O/PET, 1:5). Anal. Calcd for $C_{16}H_{16}INO_2$: C, 50.41; H, 4.23; N, 3.67. Found: C, 50.72; H, 4.09; N, 3.54.

***O*-4-Chlorobiphenyl-3-yl *N*-Isopropylcarbamate (12d).** According to General Procedure B, reaction of **11** (0.255 g, 1.0 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and hexachloroethane (0.710 g in 3 mL of Et_2O, 3.0 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:10 to 1:5) afforded **12d** (0.246 g, 0.849 mmol, 85%) as a colorless solid: mp 128−129 °C; IR (KBr) ν 3326, 3033, 2981, 1710, 1528, 1473, 1250, 1036, 1073, 886, 822, 764, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (d, J = 6.5 Hz, 6H), 3.91 (m, 1H), 5.01 (br d, 1H, NH), 7.30−7.48 (m, 6H), 7.51−7.56 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8 (CH_3), 43.7 (CH), 122.7 (CH), 125.0 (CH), 126.3 (C), 127.0 (CH), 127.8 (CH), 128.8 (CH), 130.3 (CH), 139.3 (C), 141.2 (C), 147.4 (C), 152.6 (C) ppm; TLC R_f = 0.21 (Et_2O/PET, 1:5). Anal. Calcd for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.83. Found: C, 66.62; H, 5.84; N, 4.71.

***O*-4-(Phenylsulfanyl)biphenyl-3-yl *N*-Isopropylcarbamate (12e).** According to General Procedure B, reaction of **11** (0.255 g, 1.0 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/ TMEDA, and diphenyl disulfide (0.546 g in 3 mL of Et_2O, 2.5 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:10 to 1:5) gave **12e** (0.346 g, 0.952 mmol, 95%) as a colorless solid: mp 99−100 °C; IR (KBr) ν 3355, 3066, 2972, 1709, 1526, 1471, 1074, 941, 885, 823, 762, 690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J = 6.5 Hz, 6H), 3.85 (m, 1H), 4.84 (br d, 1H, NH), 7.20−7.46 (m, 11H), 7.53−7.59 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8 (CH_3), 43.5 (CH), 120.4 (C), 122.0 (CH), 124.7 (CH), 127.0 (CH), 127.1 (CH), 127.7 (CH), 128.8 (CH), 129.2 (CH), 131.1 (CH), 132.8 (CH), 134.9 (C), 139.6 (C), 141.7 (C), 150.1 (C), 152.9 (C) ppm; TLC R_f = 0.15 (Et_2O/PET, 1:5). Anal. Calcd for $C_{22}H_{21}NO_2S$: C, 72.70; H, 5.82; N, 3.85. Found: C, 72.32; H, 5.87; N, 3.68.

***O*-4-Methylbiphenyl-3-yl *N*-Isopropylcarbamate (12f).** According to General Procedure B, reaction of **11** (0.128 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and methyl iodide (0.08 mL, 1.25 mmol, 1 h), and purification of the crude residue (FCC, Et_2O/PET, 1:5 to 1:2) yielded **12f** (0.124 g, 0.460 mmol, 92%) as a colorless solid: mp 103−104 °C; IR (KBr) ν 3324, 3060, 2976, 1703, 1532, 1249, 1045, 1126, 880, 828, 761, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, J = 6.5 Hz, 6H), 2.25 (s, 3H), 3.91 (m, 1H), 4.92 (br s, 1H, NH), 7.35−7.44 (m, 6H), 7.53−7.59 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8 (CH_3), 22.9 (CH_3), 43.5 (CH), 120.9 (CH), 124.1 (CH), 127.0 (CH), 127.2 (CH), 128.6 (CH), 129.5 (C), 131.2 (CH), 140.2 (C), 140.3 (C), 149.8 (C), 153.5 (C) ppm; TLC R_f = 0.35 (Et_2O/PET, 1:2). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.54; H, 6.93; N, 5.11.

***O*-4-(Hydroxyphenylmethyl)biphenyl-3-yl *N*-Isopropylcarbamate (12g).** According to General Procedure B, reaction of **11** (0.128 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and benzaldehyde (0.13 mL, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:2 to 2:1) gave **12g** (0.159 g, 0.440 mmol, 88%) as a colorless solid: mp 118−119 °C; IR (KBr) ν 3568, 3335, 3064, 2971, 1704, 1524, 1241, 1018, 1124, 879, 837, 763, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19/1.20 (d, J = 6.5 Hz, 6H), 3.09 (br s, 1H, OH), 3.83 (m, 1H), 4.90 (br s, 1H, NH), 6.01 (s, 1H), 7.21−7.45 (m, 11H), 7.52−7.58 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8 (CH_3), 43.6 (CH), 70.5 (CH), 121.3 (CH), 124.7 (CH), 126.4 (CH), 127.1 (CH), 128.3 (CH), 128.7 (CH), 127.3 (CH), 127.6 (CH), 129.1 (CH), 135.4 (C), 139.9 (C), 142.1 (C), 142.7 (C), 148.7 (C), 154.0 (C) ppm; TLC R_f = 0.09 (Et_2O/PET, 1:2). Anal. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.17; H, 6.45; N, 3.75.

***O*-4-(Hydroxydiphenylmethyl)biphenyl-3-yl *N*-Isopropylcarbamate (12h).** According to General Procedure B, reaction of **11** (0.128 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and benzophenone (0.228 g in 2 mL of Et_2O, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 1:2) gave **12h** (0.205 g, 0.469 mmol, 94%) as a colorless solid: mp 100−102 °C (dec); IR (KBr) ν 3418, 3335, 3061, 2970, 1715, 1532, 1019, 1120, 886, 833, 763, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, J = 6.5 Hz, 6H), 3.56 (m, 1H, CH), 4.19 (br d, 1H, NH), 4.29 (br s, 1H, OH), 6.81 (d, J = 8.2 Hz, 1H), 7.23−7.51 (m, 15H), 7.55−7.60 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5 (CH_3), 43.4 (CH), 80.9 (C), 123.0 (CH), 123.3 (CH), 127.1 (CH), 127.3 (CH), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.7 (CH), 129.1 (CH), 139.7 (C), 141.4 (C), 142.1 (C), 146.1 (C), 149.2 (C), 152.3 (C) ppm; TLC R_f = 0.26 (Et_2O/PET, 1:2). Anal. Calcd for $C_{29}H_{27}NO_3$: C, 79.61; H, 6.22; N, 3.20. Found: C, 79.48; H, 6.25; N, 2.94.

***O*-2′-Methoxy-4′,6′-dimethyl-4-(trimethylsilyl)biphenyl-3-yl *N*-Isopropylcarbamate (14a).** Following the General Procedure B, reaction of **13** (0.157 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and trimethylsilyl chloride (0.16 mL, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 1:2) gave **14a** (0.187 g, 0.485 mmol, 97%) as a colorless solid: mp 118−119 °C; IR (KBr) ν 3341, 3063, 2976, 1705, 1517, 1465, 1237, 1170, 1084, 1023, 842, 751, 719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.31 (s, 9H), 1.21 (d, J = 6.5 Hz, 6H), 2.09 (s, 3H), 2.34 (s, 3H), 3.68 (s, 3H), 3.89 (m, 1H), 4.74 (br d, 1H, NH), 6.62 (s, 1H), 6.70 (s, 1H), 6.97 (d, J = 1.3 Hz, 1H), 7.04 (dd, J = 7.5, 1.3 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.8 (CH_3), 20.4 (CH_3), 21.5 (CH_3), 22.9 (CH_3), 43.4 (CH), 55.8 (CH_3), 109.4 (CH), 123.2 (CH), 124.1 (CH), 126.9 (CH), 127.2 (C), 129.3 (C), 134.2 (CH), 137.6 (C), 137.9 (C), 140.0 (C), 153.8 (C), 155.5 (C), 156.8 (C) ppm; TLC R_f = 0.47 (Et_2O/PET, 1:2). Anal. Calcd for $C_{22}H_{31}NO_3Si$: C, 68.53; H, 8.10; N, 3.63. Found: C, 68.42; H, 7.95; N, 3.41.

***O*-4-Chloro-2′-methoxy-4′,6′-dimethylbiphenyl-3-yl *N*-Isopropylcarbamate (14b).** Following the General Procedure B, reaction of **13** (0.157 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and hexachloroethane (0.296 g in 2 mL of Et_2O, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 1:1) gave **14b** (0.163 g, 0.469 mmol, 94%) as a colorless solid: mp 108−109 °C; IR (KBr) ν 3336, 3065, 2977, 1729, 1536, 1466, 1240, 1200, 1094, 1022, 937, 835, 753, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, J = 6.5 Hz, 6H), 2.06 (s, 3H), 2.34 (s, 3H), 3.67 (s, 3H), 3.89 (m, 1H), 4.99 (br d, 1H, NH), 6.61 (s, 1H), 6.70 (s, 1H), 6.99 (dd, J = 8.2, 1.8 Hz, 1H), 7.07 (d, J = 1.8 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3 (CH_3), 21.5 (CH_3), 22.8 (CH_3), 43.6 (CH), 55.6 (CH_3), 109.3 (CH), 123.2 (CH), 126.1 (CH), 126.2 (CH), 128.5 (C), 128.5 (CH), 129.5 (CH), 137.3 (C), 137.5 (C), 138.3 (C), 146.7 (C), 152.7 (C), 156.7 (C) ppm; TLC R_f = 0.41 (Et_2O/PET, 1:2). Anal. Calcd for $C_{19}H_{22}ClNO_3$: C, 65.61; H, 6.38; N, 4.03. Found: C, 65.92; H, 6.15; N, 3.70.

***O*-2′-Methoxy-4′,6′-dimethyl-4-(methylsulfanyl)biphenyl-3-yl *N*-Isopropylcarbamate (14c).** Following the General Procedure B, reaction of **13** (0.157 g, 0.5 mmol) with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA, and dimethyl disulfide (0.12 mL, 1.25 mmol, 1 h), and purification of the crude product (FCC, Et_2O/PET, 1:5 to 2:1) gave **14a** (0.167 g, 0.465 mmol, 93%) as a colorless solid: mp 86−87 °C; IR (KBr) ν 3325, 3052, 2972, 1732, 1516, 1466, 1316, 1235, 1076, 1019, 828, 756, 713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (d, J = 6.5 Hz, 6H), 2.08 (s, 3H), 2.34 (s, 3H), 2.46 (s, 3H), 3.68 (s, 3H), 3.89 (m, 1H), 4.94 (br s, 1H, NH), 6.61 (s, 1H), 6.70 (s, 1H), 6.99 (d, J = 1.7 Hz, 1H), 7.04 (dd, J = 8.0, 1.7 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2 (CH_3), 20.4 (CH_3), 21.5 (CH_3), 22.9 (CH_3), 43.5 (CH), 55.7 (CH_3), 109.4 (CH), 123.2 (CH), 124.8 (CH), 126.4 (CH), 126.8 (C), 128.0 (CH), 129.6 (C), 135.7 (C), 137.6 (C), 138.0 (C), 147.9 (C), 153.1 (C), 156.9 (C) ppm; TLC R_f = 0.23 (Et_2O/PET, 1:2). Anal. Calcd for $C_{20}H_{25}NO_3S$: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.53; H, 6.90; N, 3.78.

***O*-4-Methoxy-2-(trimethylsilyl)biphenyl-3-yl *N*-Isopropylcarbamate (17).** Following the General Procedure B, carbamate **16** (0.114 g, 0.4 mmol) was dissolved in 10 mL of Et_2O and treated sequentially with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA (1.6 mmol, −60 °C, 2 h), and trimethylsilyl chloride (0.23 mL, 1.8 mmol, −60 °C, 1 h). Workup and purification of the crude product by FCC (Et_2O/PET, 1:5 to 1:1) afforded silane **17** (0.114 g, 0.319 mmol, 80%) as a colorless solid: mp 141−142 °C; IR (KBr) ν 3365, 3058, 2972, 1734, 1523, 1462, 1392, 1285, 1249, 1160, 1088, 1038, 1022, 868, 847, 819, 766, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.04 (s, 9H), 1.24 (d, J = 6.5 Hz, 6H), 3.85 (s, 3H), 3.93 (m, 1H), 4.88 (br d, 1H, NH), 6.95 (d, J = 8.3 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H), 7.22−7.27 (m, 2H), 7.29−7.34 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.2 (CH_3), 22.9 (CH_3), 43.4 (CH), 56.0 (CH_3), 112.5 (CH), 126.8 (CH), 127.6 (CH), 128.1 (CH), 129.7 (CH), 131.8 (C), 141.7 (C), 144.1 (C), 145.0 (C), 150.3 (C), 153.3 (C) ppm; TLC R_f = 0.20 (Et_2O/PET, 1:2). Anal. Calcd for $C_{20}H_{27}NO_3Si$: C, 67.19; H, 7.61; N, 3.92. Found: C, 67.10; H, 7.53; N, 3.78.

***O*-2′,4-Dimethoxy-4′,6′-dimethyl-2-(trimethylsilyl)biphenyl-3-yl *N*-Isopropylcarbamate (19).** Following the General Procedure B, carbamate **18** (0.103 g, 0.3 mmol) was dissolved in 7 mL of Et_2O and treated sequentially with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA (1.2 mmol, −60 °C, 4 h), and trimethylsilyl chloride (0.17 mL, 1.35 mmol, −60 °C, 1 h). Workup and purification of the crude product by FCC (Et_2O/PET, 1:5 to 1:1) yielded silane **19** (0.112 g, 0.270 mmol, 90%) as a colorless solid: mp 154−155 °C; IR (KBr) ν 3324, 3012, 2966, 1715, 1523, 1467, 1283, 1240, 1161, 1099, 1081, 1024, 938, 866, 841, 759, 727 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.10 (s, 9H), 1.24 (d, J = 6.5 Hz, 6H), 1.93 (s, 3H), 2.43 (s, 3H), 3.65 (s, 3H), 3.84 (s, 3H), 3.91 (m, 1H), 4.82 (br d, 1H, NH), 6.53 (br s, 1H), 6.65 (br s, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.97 (d, J = 8.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.4 (CH_3), 20.4 (CH_3), 21.6 (CH_3), 22.9 (CH_3), 43.4 (CH), 55.2 (CH_3), 55.8 (CH_3), 108.6 (CH), 113.2 (CH), 122.6 (CH), 128.3 (C), 129.3 (C), 132.9 (C), 136.0 (C), 137.6 (C), 138.0 (C), 145.3 (C), 149.9 (C), 153.3 (C), 157.5 (C) ppm; TLC R_f = 0.27 (Et_2O/PET, 1:1).

Anal. Calcd for $C_{23}H_{33}NO_4Si$: C, 66.47; H, 8.00; N, 3.37. Found: C, 66.44; H, 7.81; N, 3.21.

***O*-6′-Isopropyl-2′,4-dimethoxy-3′-methyl-2-(trimethylsilyl)biphenyl-3-yl *N*-Isopropylcarbamate (21).** Following the General Procedure B, carbamate **20** (0.111 g, 0.3 mmol) was dissolved in 5 mL of Et_2O and treated sequentially with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA (1.2 mmol, −60 °C, 4 h), and trimethylsilyl chloride (0.17 mL, 1.35 mmol, −60 °C, 1 h). The crude product was purified by FCC (Et_2O/PET, 1:10 to 1:5) to give silane **21** (0.113 g, 0.255 mmol, 85%) as a colorless solid: mp 155−156 °C; IR (KBr) ν 3353, 3016, 2960, 1715, 1521, 1466, 1286, 1248, 1156, 1048, 936, 869, 839, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.08 (s, 9H), 1.06/1.08 (d, J = 6.5 Hz, 6H), 1.25 (d, J = 6.1 Hz, 6H), 2.25 (s, 3H), 2.75 (septet, 1H), 3.29 (s, 3H), 3.87 (s, 3H), 3.92 (m, 1H), 4.85 (br s, 1H, NH), 6.89−7.03 (m, 3H), 7.12 (d, J = 7.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.3 (CH_3), 16.0 (CH_3), 22.9/23.1 (CH_3), 24.7 (CH_3), 29.3 (CH), 43.4 (CH), 55.8 (CH_3), 59.2 (CH_3), 112.2 (CH), 120.5 (CH), 127.7 (C), 128.8 (CH), 130.1 (CH), 133.4 (C), 135.0 (C), 135.7 (C), 145.1 (C), 146.3 (C), 149.9 (C), 153.2 (C), 156.0 (C) ppm; TLC R_f = 0.34 (Et_2O/PET, 1:1). Anal. Calcd for $C_{25}H_{37}NO_4Si$: C, 67.68; H, 8.41; N, 3.16. Found: C, 67.50; H, 8.28; N, 2.99.

***O*-2′,4′-Di-*tert*-butyl-4,6′-dimethoxy-2-(trimethylsilyl)-biphenyl-3-yl *N*-Isopropylcarbamate (23).** Following the General Procedure B, carbamate **22** (0.128 g, 0.3 mmol) was dissolved in 6 mL of Et_2O and treated sequentially with TMEDA, TBDMSOTf, *s*-BuLi/TMEDA (1.2 mmol, −60 °C, 4 h), and trimethylsilyl chloride (0.17 mL, 1.35 mmol, −60 °C, 1 h). The crude product was purified by FCC (Et_2O/PET, 1:10 to 1:5) to afford silane **23** (0.136 g, 0.272 mmol, 91%) as a colorless solid: mp 177−178 °C; IR (KBr) ν 3444, 2960, 1731, 1462, 1284, 1231, 1156, 1064, 1026, 938, 868, 840, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.12 (s, 9H), 1.15 (s, 9H), 1.35 (s, 9H), 1.23 (d, J = 6.5 Hz, 6H), 3.62 (s, 3H), 3.85 (s, 3H), 3.91 (m, 1H), 4.80 (br d, 1H, NH), 6.72 (d, J = 1.6 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 1.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.2 (CH_3), 22.9 (CH_3), 31.5 (CH_3), 33.0 (CH_3), 35.0 (C), 37.2 (C), 43.4 (CH), 55.4 (CH_3), 55.7 (CH_3), 105.0 (CH), 111.6 (CH), 116.6 (CH), 128.6 (C), 129.2 (CH), 134.4 (C), 137.3 (C), 144.8 (C), 148.2 (C), 149.7 (C), 150.5 (C), 153.3 (C), 157.8 (C) ppm; TLC R_f = 0.30 (Et_2O/PET, 1:1). Anal. Calcd for $C_{29}H_{45}NO_4Si$: C, 69.70; H, 9.08; N, 2.80. Found: C, 69.63; H, 9.01; N, 2.79.

Deprotection of *O*-Isopropylcarbamoyl-Substituted Hydroxybiaryls. Method A: 3-Benzylbiphenyl-2-ol (15a).[18] A solution of carbamate **9b** (0.173 g, 0.5 mmol), DMAP (6 mg, 0.05 mmol), and cyclohexylamine (0.57 mL, 5.0 mmol) in 2 mL of THF was heated at reflux for 6 h. After cooling, 3 mL of 2 M HCl was added and the aqueous layer was extracted with Et_2O. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by FCC (Et_2O/PET, 1:10 to 1:5) to yield phenol **15a** (0.127 g, 0.488 mmol, 98%) as a colorless oil: IR (film) ν 3543, 3060, 3021, 2924, 1599, 1492, 1453, 1431, 1323, 1222, 1078, 760, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.04 (s, 2H), 5.25 (br s, 1H, OH), 6.90 (t, J = 7.5 Hz, 1H), 7.06−7.12 (m, 2H), 7.14−7.31 (m, 5H), 7.32−7.40 (m, 1H), 7.40−7.50 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.3 (CH_2), 120.4 (CH), 126.0 (CH), 127.8 (C), 127.8 (CH), 128.2 (C), 128.3 (CH), 128.4 (CH), 128.9 (CH), 129.2 (CH), 129.3 (CH), 130.3 (CH), 137.3 (C), 140.6 (C), 150.4 (C) ppm; TLC R_f = 0.58 (Et_2O/PET, 1:5). Anal. Calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.49; H, 6.22.

Method B: 2-Hydroxybiphenyl-3-carboxylic Acid Methyl Ester (15b). Tetrabutylammonium fluoride (0.75 mL, 1.0 M in THF, 0.75 mmol) was added at room temperature to a solution of carbamate **9d** (0.157 g, 0.5 mmol) in 5 mL of THF, and stirring was continued for 2 h. The reaction was quenched with 2 mL of saturated NH_4Cl solution, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. Purification of the resulting residue was performed by FCC (Et_2O/PET, 1:20) to give phenol **15b** (0.109 g, 0.478 mmol, 96%) as a colorless oil: IR (film) ν 3088, 2952, 1672, 1612, 1430, 1329, 1286, 1247, 1200, 1149, 971, 835, 758, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.96 (s, 3H), 6.94 (dd, J = 8.0, 7.5 Hz, 1H), 7.34 (m, 1H), 7.39−7.46 (m, 2H), 7.51 (dd, J = 7.5, 1.8 Hz, 1H), 7.55−7.60 (m, 2H), 7.85 (dd, J = 8.0, 1.8 Hz, 1H), 11.27 (s, 1H, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.4 (CH_3), 112.6 (C), 119.0 (CH), 127.4 (CH), 128.1 (CH), 129.2 (CH), 129.3 (CH), 130.5 (C), 136.6 (CH), 137.2 (C), 159.0 (C), 171.0 (C) ppm; TLC R_f = 0.48 (Et_2O/PET, 1:10). Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.78; H, 5.60.

Method C: 4-Chlorobiphenyl-3-ol (15f). To a solution of carbamate **12d** (0.145 g, 0.5 mmol) in 5 mL of EtOH and 1 mL of THF was added at room temperature 2 M NaOH (1.0 mL, 2.0 mmol), and the resulting reaction mixture was stirred for 2 h. Then 3 mL of 2 M HCl and 10 mL of Et_2O were added, the aqueous layer was extracted with Et_2O, and the combined organic phases were washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. FCC (Et_2O/PET, 1:20 to 1:10) of the residue afforded phenol **15f** (0.100 g, 0.489 mmol, 98%) as a colorless oil which solidified on standing to give a colorless solid: mp 51−52 °C; IR (KBr) ν 3251, 3030, 1420, 1310, 1219, 1042, 1068, 897, 817, 866, 764, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.58 (br s, 1H, OH), 7.09 (dd, J = 8.3, 2.2 Hz, 1H), 7.25 (d, J = 2.2 Hz, 1H), 7.31−7.37 (m, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.38−7.45 (m, 2H), 7.51−7.56 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 114.8 (CH), 119.0 (C), 120.1 (CH), 127.0 (CH), 127.7 (CH), 128.8 (CH), 129.1 (CH), 139.8 (C), 141.9 (C), 151.5 (C) ppm; TLC R_f = 0.31 (Et_2O/PET, 1:5). Anal. Calcd for $C_{12}H_9ClO$: C, 70.43; H, 4.43. Found: C, 70.39; H, 4.47.

Method D: 4-(Trimethylsilyl)biphenyl-3-ol (15d). To a stirred solution of carbamate **12a** (0.196 g, 0.6 mmol) in 12 mL of EtOH was added at room temperature K_2CO_3 (0.829 g, 6.0 mmol) in one portion, and stirring was continued for 12 h. Then the reaction mixture was quenched with 9 mL of 2 M HCl, the aqueous phase was extracted with Et_2O, and the combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. FCC (Et_2O/PET, 1:20 to 1:5) of the residue yielded phenol **15d** (0.143 g, 0.590 mmol, 98%) as a colorless solid: mp 123−124 °C; IR (KBr) ν 3488, 3048, 2953, 1546, 1391, 1084, 838, 758, 719, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.34 (s, 9H), 4.82 (s, 1H, OH), 6.87 (d, J = 1.5 Hz, 1H), 7.16 (dd, J = 7.5, 1.5 Hz, 1H), 7.29−7.45 (m, 4H), 7.51−7.58 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.9 (CH_3), 113.2 (CH), 119.5 (CH), 124.1 (C), 127.1 (CH), 127.5 (CH), 128.8 (CH), 135.8 (CH), 140.7 (C), 144.0 (C), 160.7 (C) ppm; TLC R_f = 0.47 (Et_2O/PET, 1:5). Anal. Calcd for $C_{15}H_{18}OSi$: C, 74.33; H, 7.49. Found: C, 74.43; H, 7.63.

4-Iodobiphenyl-3-ol (15e). According to Method D, **12c** (0.229 g, 0.6 mmol) was stirred with K_2CO_3 in EtOH. Standard workup and FCC (Et_2O/PET, 1:20 to 1:5) afforded **15e** (0.176 g, 0.594 mmol, 99%) as a colorless solid: mp 80−81 °C; IR (KBr) ν 3247, 1562, 1399, 1205, 892, 859, 814, 758, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (br s, 1H, OH), 6.91 (dd, J = 8.2, 2.1 Hz, 1H), 7.22 (d, J = 2.1 Hz, 1H), 7.31−7.46 (m, 3H), 7.51−7.58 (m, 2H), 7.69 (d, J = 8.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.3 (C), 113.7 (CH), 121.3 (CH), 126.9 (CH), 127.9 (CH), 128.9 (CH), 138.4 (CH), 139.8 (C), 143.8 (C), 155.1 (C) ppm; TLC R_f = 0.23 (Et_2O/PET, 1:5). Anal. Calcd for $C_{12}H_9IO$: C, 48.67; H, 3.06. Found: C, 48.69; H, 3.08.

4-(Phenylsulfanyl)biphenyl-3-ol (15g). According to Method C, **12e** (0.182 g, 0.5 mmol) was treated with 2 M NaOH in 5 mL of EtOH and 1 mL of THF, and the crude product was purified after workup by FCC (Et_2O/PET, 1:20 to 1:10) to afford **15g** (0.135 g, 0.485 mmol, 97%) as a colorless oil: IR (film) ν 3430, 3062, 1601, 1583, 1555, 1476, 1191, 1024, 900, 878, 760, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.53 (s, 1H, OH), 7.31 (d, J = 2.0 Hz, 1H), 7.10−7.27 (m, 5H), 7.18 (dd, J = 8.0, 2.0 Hz, 1H), 7.33−7.39 (m, 1H), 7.40−7.47 (m, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.57−7.63 (m, 2H) ppm; ^{13}C NMR (75 MHz,

$CDCl_3$) δ 114.0 (CH), 115.3 (C), 120.1 (CH), 126.2 (CH), 127.0 (CH), 127.1 (CH), 128.0 (CH), 128.8 (CH), 129.2 (CH), 135.9 (C), 137.1 (CH), 140.0 (C), 145.7 (C), 157.4 (C) ppm; TLC R_f = 0.51 (Et_2O/PET, 1:5). Anal. Calcd for $C_{18}H_{14}OS$: C, 77.66; H, 5.07. Found: C, 77.51; H, 5.06.

4-Methylbiphenyl-3-ol (15h).[20] Following Method C, **12f** (0.135 g, 0.5 mmol) was stirred with 2 M NaOH in 5 mL of EtOH, and the crude product was purified after workup by FCC (Et_2O/PET, 1:10 to 1:5) to afford **15h** (0.091 g, 0.494 mmol, 99%) as a colorless solid: mp 78−79 °C; IR (KBr) ν 3528, 3031, 2945, 1409, 1305, 1239, 1123, 899, 823, 762, 691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 3H), 4.84 (br s, 1H, OH), 6.98 (d, J = 1.8 Hz, 1H), 7.07 (dd, J = 7.8, 1.8 Hz, 1H), 7.16 (d, J = 7.8 Hz, 1H), 7.23 (m, 1H), 7.35−7.42 (m, 2H), 7.50−7.55 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4 (CH_3), 113.6 (CH), 119.5 (CH), 122.8 (C), 126.9 (CH), 127.2 (CH), 128.7 (CH), 131.3 (CH), 140.5 (C), 140.7 (C), 154.0 (C) ppm; TLC R_f = 0.28 (Et_2O/PET, 1:5). Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.75; H, 6.43.

2-Hydroxybiphenyl-3-carbaldehyde (15c).[5b,19] Following the procedure for the synthesis of **9e**, reaction of **8** (0.255 g, 1.0 mmol) with DMF and standard workup gave the crude product, which was treated according to Method C with 2 M NaOH in 10 mL of EtOH. Workup and FCC (Et_2O/PET, 1:20 to 1:5) afforded salicylic aldehyde **15c** (0.176 g, 0.888 mmol, 89%) as a light yellow oil which solidified on standing to give a pale yellow solid: mp 41−42 °C; IR (film) ν 3058, 2849, 2745, 1656, 1451, 1430, 1386, 1279, 917, 832, 760, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.08 (t, J = 7.6 Hz, 1H), 7.31−7.64 (m, 7H), 9.92 (s, 1H), 11.51 (s, 1H, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.9 (CH), 120.9 (C), 127.6 (CH), 128.2 (CH), 129.2 (CH), 130.5 (C), 133.1 (CH), 136.1 (C), 137.7 (CH), 158.9 (C), 196.7 (CH) ppm; TLC R_f = 0.45 (Et_2O/PET, 1:5). Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.85; H, 5.20.

4-Methoxy-2-(trimethylsilyl)biphenyl-3-ol (24a). Following Method C, **17** (0.143 g, 0.4 mmol) was stirred with 2 M NaOH in 8 mL of EtOH and 2 mL of THF. The crude product was purified after workup by FCC (Et_2O/PET, 1:10) to yield **24a** (0.106 g, 0.389 mmol, 97%) as a colorless oil: IR (film) ν 3530, 3057, 2952, 1602, 1566, 1457, 1263, 1226, 1152, 1049, 863, 840, 808, 764, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 9H), 3.91 (s, 3H), 6.03 (br s, 1H, OH), 6.70 (d, J = 8.2 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 7.22−7.27 (m, 2H), 7.28−7.35 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.0 (CH_3), 55.9 (CH_3), 110.5 (CH), 121.7 (CH), 123.1 (C), 126.7 (CH), 127.5 (CH), 129.6 (CH), 142.4 (C), 144.7 (C), 144.8 (C), 150.7 (C) ppm; TLC R_f = 0.59 (Et_2O/PET, 1:5). Anal. Calcd for $C_{16}H_{20}O_2Si$: C, 70.54; H, 7.40. Found: C, 70.87; H, 7.44.

2′,4-Dimethoxy-4′,6′-dimethyl-2-(trimethylsilyl)biphenyl-3-ol (24b). Following Method C, **19** (0.481 g, 1.157 mmol) was treated with 2 M NaOH in 12 mL of EtOH and 3 mL of THF. The crude product was purified after workup by FCC (Et_2O/PET, 1:10) to afford **24b** (0.367 g, 1.110 mmol, 96%) as a colorless solid: mp 104−105 °C; IR (KBr) ν 3508, 3068, 2949, 1599, 1571, 1463, 1421, 1314, 1282, 1236, 1162, 1092, 865, 842, 808, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 9H), 2.02 (s, 3H), 2.43 (s, 3H), 3.76 (s, 3H), 3.97 (s, 3H), 6.04 (s, 1H, OH), 6.59 (d, J = 8.2 Hz, 1H), 6.63 (s, 1H), 6.73 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.1 (CH_3), 20.2 (CH_3), 21.6 (CH_3), 55.4 (CH_3), 55.6 (CH_3), 108.6 (CH), 111.0 (CH), 121.9 (CH), 122.5 (CH), 124.1 (C), 129.9 (C), 136.4 (C), 137.4 (C), 137.8 (C), 144.3 (C), 150.5 (C), 157.5 (C) ppm; TLC R_f = 0.64 (Et_2O/PET, 1:2). Anal. Calcd for $C_{19}H_{26}O_3Si$: C, 69.05; H, 7.93. Found: C, 69.11; H, 7.98.

2′,4′-Di-*tert*-butyl-4,6′-dimethoxy-2-(trimethylsilyl)biphenyl-3-ol (24c). Following method C, **23** (0.165 g, 0.33 mmol) was stirred with 2 M NaOH in 5 mL of EtOH and 2 mL of THF. Workup and purification the crude product by FCC (Et_2O/PET, 1:20) gave **24c** (0.134 g, 0.323 mmol, 98%) as a colorless solid: mp 137−138 °C; IR (KBr) ν 3512, 3066, 2964, 1602, 1558, 1455, 1402, 1300, 1269, 1231, 1206, 1064, 926, 862, 836, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.09 (s, 9H), 1.15 (s, 9H), 1.35 (s, 9H), 3.64 (s, 3H), 3.89 (s, 3H), 5.90 (br s, 1H, OH), 6.58 (d, J = 8.1 Hz, 1H), 6.72 (d, J = 1.7 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 7.15 (d, J = 1.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.1 (CH_3), 31.5 (CH_3), 33.1 (CH_3), 35.0 (C), 37.2 (C), 55.5 (CH_3), 55.5 (CH_3), 105.0 (CH), 109.6 (CH), 116.6 (CH), 123.2 (CH), 125.7 (C), 129.1 (C), 137.8 (C), 144.2 (C), 147.9 (C), 149.7 (C), 150.3 (C), 157.8 (C) ppm; TLC R_f = 0.60 (Et_2O/PET, 1:2). Anal. Calcd for $C_{25}H_{38}O_3Si$: C, 72.41; H, 9.24. Found: C, 72.66; H, 9.37.

Bis-silylation of BINOL by Directed *ortho*-Lithiation. *rac*-*O*,*O*′-[1,1′]-Binaphthyl-2,2′-diyl Di(*N*-isopropylcarbamate)(*rac*-26). A solution of *rac*-BINOL (*rac*-**25**) (2.291 g, 8.0 mmol) and DMAP (0.098 g, 0.8 mmol) in 5 mL of THF and 5 mL of CH_2Cl_2 was treated with isopropyl isocyanate (1.89 mL, 19.2 mmol). The reaction mixture was stirred at 60 °C for 2 d, cooled to room temperature, and quenched with 8 mL of 2 M HCl. The aqueous layer was extracted with Et_2O and the organic extracts were washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to FCC (Et_2O/PET, 1:5 to 1:2) to afford *rac*-**26** (3.347 g, 7.331 mmol, 92%) as a colorless solid: mp 161−162 °C; IR (KBr) ν 3347, 3055, 2967, 1698, 1522, 1454, 1363, 1314, 1224, 1076, 1042, 934, 832, 818, 788, 770, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75/1.01 (d, J = 5.8 Hz, 12H), 3.52 (m, 2H), 4.84 (br d, 2H, NH), 7.14−7.30 (m, 4H), 7.37−7.44 (m, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2/22.5 (CH_3), 43.0 (CH), 122.4 (CH), 123.5 (C), 125.3 (CH), 126.4, (CH), 126.5 (CH), 127.8 (CH), 129.2 (CH), 131.4 (C), 133.4 (C), 147.4 (C), 153.8 (C) ppm; TLC R_f = 0.15 (Et_2O/PET, 1:2). Anal. Calcd for $C_{28}H_{28}N_2O_4$: C, 73.66; H, 6.18; N, 6.14. Found: C, 73.30; H, 6.04; N, 5.98.

(*R*)-*O*,*O*′-[1,1′]-Binaphthyl-2,2′-diyl Di(*N*-isopropylcarbamate) ((*R*)-26). Following the procedure described for *rac*-**26**, a solution of (*R*)-BINOL ((*R*)-**25**) (4.295 g, 15.0 mmol, ≥99% ee),[32] DMAP (0.367 g, 3.0 mmol), and isopropyl isocyanate (3.83 mL, 39.0 mmol) in 30 mL THF was stirred at 60 °C for 2 d. (*R*)-**26** (6.701 g, 14.68 mmol, 98%) was obtained as a colorless foam: mp 64−66 °C; $[\alpha]_D^{20}$ −21 (c = 1.01, THF, ≥99% ee).

***rac*-*O*,*O*′-3,3′-Bis(trimethylsilyl)-[1,1′]-binaphthyl-2,2′-diyl Di(*N*-isopropylcarbamate (*rac*-27).** Following the General Procedure A, a solution of *rac*-**26** (0.137 g, 0.3 mmol) in 10 mL of Et_2O was sequentially treated with TMEDA (0.077 g, 0.66 mmol), TMSOTf (0.63 mmol), *s*-BuLi/TMEDA (1.5 mmol, −78 °C, 1.5 h), and trimethylsilyl chloride (0.23 mL, 1.8 mmol, −78 °C, 1 h). Standard workup and purification of the residue (FCC, Et_2O/PET, 1:5) afforded *rac*-**27** (0.175 g, 0.291 mmol, 97%) as a colorless solid: mp 158−159 °C; IR (KBr) ν 3311, 3047, 2967, 1711, 1533, 1394, 1252, 1202, 1144, 1093, 1056, 961, 848, 744, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.38 (s, 18H), 0.52/0.91 (d, J = 6.5 Hz, 12H), 3.26 (m, 2H), 4.66 (br d, 2H, NH), 7.13 (d, J = 8.5 Hz, 2H), 7.20−7.26 (m, 2H), 7.35−7.42 (m, 2H), 7.85 (d, J = 8.1 Hz, 2H), 8.07 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ −0.4 (CH_3), 22.1/22.5 (CH_3), 42.8 (CH), 124.1 (C), 125.1 (CH), 126.5 (CH), 126.9 (CH), 127.6 (CH), 131.3 (C), 133.3 (C), 134.4 (C), 136.5 (CH), 151.4 (C), 153.4 (C) ppm; TLC R_f = 0.58 (Et_2O/PET, 1:2). Anal. Calcd for $C_{34}H_{44}N_2O_4Si_2$: C, 67.96; H, 7.38; N, 4.66. Found: C, 67.95; H, 7.40; N, 4.42.

(*R*)-*O*,*O*′-3,3′-Bis(trimethylsilyl)-[1,1′]-binaphthyl-2,2′-diyl Di(*N*-isopropylcarbamate ((*R*)-27). The reaction was carried out according to the procedure described for *rac*-**27** using (*R*)-**26** (0.137 g, 0.3 mmol). (*R*)-**27** (0.173 g, 0.288 mmol, 96%) was obtained as a colorless solid: mp 175−177 °C; $[\alpha]_D^{20}$ −77 (c = 1.00, THF, ≥99% ee).

(32) (*R*)-BINOL ((*R*)-**25**) (≥99% ee) was purchased from Merck. The enantiomeric purity was checked by HPLC analysis (CHIRA GROM 1 column, 60 × 2 mm, 2-propanol/hexane, 1:100, flow rate 3.0 mL/min, t_R = 25.6 min for (*S*)-**25**, t_R = 35.4 min for (*R*)-**25**).

(33) (a) Mínguez, J. M.; Castellote, M. I.; Vaquero, J. J.; García-Navio, J. L.; Alvarez-Builla, J.; Castano, O.; Andrés, J. L. *J. Org. Chem.* **1996**, *61*, 4655−4665. (b) Terrian, D. L.; Mohammad, T.; Morrison, H. *J. Org. Chem.* **1995**, *60*, 1981−1984.

***rac*-3,3′-Bis(trimethylsilyl)-[1,1′]-binaphthyl-2,2′-diol (*rac*-28).**[25a] According to Method C, *rac*-**27** (0.180 g, 0.3 mmol) was stirred with 2 M NaOH (0.75 mL, 1.5 mmol, rt, 2.5 h) in 10 mL of EtOH. The crude product was purified after workup by FCC (Et_2O/PET, 1:20) to yield *rac*-**28** (0.128 g, 0.297 mmol, 99%) as a colorless solid: mp 153−154 °C; IR (KBr) ν 3520, 3041, 2947, 1581, 1413, 1246, 1179, 1042, 997, 848, 749, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.41 (s, 18H), 5.22 (br s, 2H, OH), 7.05−7.12 (m, 2H), 7.23−7.38 (m, 4H), 7.85−7.91 (m, 2H), 8.07 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.9 (CH_3), 109.6 (C), 123.7 (CH), 124.6 (CH), 127.6 (CH), 128.5 (CH), 129.0 (C), 129.3 (C), 134.3 (C), 137.8 (CH), 156.9 (C) ppm; TLC R_f = 0.78 (Et_2O/PET, 1:10). Anal. Calcd for $C_{26}H_{30}O_2Si_2$: C, 72.51; H, 7.02. Found: C, 72.84; H, 7.09.

(*R*)-3,3′-Bis(trimethylsilyl)-[1,1′]-binaphthyl-2,2′-diol ((*R*)-28).[25] According to the procedure described for *rac*-**28**, (*R*)-**27** (0.150 g, 0.25 mmol) was deprotected with 2 M NaOH (0.63 mL, 1.25 mmol, rt, 4 h) in 5 mL EtOH to furnish (*R*)-**28** (0.107 g, 0.248 mmol, 99%) as a colorless foam: mp 71−73 °C; $[\alpha]_D^{20}$ +139 (c = 1.00, THF, ≥99% ee) (lit.[25a] $[\alpha]_D^{20}$ +142 (c = 0.52, THF), lit.[25b] $[\alpha]_D$ +143 (c = 0.985, THF)). The enantiomeric excess was determined by HPLC analysis (CHIRA GROM 2 column, 250 × 2 mm, pentane, flow rate 3.0 mL/min, t_R = 6.4 min for (*S*)-**28**, t_R = 7.3 min for (*R*)-**28**).

Pd-catalyzed Cross-coupling Reactions. Negishi Coupling of Carbamate 8: *O*-[1,1′:3′,1″]-Terphenyl-2′-yl *N*-Isopropylcarbamate (30). Following the General Procedure A, a solution of carbamate **8** (0.128 g, 0.5 mmol) in 5 mL of THF was sequentially treated with TMEDA (0.064 g, 1.1 mmol), TBDMSOTf (1.05 mmol), *s*-BuLi/TMEDA (1.25 mmol, −78 °C, 1 h), and zinc(II) chloride (2.63 mL, 0.5 M in THF, 1.31 mmol, −78 °C, 15 min). The reaction mixture was allowed to warm to room temperature and stirring was continued for 45 min. The mixture was then transferred into a solution of iodobenzene (0.17 mL, 1.5 mmol) and $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) in 1 mL of THF and the whole was heated at reflux for 6 h. Quenching was effected at room temperature with 5 mL of 2 M HCl, the aqueous phase was then extracted with Et_2O, and the combined organic layers were washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated in vacuo. The resulting residue was purified by FCC (Et_2O/PET, 1:10 to 1:2) to yield starting material **8** (0.027 g, 0.106 mmol, 21%) and **30** (0.120 g, 0.362 mmol, 72%) as a colorless solid: mp 163−164 °C; IR (KBr) ν 3327, 3060, 2977, 1703, 1527, 1421, 1257, 1212, 1172, 1039, 786, 767, 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, J = 6.5 Hz, 6H), 3.49 (m, 1H), 4.40 (br s, 1H, NH), 7.26−7.50 (m, 13H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5 (CH_3), 43.0 (CH), 125.9 (CH), 127.2 (CH), 128.1 (CH), 129.1 (CH), 130.0 (CH), 136.4 (C), 138.2 (C), 145.2 (C), 153.0 (C) ppm; TLC R_f = 0.12 (Et_2O/PET, 1:2). Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.72; H, 6.42; N, 4.14.

Stille Coupling of Carbamate 9g.[9] Following the General Procedure B, stannane **9g** (0.109 g, 0.2 mmol) was *N*-silylated with *i*-Pr_2NEt (0.054 g, 0.42 mmol) and TBDMSOTf (0.21 mmol) in 2 mL of THF. The mixture was then transferred into a solution of iodobenzene (0.04 mL, 0.3 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) in 2 mL of THF, and the whole was stirred at 60 °C for 2 d. Workup and purification was performed as described for the Negishi coupling to give **30** (0.037 g, 0.112 mmol, 56%) along with starting material **9g** (0.038 g, 0.070 mmol, 35%).

Heck Coupling of Carbamate 31:[9] **(*E*)-3-(2-Hydroxyphenyl)acrylic Acid Methyl Ester (32).**[33] A mixture of Bu_4NCl (0.278 g, 1.0 mmol), KOAc (0.245 g, 2.5 mmol), $Pd(OAc)_2$ (7 mg, 0.03 mmol), and acrylic acid methyl ester (0.065 g, 0.75 mmol) in 2 mL of DMF was stirred at room temperature for 10 min. Then, a solution of carbamate **31** (0.153 g, 0.5 mmol) in 2 mL of DMF was added, and the whole was heated to 80 °C for 16 h. After cooling, quenching was effected with 5 mL of 2 M HCl and 20 mL of Et_2O. The aqueous layer was then extracted with Et_2O, and the combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. FCC (Et_2O/PET, 1:5 to 1:1) provided **32** (0.082 g, 0.460 mmol, 92%) as a colorless solid: mp 135 °C; IR (KBr) ν 3383, 3033, 2957, 1695, 1628, 1461, 1330, 1199, 1176, 993, 871, 804, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.42 (br s, 1H, OH), 3.80 (s, 3H), 6.57 (d, J = 16.1 Hz, 1H), 6.80−6.91 (m, 2H), 7.21 (ddd, J = 8.1, 7.7, 1.7 Hz, 1H), 7.45 (dd, J = 7.7, 1.7 Hz, 1H), 7.99 (d, J = 16.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.4 (CH_3), 116.0 (CH), 117.3 (CH), 119.7 (CH), 121.4 (C), 128.9 (CH), 131.3 (CH), 141.0 (CH), 156.4 (C), 168.6 (C) ppm; TLC R_f = 0.37 (Et_2O/PET, 1:1). Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.28; H, 5.74.

Sonogashira Coupling of Carbamate 31:[9] ***O*-2-(Phenylethynyl)phenyl *N*-Isopropylcarbamate (33).** To a stirred solution of carbamate **31** (0.153 g, 0.5 mmol) and phenylacetylene (0.11 mL, 1.0 mmol) in 3 mL of NEt_3 were added $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol) and CuI (2 mg, 0.01 mmol) in one portion. The dark reaction mixture was stirred at room temperature for 4 h and quenched with 5 mL of saturated NH_4Cl solution and 5 mL of 2 M HCl. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with 5 M HCl, saturated $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was subjected to FCC (Et_2O/PET, 1:5 to 1:2) to give **33** (0.138 g, 0.494 mmol, 99%) as a colorless solid: mp 126 °C; IR (KBr) ν 3364, 3061, 2970, 2218, 1712, 1523, 1493, 1209, 1021, 782, 756, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J = 6.5 Hz, 6H), 3.90 (m, 1H), 5.01 (br s, 1H, NH), 7.13−7.22 (m, 2H), 7.27−7.38 (m, 4H), 7.45−7.58 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8 (CH_3), 43.5 (CH), 84.6 (C), 93.6 (C), 117.7 (C), 122.7 (CH), 123.2 (C), 125.4 (CH), 128.2 (CH), 128.4 (CH), 129.3 (CH), 131.6 (CH), 132.9 (CH), 151.7 (C), 153.2 (C) ppm; TLC R_f = 0.09 (Et_2O/PET, 1:5). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.13; H, 6.02; N, 4.84.

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