Lewis Acid-Promoted Reactions of N^1,N^4-Dibenzoyl-1,4-benzoquinone Diimines with (*E*)-Propenylbenzenes: An Unexpected Reaction

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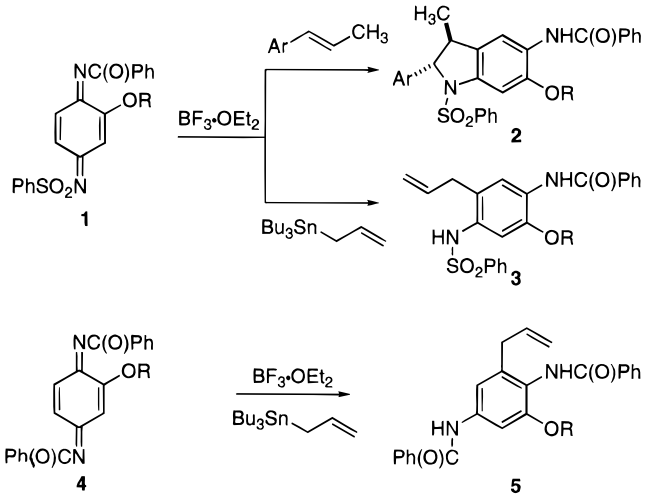
BF_3-promoted reactions of 2-alkoxy-N^1,N^4-dibenzoyl-1,4-benzoquinone diimines (**4**) with (*E*)-propenylbenzenes yield (1*R**,2*R**)-2-[[2-alkoxy-4-(benzoylamino)phenyl]amino]-1-phenylpropyl benzoates (**7/8**) stereoselectively.

Recent developments in the alkylation of quinone diimines with alkenyl systems (enol ethers, malonates, enamines, allylstannanes, and propenylbenzenes) have provided new regioselective routes to highly substituted indoles and dihydroindoles.[1] For example, BF_3-promoted reactions of 2-alkoxy-N^1-benzoyl-N^4-(phenylsulfonyl)-1,4-benzoquinone diimine (**1**) with propenylbenzenes or allyltributylstannane selectively produce dihydroindoles **2** and allylphenylenediamine derivatives **3**, respectively, presumably from selective Lewis acid coordination with the N^1-benzoyl imine. Reactions of N^1,N^4-dibenzoyldiimine **4** with allyltributylstannane afford **5** due to preferential Lewis acid coordination of the BF_3 to the imidate-like N^4-benzoylimine. Allylphenylenediamines **3** and **5** have both been converted to indoles.[1c−e]



The use of monodentate versus bidentate Lewis acids has been used to effect regioselective Lewis acid-directed Diels−Alder reactions of substituted 1,4-benzoquinones.[2] Seeking to exert similar regiocontrol over reactions of diimine **4**, and thus develop a synthesis of 7-alkoxy-2-aryl-2,3-dihydroindoles isomeric with **2**, we explored Lewis acid-promoted reactions of **4** with (*E*)-propenylbenzenes. Herein we report that BF_3 promotes these reactions to give products unlike those previously reported, revealing yet another reaction pathway available to these remarkably versatile systems.[3]

Thus, addition of $BF_3{\cdot}OEt_2$ to a mixture of diimines **4** and propenylbenzenes **6** in CH_2Cl_2 at −78 °C, followed by warming to −40, −20, or −10 °C and then aqueous workup[4a] and silica gel chromatography, afforded a single product in good to excellent yields (Table 1). Mass spectroscopy indicated that these products resulted from a combination of the two starting materials plus a molecule of water. Their IR spectra showed absorbances at 1668 and 1717 cm^{-1}. The former was consistent with a benzamide moiety but the latter was not; it was, however, suitable for a benzoate, suggesting a benzoyl-shift of some type. The ^1H NMR spectra in $CDCl_3$ showed

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(3) Lewis acid-promoted reactions of quinones and imide derivatives with dienes, styrenes, and alkenes have been found to give products of 4 + 2, 5 + 2, 2 + 2, and 3 + 2 cycloaddition, as well as simple alkylation. For examples and leading references, see refs 1 and 2 and: (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O., Jr.; Ray, J. E. *J. Org. Chem.* **1994**, *59*, 6567−6587. (b) Engler, T. A.; Wei, D.; Letavic, M. A.; Combrink, K. D.; Reddy, J. P. *J. Org. Chem.* **1994**, *59*, 6588−6599. (c) Engler, T. A.; Reddy, J. P.; Combrink, K. D.; Vander Velde, D. *J. Org. Chem.* **1990**, *55*, 1248−1254. (d) Engler, T. A.; Gfesser, G. A.; Draney, B. W. *J. Org. Chem.* **1995**, *60*, 3700−06. (e) Engler, T. A.; Chai, W. *Tetrahedron Lett.* **1996**, *37*, 6969−6970. (f) Engler, T. A.; Chai, W.; LaTessa, K. O *J. Org. Chem.* **1996**, *61*, 9297−9308. (g) Engler, T. A.; Agrios, K.; Reddy, J. P.; Iyengar, R. *Tetrahedron Lett.* **1996**, *37*, 327−330. (h) Murphy, W. S.; Neville, D. *Tetrahedron Lett.* **1996**, *37*, 9397−9340. (i) Neville, D.; Murphy, W. S. *Tetrahedron Lett.* **1996**, *37*, 5221−5224. (j) Adams, R.; Reifschneider, W. *Bull. Soc. Chim. Fr.* **1958**, *1*, 23−65 and references therein.

(4) (a) Analysis of reactions in progress by TLC was problematic. In many cases only starting propenylbenzene and base-line material were observed. Products were apparent only after aqueous quench; apparently, H_2O traps cationic intermediate **11**. This made it difficult to judge when reactions were complete. (b) Many crude reaction mixtures contained unreacted propenylbenzene and reduced diimine and were thus routinely subjected to flash chromatography as part of the workup. All fractions were carefully examined for the presence of other stereoisomeric products, to no avail.

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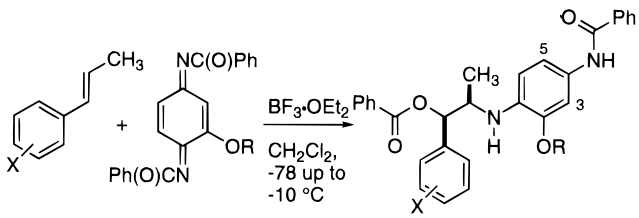
Table 1. Summary of BF_3-Promoted Reactions of Diimines 4 with Propenylbenzenes 6[a]

propenylbenzene	diimine	T[b] (°C)	product	% yield[c]
6a	**4a**	−40	**7a**	59
6b	**4a**	−78	**7b**	48
6c	**4a**	−40	**7c**	92
6d	**4a**	−40	**7d**	89
6e	**4a**	−40	**7e**	79
6a	**4b**	−40	**8a**	74
6b	**4b**	−40	**8b**	52
6c	**4b**	−20	**8c**	88
6d	**4b**	−20	**8d**	87
6e	**4b**	−10	**8e**	80
6f	**4b**	−20	**8f**	87
6g	**4b**	−40	**8g**	20

(a) All reactions were conducted in CH_2Cl_2 with 1.3 equiv of BF_3•OEt_2. (b) The BF_3•OEt_2 was added at −78 °C and the mixture then allowed to warm to this temperature over the time indicated in the Experimental. (c) Isolated yields after chromatography and/or crystallization.

a number of resonances not unlike those expected (CH_3 doublet at 1.16−1.19 and a doublet at 6.04−6.24 ppm, respectively, plus an amide NH at 7.54−7.75 ppm), but the chemical shift of a multiplet at 4.05−4.16 ppm was further downfield than expected and the integration of the aromatic region was "off" by a proton. Furthermore, spectra of **7e** and **8b**−**g** exhibited a doublet (J = 8 Hz) and a doublet-of-doublets (dd, J = 8, 2 Hz) at ∼6.85 and 6.9 ppm, respectively, and the latter was coupled to another proton buried in the rest of the aromatic region. For all of the other compounds, spectra in C_6D_6 revealed a dd ($J \approx$ 8, 2 Hz) at 6.8 ppm coupled to a broad singlet at 7.8−7.9 ppm. These signals indicated that one fragment of the product was a 1,2,4-trisubstituted aromatic system (i.e., two hydrogens ortho to one another and the third meta to one and para to the other), which likely originated from the starting diimine **4**. Finally, a D_2O-labile doublet was observed at 4.11−4.26 ppm, which was coupled to the multiplet at 4.05−4.16 ppm. The unexpected spectral features prompted us to determine the structure of the product from **6e** and **4a** by single-crystal X-ray analysis which revealed **7e**;[5] the structures of the other products were assigned as **7**/**8** by spectral comparison.

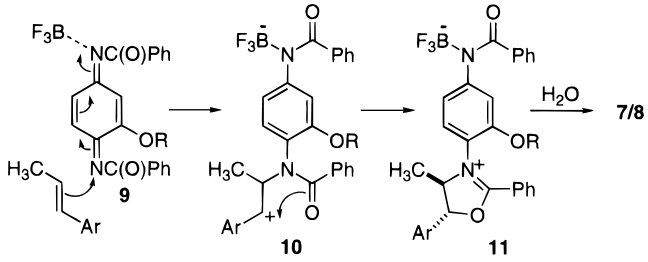


6a, X=4-OCH_3 **4a**, R=CH_3
6b, X=3,4-$(OCH_3)_2$ **4b**, R=CH_2Ph
6c, X=3,4-OCH_2O-
6d, X=4-CH_3
6e, X=H
6f, X=4-Cl
6g, X=4-NO_2

7, R=CH_3
8, R=CH_2Ph
(**a**-**g** as in **6**)

Both electron-donating and electron-withdrawing groups are tolerated on the propenylbenzene, although yields are significantly lower with the latter. Reactions of alkoxy-substituted propenylbenzenes are accompanied by considerable amounts of N^1,N^4-dibenzoyl-2-alkoxy-1,4-phenylenediamines from reduction of the diimines,[6] consistent with a competitive electron-transfer process. Notably, although products **7**/**8** possess two new acyclic stereogenic centers, only one diastereomer is isolated.[4b]

A straightforward rationale for the formation of **7**/**8** involves alkylation *on nitrogen*[7] of the BF_3-activated diimine **9** by the propenylbenzene to afford carbocation **10**, which is trapped intramolecularly by the benzamide to give **11**. Hydrolytic workup then produces the observed products.[4] The stereoselectivity is consistent with preferential formation of a *trans*-dihydrooxazolium ion **11**.



The mechanistic details remain to be defined, but the results establish that BF_3-promoted reactions of quinone diimines **4** with propenylbenzenes **6** do not afford products of carbon−carbon bond formation, rather products resulting from a mechanism involving initial C−N bond formation are found. Reactions involving other Lewis acids and alkenes are currently underway.

Experimental Section

All reactions were done in oven- and/or flame-dried glassware under an atmosphere of nitrogen with magnetic stirring. All compounds were prepared as racemic mixtures. ^{1}H NMR spectra were recorded on samples dissolved in deuteriochloroform ($CDCl_3$) or deuteriobenzene (C_6D_6), and chemical shifts are reported in parts per million (δ) relative to residual chloroform, benzene, or internal tetramethylsilane (TMS) unless otherwise noted. ^{13}C NMR spectra were recorded on samples dissolved in $CDCl_3$. Abbreviations for NMR multiplicities are as follows: s, singlet; d, doublet; m, multiplet; dd, doublet-of-doublets; bs, broad singlet; bd, broad doublet; AB q, AB quartet. Coupling constants (J) are reported in Hertz (Hz). Melting points are uncorrected. Thin-layer chromatography (TLC) was done on precoated silica plates (Art. #5715, Merck) containing a 254 nm fluorescent indicator and developed in the indicated solvent systems. Visualization was effected by UV and/or by staining with either *p*-anisaldehyde/H_2SO_4 or phosphomolybdic acid solutions. Chromatographic separations were done by flash chromatography with MN-Keiselgel 60 silica gel (0.04−0.063 mm mesh). Solvents

(5) The X-ray data for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

(6) Adams, R.; Acker, D. S. *J. Am. Chem. Soc.* **1952**, *74*, 5872−5876.

(7) Nucleophilic attack on nitrogen in unsubstituted benzoquinone diimines has been observed (Brown, E. R. In *The Chemistry of the Quinonoid Compounds*; Patai, S., Rappaport, Z., Eds.; Wiley: Chichester, 1988; Vol. 2, Part 2, Chapter 21), but this type of reactivity is rare for reactions of *N*-sulfonyl- or *N*-benzoylbenzoquinone diimines. Adams reported such products in reactions of aniline with *N*,*N*-dibenzoyl-1,4-benzoquinone diimine (Adams, R.; Werbel, L. *J. Org. Chem.* **1957**, *22*, 1287−1291) and *N*,*N*-bis(phenylsulfonyl)-2,3,5,6-tetrachloro-1,4-benzoquinone diimine (Adams, R.; Braun, B. *J. Am. Chem. Soc.* **1952**, *74*, 5869−5871). Contradicting Adams' structural assignment of the products of addition of phenols to *N*,*N*-bis(phenylsulfonyl)benzoquinone diimines (Adams, R.; Blomstrom, D. *J. Am. Chem. Soc.* **1953**, *75*, 3405−3408), Nishiyama suggested that bond formation occurred at nitrogen rather than carbon (Nishiyama, Y.; Ikagami, Y.; Seto, S. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 72−76). For a summary of Adams' work in this area, see ref 3j.

weredistilled under nitrogen from appropriate drying agents. $BF_3{\cdot}OEt_2$ was distilled from calcium hydride just prior to use. 1,2-Dimethoxy-4-propenylbenzene [(*E*):(*Z*) ≈ 14:1], 1,2-(methylenedioxy)-4-propenylbenzene (isosafrole) [(*E*):(*Z*) ≈ 5:1], (*E*)-propenylbenzene, and (*E*)-1-methoxy-4-propenylbenzene (*trans*-anethole) were purchased from Aldrich Chemical Co. and were used without further purification. (*E*)-1-Chloro-4-propenylbenzene [(*E*):(*Z*) = 9:1],[3a] (*E*)-1-nitro-4-propenylbenzene [(*E*):(*Z*) = 10:1],[8] and (*E*)-4-methyl-1-propenylbenzene [(*E*):(*Z*) ≈ 10:1][3a] were synthesized by known procedures. Benzoquinone diimines **4a** and **4b** were prepared according to the methods described by Adams[9] and Boger,[1e] respectively.

General Procedure for Addition of Propenylbenzenes to Diimines 4. The propenylbenzenes **6** were added neat to a solution of the diimine **4** in CH_2Cl_2 at rt. The mixture was cooled to −78 °C, stirred for 30−60 min, and then treated with $BF_3{\cdot}OEt_2$. After warming to −40, −20, or −10 °C over the time indicated, the reaction mixture was poured rapidly into saturated aqueous $NaHCO_3$ (50−75 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The combined extracts were dried (Na_2SO_4), decanted, and concentrated. Flash chromatography of the residue was done with the indicated solvent systems as eluents.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-methoxyphenyl]amino]-1-(4-methoxyphenyl)propyl Benzoate (7a).** According to the general procedure, (*E*)-4-methoxy-1-propenylbenzene (**6a**, 78 μL, 0.52 mmol) was added to a solution of diimine **4a** (180 mg, 0.52 mmol) in CH_2Cl_2 (4 mL), followed by $BF_3{\cdot}Et_2O$ (83 μL, 0.68 mmol). After the mixture was warmed to −40 °C over 5 h, workup and chromatography of the residue with 1:1:6 CH_2Cl_2/Et_2O/hexanes afforded **7a** (153 mg, 59%) as a light yellow solid: mp 182−183 °C (CH_2Cl_2/hexanes); TLC R_f = 0.36 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.17 (d, *J* = 6.4, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 4.06 (m, 1H), 4.14 (bd, *J* = 8.7, NH), 6.10 (d, *J* = 5.3, 1H), 6.87−6.91 (m, 4H), 7.29 (d, *J* = 8.7, 2H), 7.42−7.57 (m, 7H), 7.75 (bs, NH), 7.86 (d, *J* = 7.1, 2H), 8.04 (d, *J* = 7.1, 2H); ^{1}H NMR (400 MHz, C_6D_6) 1.11 (d, *J* = 6.3, 3H), 3.27 (s, 3H), 3.41 (s, 3H), 4.12 (m, 1H), 4.35 (bd, *J* = 9.4, NH), 6.41 (d, *J* = 5.4, 1H), 6.74 (d, *J* = 8.7, 2H), 6.79 (dd, *J* = 2.2, 8.4, 1H), 7.01−7.15 (m, 8H), 7.28 (d, *J* = 8.7, 2H), 7.63 (d, *J* = 7.0, 2H), 7.82 (bs, 1H, H-3), 8.17 (d, *J* = 7.8, 2H); ^{13}C NMR (100 MHz) 16.7, 51.7, 55.3, 55.6, 77.2, 104.3, 110.5, 113.3, 113.6, 126.9, 128.1, 128.4, 128.5, 128.7, 129.0, 129.7, 130.3, 131.5, 133.0, 134.3, 135.3, 146.7, 159.4, 165.4, 165.8. Anal. Calcd for $C_{31}H_{30}N_2O_5$: C, 72.92; H, 5.92; N, 5.49. Found: C, 72.72; H, 5.80; N, 5.40.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-methoxyphenyl]amino]-1-(3,4-dimethoxyphenyl)propyl Benzoate (7b).** According to the general procedure, (*E*)-3,4-dimethoxy-1-propenylbenzene (**6b**, 60 μL, 0.35 mmol) was added to a solution of diimine **4a** (101 mg, 0.29 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (46 μL, 0.38 mmol). After 10 min at −78 °C, workup and chromatography of the residue with 2:3:5 CH_2Cl_2/Et_2O/hexanes afforded **7b** (76 mg, 48%) as white crystals: mp 142−143 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.29 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.19 (d, *J* = 6.2, 3H), 3.83 (s, 6H), 3.88 (s, 3H), 4.09 (m, 1H), 4.16 (bd, *J* = 9.3, NH), 6.11 (d, *J* = 5.0 Hz, 1H), 6.82 (d, *J* = 1.8, 1H), 6.85 (d, *J* = 8.3, 1H), 6.89 (bs, 2H), 6.97 (dd, *J* = 1.8, 8.3, 1H), 7.44−7.59 (m, 7H), 7.69 (bs, NH), 7.87 (d, *J* = 7.2, 2H), 8.07 (d, *J* = 7.1, 2H); ^{1}H NMR (400 MHz, C_6D_6) 1.08 (d, *J* = 6.5, 3H), 3.37 (s, 3H), 3.38 (s, 3H), 3.39 (s, 3H), 4.18 (m, 1H), 4.38 (bd, *J* = 9.4, NH), 6.47 (d, *J* = 5.2, 1H), 6.56 (d, *J* = 8.3, 1H), 6.75 (dd, *J* = 2.2, 8.4, 1H, H-5), 6.89 (d, *J* = 1.9, 1H), 7.01 (dd, *J* = 1.9, 8.3, 1H), 7.02−7.15 (m, 8H), 7.63 (d, *J* = 7.0, 2H), 7.86 (bs, 1H, H-3), 8.22 (d, *J* = 7.8, 2H); ^{13}C NMR (125 MHz) 16.6, 51.3, 55.6, 55.8, 55.9, 76.8, 104.2, 110.4, 110.6, 110.8, 113.2, 119.5, 126.7, 128.1, 128.4, 128.7, 129.2, 129.6, 130.2, 131.6, 133.1, 134.1, 135.2, 146.5, 148.6, 148.8, 165.4, 165.8. Anal. Calcd for $C_{32}H_{32}N_2O_6$: C, 71.09; H, 5.97; N, 5.18. Found: C, 70.80; H, 6.00; N, 5.40.

(1*R,2*R**)-1-Benzo[1,3]dioxol-5-yl-2-[[4-(benzoylamino)-2-methoxyphenyl]amino]propyl Benzoate (7c).** According to the general procedure, (*E*)-1,2-(methylenedioxy)-4-propenylbenzene (**6c**, 21 μL, 0.15 mmol) was added to a solution of diimine **4a** (51 mg, 0.15 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (23 μL, 0.19 mmol). After warming to −40 °C over 3 h, workup and chromatography of the residue with 2:2:6 CH_2Cl_2/Et_2O/hexanes afforded **7c** (70 mg, 92%) as yellow crystals: mp 170.0−171.5 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.33 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.18 (d, *J* = 6.5, 3H), 3.84 (s, 3H), 4.05 (m, 1H), 4.15 (bd, *J* = 9.3, N−H), 5.95 (s, 2H), 6.04 (d, *J* = 5.4, 1H), 6.77 (d, *J* = 8.0, 1H), 6.81 (dd, *J* = 1.5, 8.0, 1H), 6.85 (d, *J* = 8.4, 1H, H-6), 6.88 (dd, *J* = 2.0, 8.4, 1H, H-5), 6.89 (d, *J* = 1.5, 1H), 7.42−7.58 (m, 7H), 7.69 (bs, N−H), 7.87 (d, *J* = 7.0, 2H), 8.04 (d, *J* = 7.0, 2H); ^{13}C NMR (100 MHz) 16.8, 51.8, 55.7, 77.2, 101.1, 104.3, 107.7, 108.0, 110.6, 113.2, 120.9, 126.9, 128.1, 128.4, 128.8, 129.7, 130.1, 130.7, 131.6, 133.1, 134.3, 135.3, 146.7, 147.4, 147.6, 165.4, 165.7. Anal. Calcd for $C_{31}H_{28}N_2O_6$: C, 70.98; H, 5.38; N, 5.34. Found: C, 70.95; H, 5.40; N, 4.98.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-methoxyphenyl]amino]-1-*p*-tolylpropyl Benzoate (7d).** According to the general procedure, (*E*)-4-methyl-1-propenylbenzene (**6d**, 74 μL, 0.56 mmol) was added to a solution of diimine **4a** (190 mg, 0.56 mmol) in CH_2Cl_2 (4 mL), followed by $BF_3{\cdot}Et_2O$ (89 μL, 0.73 mmol). After the mixture was warmed to −40 °C over 2 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **7d** (250 mg, 89%) as light yellow crystals: mp 185−185.5 °C (CH_2Cl_2/hexanes); TLC R_f = 0.47 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.17 (d, *J* = 6.3, 3H), 2.35 (s, 3H), 3.84 (s, 3H), 4.10 (m, 1H), 4.15 (bd, *J* = 9.2, NH), 6.11 (d, *J* = 5.2, 1H), 6.90 (bs, 2H), 7.15 (d, *J* = 7.9, 2H), 7.25 (d, *J* = 7.9, 2H), 7.42−7.58 (m, 7H), 7.54 (bs, NH), 7.87 (d, *J* = 7.2, 2H), 8.05 (d, *J* = 7.1, 2H); ^{1}H NMR (400 MHz, C_6D_6) 1.01 (d, *J* = 6.6, 3H), 2.08 (s, 3H), 3.41 (s, 3H), 4.14 (m, 1H), 4.34 (bd, *J* = 9.1, NH), 6.41 (d, *J* = 5.4, 1H), 6.80 (dd, *J* = 2.1, 8.4, 1H), 6.96 (d, *J* = 7.9, 2H), 7.03−7.11 (m, 8H), 7.18 (bs, NH), 7.29 (d, *J* = 7.9, 2H), 7.64 (d, *J* = 7.1, 2H), 7.81 (bs, 1H, H-3), 8.16 (d, *J* = 7.9, 2H); ^{13}C NMR (100 MHz) 16.6, 21.2, 51.6, 55.6, 77.3, 104.3, 110.5, 113.3, 126.9, 127.2, 128.1, 128.4, 128.7, 128.8, 129.7, 130.3, 131.5, 133.0, 133.8, 134.3, 135.3, 137.8, 146.7, 165.4, 165.8. Anal. Calcd for $C_{31}H_{30}N_2O_4$: C, 75.28; H, 6.11; N, 5.66. Found: C, 74.88; H, 6.41; N, 5.30.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-methoxyphenyl]amino]-1-phenylpropyl Benzoate (7e).** According to the general procedure, (*E*)-1-propenylbenzene (**6e**, 100 μL, 0.77 mmol) was added to a solution of diimine **4a** (260 mg, 0.77 mmol) in CH_2Cl_2 (4 mL), followed by $BF_3{\cdot}Et_2O$ (120 μL, 1.00 mmol). After the mixture was warmed to −40 °C over 5 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **7e** (290 mg, 79%) as light yellow crystals: mp 184.0−184.5 °C (CH_2Cl_2/hexanes); TLC R_f = 0.43 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) 1.18 (d, *J* = 5.7, 3H), 3.83 (s, 3H), 4.11 (bs, 2H), 6.16 (d, *J* = 4.9, 1H), 6.89 (bs, 2H), 7.32−7.55 (m, 12H), 7.73 (bs, NH), 7.87 (d, *J* = 7.2, 2H), 8.07 (d, *J* = 7.1, 2H); ^{1}H NMR (400 MHz, C_6D_6) 0.96 (d, *J* = 6.6, 3H), 3.40 (s, 3H), 4.10 (m, 1H), 4.31 (bd, *J* = 8.2, NH), 6.41 (d, *J* = 5.4, 1H), 6.78 (dd, *J* = 2.1, 8.4, 1H, H-5), 6.95−7.20 (m, 10H), 7.31 (bs, NH), 7.34 (d, *J* = 8.3, 2H), 7.64 (d, *J* = 8.2, 2H), 7.81 (bs, 1H, H-3), 8.15 (d, *J* = 8.0, 2H); ^{13}C NMR (125 MHz) 16.6, 51.5, 55.6, 77.2, 104.3, 110.5, 113.2, 126.9, 127.2, 128.0, 128.1, 128.4, 128.7, 129.7, 130.1, 131.5, 133.1, 134.2, 135.2, 136.7, 146.6, 165.4, 165.8 (1C buried under either 128.1 or 128.4). Anal. Calcd for $C_{30}H_{28}N_2O_4$: C, 74.98; H, 5.87; N, 5.83. Found: C, 74.61; H, 5.60; N, 6.20.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-(4-methoxyphenyl)propyl Benzoate (8a).** According to the general procedure, (*E*)-4-methoxy-1-propenylbenzene (**6a**, 27 μL, 0.18 mmol) was added to a solution of

(8) Broos, R.; Anteunis, M. J. O. *Bull. Soc. Chim. Belg.* **1986**, *95*, 135−138.

(9) Adams has reported **4a** as an unstable oil (Adams, R.; Neumiller, H., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 3808−3812). In our hands, **4a** is obtained as a yellow solid, stable for weeks open to the atmosphere at rt. Experimental procedures for the preparation of **4a** are included in the Supporting Information.

diimine **4b** (77 mg, 0.18 mmol) in CH_2Cl_2 (2 mL) followed by $BF_3{\cdot}Et_2O$ (30 μL, 0.24 mmol). After the mixture was warmed to −40 °C over 90 min, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8a** (80 mg, 74%) as a white solid: mp 102−104 °C (CH_2Cl_2/hexanes); TLC R_f = 0.39 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.16 (d, J = 6.5, 3H), 3.77 (s, 3H), 4.09 (m, 1H), 4.25 (bd, J = 8.7, N−H), 5.08 (s, 2H), 6.10 (d, J = 5.2, 1H), 6.85 (m, 3H), 6.91 (dd, J = 1.8, 8.4, 1H), 7.30−7.57 (m, 14H), 7.68 (bs, N−H), 7.86 (d, J = 7.1, 2H), 8.02 (d, J = 7.2, 2H); ^{13}C NMR (125 MHz) 16.7, 51.7, 55.2, 70.5, 77.2, 105.7, 110.6, 113.7 (2C), 126.9, 127.6, 127.9, 128.0, 128.4, 128.5 (2C), 128.7, 129.0, 129.7, 130.2, 131.6, 133.0, 134.6, 135.3, 136.9, 145.8, 159.4, 165.4, 165.8. Anal. Calcd for $C_{37}H_{34}N_2O_5$: C, 75.75; H, 5.84; N, 4.77. Found: C, 75.36; H, 5.99; N, 4.50.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-(3,4-dimethoxyphenyl)propyl Benzoate (8b).** According to the general procedure, (*E*)-3,4-dimethoxy-1-propenylbenzene (**6b**, 42 μL, 0.25 mmol) was added to a solution of diimine **4b** (105 mg, 0.25 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (40 μL, 0.32 mmol). After the mixture was warmed to −40 °C over 4 h, workup and chromatography of the residue with 1:1:6 CH_2Cl_2/Et_2O/hexanes afforded **8b** (79 mg, 52%) as a white foam: mp 75−80 °C (CH_2Cl_2/hexanes); TLC R_f = 0.28 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.18 (d, J = 6.5, 3H), 3.78 (s, 3H), 3.83 (s, 3H), 4.09 (bs, 1H), 4.31 (bd, J = 7.8, NH), 5.10 (s, 2H), 6.12 (d, J = 5.1, 1H), 6.79 (d, J = 8.3, 1H), 6.84 (d, J = 8.5, 1H), 6.89 (d, J = 1.8, 1H), 6.91 (dd, J = 2.0, 8.5, 1H), 6.95 (dd, J = 1.8, 8.3, 1H), 7.32−7.56 (m, 12H), 7.67 (bs, NH), 7.87 (d, J = 7.1, 2H), 8.04 (d, J = 7.2, 2H); ^{13}C NMR (100 MHz) 16.8, 51.6, 55.7, 55.8, 70.4, 77.2, 105.6, 110.3, 110.4, 110.7, 113.7, 119.5, 126.9, 127.5, 127.9 (2C), 128.4, 128.5, 128.7, 129.4, 129.6, 130.1, 131.5, 133.1, 134.3, 135.1, 136.7, 145.7, 148.6, 148.7, 165.4, 165.7; FABMS m/z 616 (M^+); HRMS m/z 617.2647 (M^+ + 1) (calcd for $C_{38}H_{37}N_2O_5$ − 617.2652).

(1*R,2*R**)-1-Benzo[1,3]dioxol-5-yl-2-[[4-(benzoylamino)-2-(benzyloxy)phenyl]amino]propyl Benzoate (8c).** According to the general procedure, (*E*)-1,2-(methylenedioxy)-4-propenylbenzene (**6c**, 25 μL, 0.17 mmol) was added to a solution of diimine **4b** (73 mg, 0.17 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (28 μL, 0.23 mmol). After the mixture was warmed to −20 °C over 90 min, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8c** (92 mg, 88%) as a white powder: mp 100.5−102 °C (CH_2Cl_2/Et_2O, hexanes); TLC R_f = 0.38 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.18 (d, J = 6.6, 3H), 4.06 (m, 1H), 4.25 (d, J = 9.5, NH), 5.08 (s, 2H), 5.93 (AB q, J = 1.4, $\Delta\nu$ = 13.5, 2H), 6.05 (d, J = 5.1, 1H), 6.73 (d, J = 8.0, 1H), 6.83 (dd, J = 1.6, 8.0, 1H), 6.84 (d, J = 8.5, 1H, H-6), 6.89 (d, J = 1.6, 1H), 6.92 (dd, J = 1.9, 8.5, 1H, H-5), 7.31−7.57 (m, 12H), 7.67 (bs, NH), 7.87 (d, J = 7.1, 2H), 8.02 (d, J = 7.1, 2H); ^{1}H NMR (400 MHz, C_6D_6) 0.93 (d, J = 6.6, 3H), 4.00 (m, 1H), 4.45 (bd, J = 6.5, NH), 4.81 (s, 2H), 5.27 (AB q, J = 1.3, $\Delta\nu$ = 11.0, 2H), 6.22 (d, J = 5.4, 1H), 6.57 (d, J = 8.0, 1H), 6.73 (dd, J = 1.4, 8.0), 6.89 (d, J = 8.5, 1H, H-6), 6.97 (dd, J = 1.9, 8.5, 1H, H-5), 6.98 (d, J = 1.4, 1H), 7.02−7.13 (m, 5H), 7.24 (d, J = 7.5, 2H), 7.58 (bs, NH), 7.71 (d, J = 7.0, 2H), 7.84 (bs, 1H, H-3), 8.08 (d, J = 7.0, 2H); ^{13}C NMR (125 MHz) 16.7, 51.7, 70.5, 77.2, 101.1, 105.7, 107.7, 108.0, 110.5, 113.6, 120.8, 126.9, 127.6 (2C), 127.9, 128.4, 128.5, 128.7, 129.7, 130.0, 130.7, 131.5, 133.1, 134.4, 135.2, 136.8, 145.8, 147.4, 147.6, 165.4, 165.7; EIMS (relative intensity) m/z 600 (M^+, <1); HRMS m/z 601.2355 (M^+ + 1) (calcd for $C_{37}H_{33}N_2O_6$ − 601.2339).

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-*p*-tolylpropyl Benzoate (8d).** According to the general procedure, (*E*)-4-methyl-1-propenylbenzene (**6d**, 20 μL, 0.17 mmol) was added to a solution of diimine **4b** (73 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) followed by $BF_3{\cdot}Et_2O$ (28 μL, 0.23 mmol). After the mixture was warmed to −20 °C over 2 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8d** (99 mg, 87%) as a white solid: mp 101.5−102.5 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.50 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.16 (d, J = 6.5, 3H), 2.32 (s, 3H), 4.10 (m, 1H), 4.25 (bd, J = 9.1, NH), 5.07 (s, 2H), 6.12 (d, J = 5.2, 1H), 6.86 (d, J = 8.5, 1H), 6.91 (dd, J = 1.8, 8.5, 1H), 7.11 (d, J = 8.0, 2H), 7.26 (d, J = 8.0, 2H), 7.32−7.57 (m, 12H), 7.67 (bs, NH), 7.86 (d, J = 7.1, 2H), 8.03 (d, J = 7.2, 2H); ^{13}C NMR (100 MHz) 16.6, 21.2, 51.5, 70.5, 77.2, 105.7, 110.5, 113.7, 126.9, 127.1, 127.6, 127.8, 127.9, 128.4, 128.5, 128.7, 128.9, 129.7, 130.2, 131.6, 133.0, 133.8, 134.5, 135.3, 136.9, 137.8, 145.8, 165.4, 165.6. Anal. Calcd for $C_{37}H_{34}N_2O_4$: C, 77.87; H, 6.01; N, 4.91. Found: C, 77.54; H, 6.21; N, 4.77.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-phenylpropyl Benzoate (8e).** According to the general procedure, (*E*)-1-propenylbenzene (**6e**, 26 μL, 0.20 mmol) was added to a solution of diimine **4b** (85 mg, 0.20 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (32 μL, 0.26 mmol). After the mixture was warmed to −10 °C over 4 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8e** (95 mg, 80%) as a white solid: mp = 112.0−112.5 °C (CH_2Cl_2/Et_2O/pentanes); TLC R_f = 0.41 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.18 (d, J = 6.5, 3H), 4.11 (m, 1H), 4.26 (bd, J = 8.6, N−H), 5.09 (s, 2H), 6.16 (d, J = 5.1, 1H), 6.87 (d, J = 8.5, 1H), 6.91 (dd, J = 1.9, 8.5, 1H), 7.29−7.66 (m, 17H), 7.66 (bs, N−H), 7.86 (d, J = 7.2, 2H), 8.05 (d, J = 7.1, 2H); ^{13}C NMR (125 MHz) 16.7, 51.6, 70.5, 77.2, 105.7, 110.5, 113.7, 126.9, 127.1, 127.6 (2C, 1 quaternary buried), 128.0 (2C), 128.2, 128.4, 128.5, 128.7, 129.7, 130.1, 131.5, 133.1, 134.4, 135.3, 136.8, 136.9, 145.8, 165.4, 165.7; EIMS (relative intensity) m/z 556 (M^+, <1); HRMS m/z 557.2437 (M^+ + 1) (calcd for $C_{36}H_{33}N_2O_4$ − 557.2440).

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-(4-chlorophenyl)propyl Benzoate (8f).** According to the general procedure, (*E*)-1-chloro-4-propenylbenzene (**6f**, 30 μL, 0.19 mmol) was added to a solution of diimine **4b** (81 mg, 0.19 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (30 μL, 0.25 mmol). After the mixture was warmed to −20 °C over 2 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8f** (99 mg, 87%) as a white solid: mp 84.5−86.5 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.49 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.16 (d, J = 6.4, 3H), 4.10 (m, 1H), 4.18 (bd, J = 9.3, NH), 5.08 (s, 2H), 6.13 (d, J = 4.8, 1H), 6.84 (d, J = 8.5, 1H), 6.91 (dd, J = 1.8, 8.5, 1H), 7.25−7.60 (m, 16H), 7.71 (bs, N−H), 7.87 (d, J = 7.2, 2H), 8.04 (d, J = 7.2, 2H); ^{13}C NMR (100 MHz) 16.5, 51.4, 70.6, 76.5, 105.7, 110.5, 113.7, 126.9, 127.6, 128.1 (2C), 128.4, 128.5 (2C), 128.6, 128.8, 129.7, 129.9, 131.6, 133.3, 133.9, 134.1, 135.2, 135.4, 136.8, 145.8, 165.4, 165.6. Anal. Calcd for $C_{36}H_{31}N_2O_4Cl$: C, 73.15; H, 5.29; N, 4.74. Found: C, 73.04; H, 5.56; N, 4.38.

(1*R,2*R**)-2-[[4-(Benzoylamino)-2-(benzyloxy)phenyl]amino]-1-(4-nitrophenyl)propyl Benzoate (8).** According to the general procedure, (*E*)-4-nitro-1-propenylbenzene (**6g**, 29 mg, 0.18 mmol) was added to a solution of diimine **4b** (74 mg, 0.18 mmol) in CH_2Cl_2 (2 mL), followed by $BF_3{\cdot}Et_2O$ (28 μL, 0.30 mmol). After the mixture was warmed to −40 °C over 4 h, workup and chromatography of the residue with 1:1:8 CH_2Cl_2/Et_2O/hexanes afforded **8g** (21 mg, 20%) as a yellow solid: mp 120−122 °C (Et_2O/pentanes); TLC R_f = 0.41 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) 1.19 (d, J = 5.9, 3H), 4.16 (bs, 2H), 5.11 (AB q, J = 11.8, $\Delta\nu$ < 5.3, 2H), 6.24 (d, J = 3.1, 1H), 6.82 (d, J = 8.5, 1H), 6.91 (dd, J = 1.8, 8.5, 1H), 7.33−7.62 (m, 14H), 7.76 (bs, NH), 7.87 (d, J = 7.1, 2H), 8.06 (d, J = 7, 2H), 8.12 (d, J = 8.7, 2H); ^{1}H NMR (400 MHz, C_6D_6) 0.79 (d, J = 6.6, 3H), 3.92 (m, 1H), 4.21 (bd, J = 9.3, N−H), 4.80 (AB q, J = 11.2, $\Delta\nu$ = 11.3, 2H), 6.19 (d, J = 4.6, 1H), 6.81 (dd, J = 2.1, 8.4, 1H), 6.88 (d, J = 8.4, 1H), 6.99 (d, J = 8.7, 2H), 7.03−7.20 (m, 11H), 7.26 (bs, N−H), 7.66 (d, J = 7.0, 2H), 7.75 (d, J = 8.7, 2H), 7.94 (bs, 1H, H-3), 8.10 (d, J = 7.0, 2H); ^{13}C NMR (125 MHz) 16.6, 51.4, 70.7, 75.9, 105.8, 110.6, 113.7, 123.3, 126.9, 127.7, 127.8, 128.3, 128.4, 128.7, 128.8, 129.5, 129.7, 131.7, 133.6, 133.7, 135.2, 136.6, 144.2, 145.8, 147.6, 165.4, 165.7, 177.5. Anal. Calcd for $C_{36}H_{31}N_3O_6$: C, 71.87; H, 5.19; N, 6.98. Found: C, 71.76; H, 5.34; N, 6.58.

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Supporting Information Available: Experimental procedures for the preparation of **4a/b** and **6g**, IR and mass spectral data for compounds **7** and **8** (all), ^{1}H and ^{13}C NMR spectra for all compounds with HRMS data (**4a**, **8b**, **8c**, and **8e**), crystallographic data and an ORTEP drawing of **7e** (42 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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