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Facile Syntheses and Multi-orthofunctionalizations of Tertiary Benzamides

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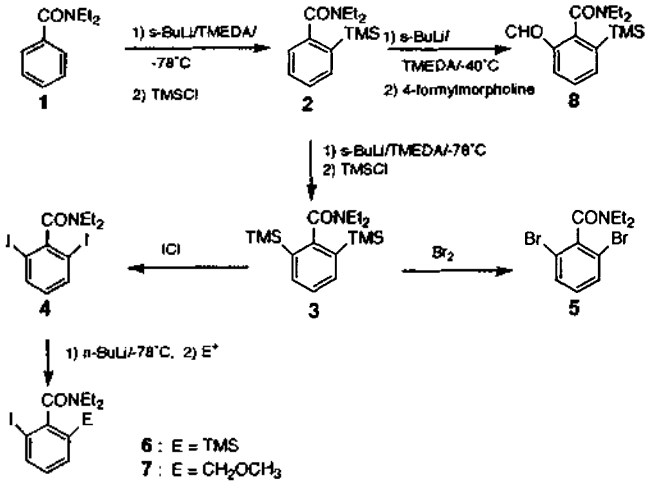
Good yields were usually obtained in Pd(O)-catalyzed Suzuki aryl-aryl coupling reaction, even when both coupling partners had an ortho tertiary benzamide functional group. The direct ortho functionalization of oligomeric tertiary benzamides at Snieckus condition is dependent on the chain length. Tertiary benzamide **1** can be o,o-dilithiated only by metal-halogen exchange of the 2,6-dihalo-compound. Bis-tertiary benzamide **9** can be o,o'-dilithiated with excess (4.1 equivalents) s-butyllithium/TMEDA as the lithiating agent. Tris-tertiary benzamide **21** is hard to o,o''-difunctionalize due to steric interactions among the tertiary benzamide functional groups, and due to steric interactions between these functional groups and others (if present) on the termini of the terphenyl unit.

Introduction

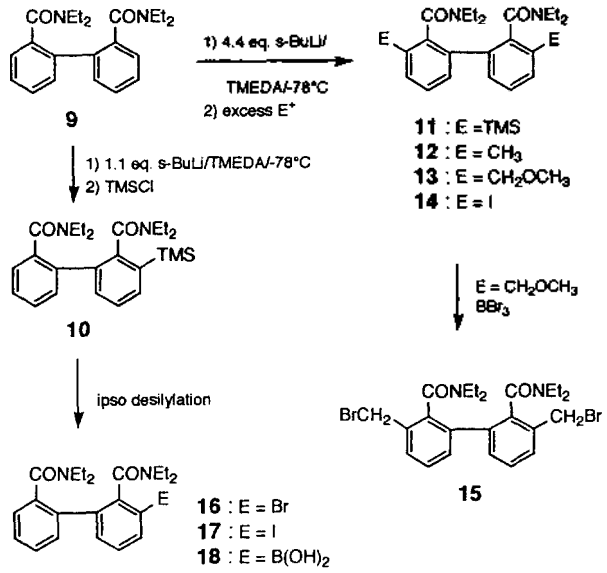
The carbonyl group is one of the most important functional groups in biological systems. The base pairing within nucleic acids is based on hydrogen bonding to carbonyl oxygens[1] and many ionophores use carbonly oxygens as ligands.[2] Valiomycin and enniatin B are antibiotics capable of inducing alkali metal permeability in various artificial and biological membranes.[3] These bind potassium ion in preference to sodium ion, and their antibiotic activities are due to their interference with the ion balances of bacterial cells. In the potassium ion complex of valinomycin, all the six ester carbonyls are coordinated to potassium, forming a distorted octahedral ligand system. The structural framework of this ionophore is stabilized by hydrogen bonds. In the conformation of the potassium complex of enniatin B, six carbonyl oxygens from an equal number of amide and ester are coordinated to cation.[4]

Even though the carbonyl group has such important biological functions, only a few hosts have been designed and synthesized whose only binding sites are carbonyl oxygens. The cyclic urea system[5] and the calixarene derivatives[6-8] have recently been reported. The use of amide groups is especially attractive because the highly polarized carbonyl of this functional group should be a superior binding site.

The observed stability order of the 1 : 1 complexes of potassium cation and solvents (K^+L) in the gas phase is as follows: dimethyl sulfoxide (25), dimethyl acetamide (24), dimethyl formamide (23), 1,2-dimethoxyethane (23), 1,2-diaminoethane (19), acetone (19), acetonitrile (18), aniline (16), diethyl ether (15), pyridine (15), dimethyl ether (13), trimethyl amine (13), methyl amine (13), benzene (12), ammonia (12), water (11), where the numbers in parenthesis are the values of $-\Delta G^\circ_{300}$ in kcal/mol.[9] The strong bonding of dimethyl sulfoxide, dimethyl acetamide, and dimethyl formamide to potassium ion is due to the high dipole moment of these compounds. These bond even more strongly than the bidentate ligands, 1,2-dimethoxyethane and 1,2-diaminoethane.



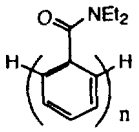
Scheme 1. The Orthofunctionalizations of N,N-Diethylbenzamide, **1**.



Scheme 2. The Orthofunctionalizations of Bis-tertiary Benzamide, **9**.

Synthetic studies of tertiary benzamides were therefore undertaken with the goal of developing new synthetic routes for the preparation of hosts using amide oxygens as ligands. Beak and Snieckus[10] have reported that tertiary benzamides can be substituted in the ortho position by lithiating with s-BuLi/TMEDA at −78℃ and quenching with an appropriate electrophiles. No systematic study has been reported, however, concerning the application of this process to biphenyl or terphenyl systems such as **9** and **21**.

In this paper the synthesis and the feasibility of orthofunctionalization of tertiary benzamide **1**, bis-tertiary benzamide **9**, and tris-tertiary benzamide **21** were presented.

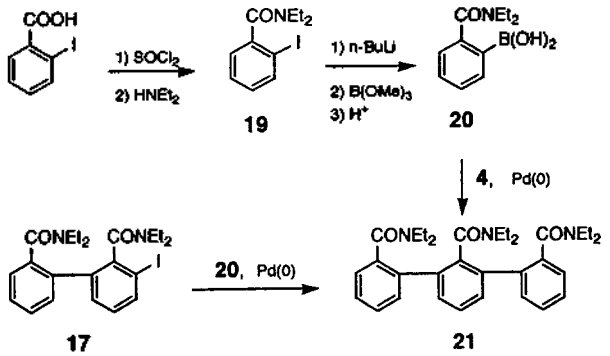


1 n=1 tertiary benzamide
9 n=2 bis-tertiary benzamide
21 n=3 tris-tertiary benzamide

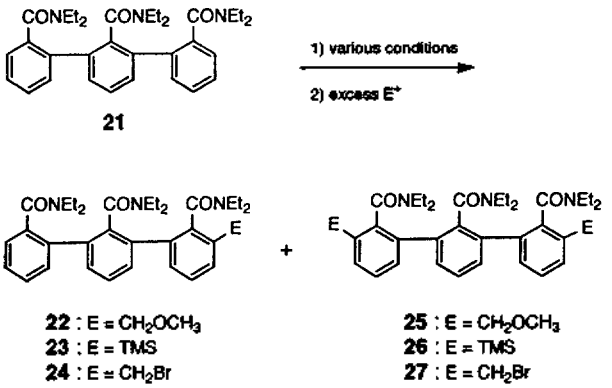
Results

Orthofunctionalizations of N,N-Diethylbenzamide, 1. The N,N-diethylbenzamide **1** was obtained from the reaction of benzoyl chloride and Et_2NH in 86.6% yield (bp. 140-145℃ at 10 torr, lit.[11] 90-95℃ at 0.6 torr) after fractional distillation. Compound **3** was obtained in 90% yield *via* an one-pot procedure involving ortholithiation of **1** with s-BuLi/TMEDA, quenching with trimethylsilyl chloride (TMSCl), lithiating the remaining open ortho position of intermediate **2** with fresh s-BuLi/TMEDA, and a second TMSCl quench.[12] In a few runs the intermediate **2** was isolated as crystalline product (mp. 55.5-56.0℃, from pentane).[10a] Snieckus *et al.*[13] reported that compound **3** could be obtained by the direct addition of 2.2 equivalents of s-BuLi/TMEDA in THF at −78 ℃ followed by quenching with excess TMSCl. Only monosubstituted products (40-60% yield) were obtained when the mixture was quenched with more reactive electrophiles, which would be possible due to a stepwise lithiation mechanism. When compound **2** was treated with 1.2 equivalents of s-BuLi/TMEDA in THF at −78℃ and quenched the resulting mixture with 4-formylmorpholine,[14] none of the desired product **8** was obtained. When the lithiating temperature was raised to −40℃, compound **8** was obtained quantitatively. From these results it is clear that the compound **2** needs more activation energy for further lithiation due to the steric hindrance between the trimethylsilyl and N,N-diethylamino groups. Compound **3** was transformed to diiodide **4** (91.8%) and dibromide **5**[12] (67%) by desilylation with iodine monochloride and bromine respectively.[15] Compound **4** was easily further functionalized to compounds **6** and **7** by mono metal-halogen exchange with 1.1 equivalent of n-BuLi followed by quenching with the appropriate electrophiles.[20]

Orthofunctionalizations of Bis-tertiary benzamide, 9. Compound **9** was obtained from commercially available diphenic acid *via* its bis-acid chloride (91.4%). Monolithiation of compound **9** with 1.2 equivalents of s-BuLi/TMEDA in THF at −78℃ followed by quenching with 1.2 equivalents of TMSCl gave mono functionalized compound **10** in 44% yield. The difunctionalized compound **11** was obtained in 47% yield from **9** by the sequential lithiation-quenching procedure described above for N,N-diethylbenzamide. But when compound **9** was dilithiated with 4.1 equivalents of s-BuLi /TMEDA in THF at −78℃ and quenched with excess electrophile (TMSCl, methyl iodide, bromomethyl methyl ether, or iodine), the disubstituted products **11**, **12**, **13**, and **14** were obtained in high yields (90.0, 92.6, 88.0, 70.2% respectively). The mono-TMS compound **10** was transformed to the bromo-(**16**, 49%) and iodo-(**17**, 80.3%) compounds, and to the boronic acid (**18**, 40%) by ipso desilylation with bromine, iodine monochloride, and boron tribromide respectively. These monosubstituted compounds are hard to separate from the disubstituted compounds which are byproducts in the direct monofunctionalization reaction. Compound **11** was also converted to compound **14** by treatment with iodine monochloride in 45.8% yield. Treatment of compound **12** with NBS failed to give the desired product **15**. This compound was



Scheme 3. The Synthesis of Tris-tertiary Benzamide, **21**.



Scheme 4. The Orthofunctionalizations of Tris-tertiary Benzamide, **21**.

successfully obtained in 53.8% yield by treating compound **13** with boron tribromide in dichloromethane.

Synthesis and orthofunctionalizations of Tris-tertiary benzamide, 21

Synthesis. Tris-tertiary benzamide **21** was obtained by the synthetic routes in Scheme 3. using the Suzuki reaction.[17] Boronic acid **20** was prepared from *o*-iodobenzoic acid in 69% overall yield. It was coupled by Pd(O) with 2,6-diiodo-N,N-diethylbenzamide **4** or with compound **17** to give tris-tertiary benzamide **21** in 40.2 and 40.8% yields respectively.[18]

Orthofunctionalizations. The o,o″-dilithiation of tris-tertiary benzamide **21** turned out to be extremely difficult. Treatment of **21** even with a large excess of s-BuLi followed by quenching with electrophiles gave mainly monosubstituted products. When the electrophile was TMSCl, the results were even worse. Raising the reaction temperature gave only unidentifiable side products (streaks on TLC). It is interesting that 1.2 equivalent of s-BuLi gave only starting material. It is probable that 1 equivalent of s-BuLi could be deactivated by complexation to the three carbonyl oxygens of **21**. Compound **22** and **25** could not be separated from each other. But when the mixture was treated with boron tribromide in dichloromethane, the products **24** and **27** could be separated by dry column chromatography in 17% and 6.6% yield (for two steps) respectively.

Discussion

The direct o,o-dilithiation of N,N-diethylbenzamide is unlikely, but the corresponding dilithiate can be generated by the metal-halogen exchange of 2,6-dihalo-N,N-diethylbenzamide.[13] Selective monolithiation of 2,6-diiodo-N,N-diethylbenzamide with 1.1 equivalent n-BuLi followed by quenching with various electrophiles gave important unsymmetrically substituted intermediates. The N,N-diethylamide group is known as the smallest stable tertiary amide group for the directing of ortho lithiation by s-butyllithium/TMEDA at −78℃ in THF.[10c] The N,N-diethylamide group also turned out to be stable to this reagent up to −40℃ in the conversion of **2** to **8**. The higher temperature required for successful lithiation of **2** compared to **1** is undoubtedly due to unfavorable steric interactions between the trimethylsilyl group and the diethylamino group in the transition state of the carbonyl directed ortho lithiation.

The bis-tertiary benzamide **9** was efficiently difunctionalized with 4.4 equivalent s-BuLi/TMEDA in THF at −78℃ followed by various E^+, but when 2.2 equivalents of reagent were used, significant amounts of monosubstituted product were obtained. It is probable that one equivalent s-BuLi is chelated by the two carbonyl oxygens of **9**, and is unavailable for deprotonation of the aryl ring. For the same reason the treatment of compound **9** with 1.0 equivalent of lithiating reagent followed by TMSCl gave only a 44% yield of compound **10**. Likewise the one pot sequential difunctionalization of **9** gave only a 47% yield of compound **11**. By contrast, the same treatment of N,N-diethylbenzamide **1** gave a 90% yield of disubstituted product **3**. Similar results were reported by Sineckus for the lithiation of N,N-diethyl phthalamide.[13] Treatment of N,N-diethyl phthalamide with 1.0 equivalent of s-BuLi/TMEDA in THF at −78℃ followed by a TMSCl quench gave only starting material. The use of 2.2 equivalents of lithiating agent gave 52% of monosilylated and 20% of disilylated products. But the use of 3.0 equivalents of lithiating agent gave disilylated phthalamide in 64% yield.

The dilithiation of tris-tertiary benzamide **21** turned out to be extremely difficult. Under a wide variety of reaction conditions the monosubstituted product always predominated. Even the stepwise difunctionalization was unsuccessful. This can be explained as follows: First, the relay of steric hindrance from one end of the terphenyl unit to the other might be critical. Once one side is lithiated or substituted, the bulky diethyl groups could force the other amide groups to be oriented in the wrong direction for the second lithiation. The bigger the electrophile is, the more serious this effect becomes (MOM *vs.* TMS). Secondly, the charge-dipole interaction between the lithium cation and the carbonyl oxygens might also be an unfavorable factor for dilithiation. The gas phase binding energy of N,N-dimethylformamide toward lithium ion is reported to be about 50 kcal/mole.[19] ^{1}H-NMR studies have show that the activation energy for internal rotation of N-CO bond in N,N-dimethylacetamide is increased by 2.3 kcal/mole on 1 : 1 complexation with lithium ion, which implies strong binding between the carbonyl oxygen and lithium ion.[20]

Among the three conformational isomers (**A**, **B**, **C**) in Figure 1, conformation **A** becomes the most stable when lithium ion is present, due to the converging carbonyl oxygens which can cooperatively bind the lithium ion (but the exact aggregation state of alkyllithium in solution is not well known).[21] Lithiation of the aromatic ring can occur only by breaking

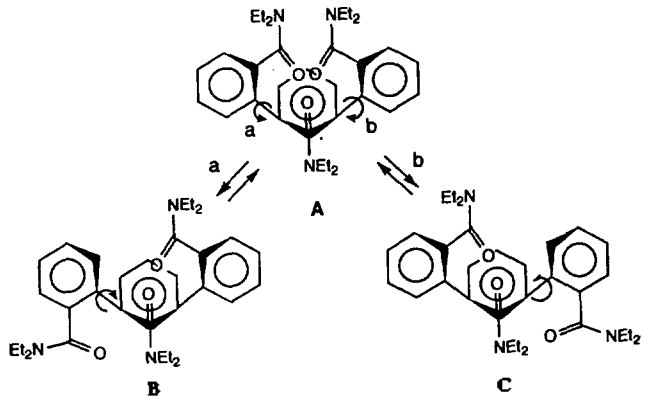


Figure 1. The Proposed Isomerization among the Three Conformers of **21**.

up the complex between conformer **A** and the lithiating agent. In fact, the use of 1.2 equivalent of lithiating reagent gave only recovered starting material. Examination of CPK molecular models suggests that conformer **A** is further enforced to be a stable complex with Li^+ by the presence of bulky substituents in the 3 and 3″ positions of the terphenyl unit.

Conclusion

The direct ortho functionalization of oligomeric tertiary benzamides is dependent on the chain length. Tertiary benzamide **1** can be o,o-dilithiated only by metal-halogen exchange of the 2,6-dihalo-compound. Bis-tertiary benzamide **9** can be o,o′-dilithiated with excess (4.1 equivalents) s-BuLi/TMEDA as the lithiating agent. Tris-tertiary benzamide **21** is hard to o,o″-difunctionalize due to steric interactions among the tertiary benzamide functional groups, and due to steric interactions betwen these functional groups and others (if present) on the termini of the terphenyl unit. The ability of three carbonyl oxygens of **21** to cooperatively bind lithium ion may also contribute to the difficulties which were encountered in attempts to difunctionalize this compound. Good yields were usually obtained in Suzuki aryl-aryl coupling reaction, even when both coupling partners had an ortho tertiary benzamide functional group. The reaction of suitably pre-functionalized coupling partners would be a potentially useful method for the preparation of difunctionalized terphenyls.

Experimental

General. All chemicals were reagent grade and purchased from common vendors. Where necessary, chemicals were purified according to procedures reported.[22] THF and diethyl ether were freshly distilled from sodium benzophenone ketyl prior to use. Where anhydrous CH_2Cl_2 was needed, it was distilled twice over calcium hydride. All anhydrous reactions were conducted under an argon atmosphere. Flash chromatography was carried out using silica gel 60 (E. M. Merch, particle size 0.040-0.063 mm, 230-400 mesh ASTM). Gravity columns were packed with silica gel 60 (E. M. Merck, Particle size 0.063-0.200 mm, 70-230 mesh ASTM). Preparative thin layer chromatography was effected on 0.5 mm, 1 mm or 2 mm silica gel plates (E. M. Merck, 60 F254) or 1 mm reverse phase silica gel plates (PLKC 18F, Whatman). Thin layer chromatography was conducted on plastic-backed precoated silica gel plates (E. M. Merch, F254, 0.2 mm thickness). Melting points below 240℃ were measured on Thomas-Hoover melting point apparatus. Those above 240℃ were measured on Mel-Temp apparatus. All melting points are uncorrected. Infra-red spectra were obtained on Perkin-Elmer 297 grating spectrophotometer (KBr pellets). Mass spectrum was obtained on an AE1 model MS-9 double focusing spectrometer interfaced by Kratos Company to a Data General Nova 3. Regular mass spectra were recorded at 16 or 70 eV at the temperatures indicated. FAB mass spectra were recorded using xenon ionization techniques on a ZAB SE instrument using m-nitrobenzyl alcohol (NOBA) as matrix. Proton NMR spectroscopy were obtained in $CDCl_3$ solution at 200.1 MHz on a Bruker WP-200 spectrometer unless otherwise specified. Carbon-13 NMR spectroscopy were obtained on a Bruker AF-200 in $CDCl_3$ solution unless otherwise specified. All proton chemical shifts (δ values) are reported in parts per million using tetramethyl silane at 0.00 ppm or chloroform at 7.24 ppm as references. Coupling constants are reported in hertz (Hz) and splitting patterns are designated as s(singlet), d(doublet), t(triplet), q(quartet), and m(multiplet). Splitting pattern designations preceeded by "b" indicate the peaks to be slightly broadened.

2,6-Bis(trimethylsilyl)-N,N-diethylbenzamide (3)[12]. Dry THF (150 m*l*), TMEDA (8.7 m*l*, 57.6 mmol), and s-BuLi (45 m*l*, 63 mmol, 1.4 M in cyclohexene) were mixed in 1-L round-bottom flask and cooled to −78℃. A solution of N,N-diethylbenzamide (10.0 m*l*, 57.9 mmol) and THF (50 m*l*) was added with stirring over 10 min. After an additional stirring for 45 min the reaction was quenched at −78℃ with TMSCl (8.0 m*l*, 63.0 mmol). The reaction mixture was slowly warmed to room temperature. Meanwhile THF (150 m*l*), TMEDA (8.7 m*l*), and 1.4 M s-BuLi (45.0 m*l*) were combined in another 1 L round-bottom flask equipped with a 500 m*l* dropping funnel and cooled to −78℃. The reaction mixture in the first 1 L round-bottom flask was cannulated into the dropping funnel, then added to the cooled lithiating reagent over 20 min. The whole mixture turned black. It was stirred for 45 min then quenched with 8.0 m*l* (63.0 mmol) of TMSCl. After stirring for an additional 15 min, the solution was warmed to room temperature, then the solution turned transparent yellow. Water (10 m*l*) was added. The solution was concentrated under reduced pressure and the residue was partitioned between Et_2O (250 m*l*) and water (100 m*l*). The organic phase was separated and the aqueous phase was extracted with Et_2O (50 m*l*). The combined organic phases were dried with brine then with anhydrous $MgSO_4$. Analysis of the reaction mixture by TLC showed no starting material, traces of monosubstituted compound **2**, and mainly disubstituted compound **3**. The solvent was evaporated under reduced pressure. An analytical sample was purified by chromatography on a 2 mm-preparative TLC plate (silical gel, 3% EtOAc in CH_2Cl_2. The rest of the product was stirred at room temperature at 30 torr overnight, and used for the next step. The yield was 90% (18.6 g oil): IR (neat) 3000, 1650, 1450, 1280, 870; ^{1}H-NMR ($CDCl_3$) δ 0.26 (s, 18H Si-CH_3), 0.97 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.28 (t, 3H, J=7.0 Hz, CH_2CH_3), 3.06 (q, 2H, J=7.0 Hz, CH_2CH_3), 3.56

(q, 2H, J=7.0 Hz, CH_2CH_3), 7.30 (t, 1H, J=7.5 Hz, Ar-*H*) 7.55 (d, 2H, J=7.5 Hz, Ar-H); MS m/e (relative intensity) 321 (3.0, M^+), 306 (100, M^+-CH_3), 249 (59.5, M^+-NEt_2).

2,6-Diiodo-N,N-diethylbenzamide (4). In a 500 m*l* round-bottom flask, CCl_4 (250 m*l*), compound **3** (10 g, 31.2 mmol), and ICl (6.5 g) were combined. The dark violet solution was refluxed for 5 h and cooled to 25℃. Saturated aq. $NaHSO_3$ solution (30 m*l*) was added to destroy the excess ICl then the solution was stirred for 1 h. The reaction mixture was washed twice with water (100 m*l*), dried with brine, and then with anhydrous $MgSO_4$. The filtered organic solution was concentrated, and hexane (100 m*l*) was added. The product was obtained as fine white crystals which were collected by filtration and then washed with pentane (12.3 g, 91.8%): mp. 110-110.5℃ (lit.[13] 112-114℃); IR (KBr) 3005, 2970, 2900, 1641, 1425, 1300, 785; ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, 3H, J=7.3 Hz, CH_2CH_3), 1.32 (t, 3H, J=7.3 Hz, CH_2CH_3), 3.17 (q, 2H, J=7.3 Hz, CH_2CH_3), 3.61 (q, 2H, J=7.3 Hz, CH_2CH_3), 6.70 (t, 1H, J=7.9 Hz, Ar-*H*), 7.79 (d, 2H, J=7.9 Hz, Ar-*H*); MS m/e (relative intensity) 429 (54.6, M^+), 357 (100, M^+-NEt_2), 302 (98.5, M^+-I); Anal. Calcd. For $C_{11}H_{13}I_2NO$: C, 30.79; H, 3.05; N, 3.26. Found: C, 30.79; H, 3.03; N, 3.27.

2-Iodo-6-trimethylsilyl-N,N-diethylbenzamide (6). In a 500 m*l* round-bottom flask compound **4** (3.0 g, 6.99 mmol) was dissolved in THF (200 m*l*) and cooled to −78℃. n-BuLi (3.0 m*l*, 7.5 mmol, 2.5 M in hexane) was added. The solution was stirred for 15 min, then quenched with TMSCl (0.9 g, 8.3 mmol). After an additional 20 min at −78℃ the solution was warmed to room temperature. Water (10 m*l*) was added, and the mixture was stirred for 20 min. The solution was washed with brine twice, and the organic phase was dried over anhydrous $MgSO_4$. The solution was concentrated under reduced pressure. The residue was flash chromatogaphed (silica gel, 5×25 cm, CH_2Cl_2 then 5% EtOAc in CH_2Cl_2) to give 1.91 g (73%, oil) of product: IR (neat) 3000, 2940, 1650, 1450, 1300, 1125, 1070, 850, 775; ^{1}H-NMR ($CDCl_3$) δ 0.26 (s, 9H, Si-CH_3), 1.13 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.33 (t, 3H, J=7.0 Hz, CH_2CH_3), 3.11-3.91 (m, 4H, 2×CH_2CH_3), 7.00 (t, 1H, J=7.5 Hz, Ar-*H*), 7.55 (d, 1H, J=7.5 Hz, Ar-*H*), 7.80 (d, 1H, J=8.1 Hz, Ar-*H*); ^{13}C-NMR (500 NHz, $CDCl_3$), 0.03 (Si-CH_3), 12.31, 13.42 (CH_2CH_3); 38.99, 43.48 (CH_2CH_3); 95.14, 129.10, 134.68, 139.78, 139.97, 146.84 (aromatic C); 170.77 (*C*=O); MS m/e (relative intensity) 375 (5.8, M^+), 360 (100, M^+-CH_3), 303 (58.6, M^+-TMS); Anal. Calcd. for $C_{14}H_{22}$ INOSi: C, 44.80; H, 5.91; N, 3.73. Found: C, 44.87; H, 6.03; N, 3.65.

2-Iodo-6-methoxymethyl-N,N-diethybenzamide (7). This compound was prepared by the same procedure as that described for the preparation of compound **6** except that MOMBr (9.0 m*l*, 11 mmol) was used in place of TMSCl. Yield: 65% (1.58 g, oil): IR (neat) 3000, 1640, 1460, 1300 700; ^{1}H-NMR ($CDCl_3$) δ 1.11 (t, 3H, J=7.2 Hz, CH_2CH_3), 1.30 (t, 3H, J=7.2 Hz, CH_2CH_3), 3.08-3.71 (m, 4H, 2×CH_2CH_3), 3.38 (s, 3H, CH_2OCH_3): 4.39 (d, 2H, CH_2OCH_3), 7.05 (t, 1H, J=7.6 Hz, Ar-*H*), 7.45 (d, 1H, J=7.6 Hz, Ar-*H*), 7.73 (d, 1H, J=7.9 Hz, Ar-*H*); ^{13}C-NMR (500 MHz, $CDCl_3$): 12.30, 13.35 (CH_2CH_3); 38.47, 42.85 (CH_2CH_3); 58.48 (CH_2OCH_3), 71.95 (CH_2OCH_3), 93.25, 128.13, 129.76, 136.63, 138.08, 141.13 (aromatic C); 168.69 (*C*=O); MS m/e (relative intensity) 347 (30.2, M^+), 332 (28.2, M^+-CH_3), 275 (100, M^+-NEt_2); Anal. Calcd. for $C_{13}H_{18}INO_2$: C, 44.97; H, 5.23; N, 4.03. Found: C, 45.06; H, 5.27; N, 4.03.

2-Formyl-6-trimethylsilyl-N,N-diethylbenzamide (8). Compound **2** (1.0 g, 4.0 mmol) was dissolved in THF (40 m*l*) in a 100 m*l* round-bottom flask. The solution was cooled to −78℃. To this solution TMEDA (0.7 m*l* 4.6 mmol) and s-BuLi (3.5 m*l*, 4.9 mmol, 1.4 M in cyclohexane) were added. After stirring for 20 min at −78℃, the solution was warmed to −40℃, and stirred at this temperature for 20 min. The reaction was quenched with 4-formylmorpholine (3.0 m*l*, 29.8 mmol). The solution was stirred for 20 min at −40℃ then poured into 50 m*l* of stirred 2 N HCl. Ether (50 m*l*) and brine (50 m*l*) were added to the solution and the organic phase was separated. The organic phase was dried with brine then with anhydrous $MgSO_4$. The solution was concentrated to give. 1.1 g of crude product (oil, 99%): IR (neat) 3010, 1705, 1650, 1450, 1250; ^{1}H-NMR ($CDCl_3$) δ 1.00 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.34 (t, 3 H J=7.0 Hz, CH_2CH_3), 3.04-3.88 (m, 4H, 2×CH_2CH_3), 7.50 (t, 1H, J=7.5 Hz, Ar-*H*), 7.84 (d, 1H, J=6.1 Hz, Ar-*H*), 7.93 (d, 1H, J=7.9 Hz, Ar-*H*), 10.06 (s, 1H, *CH*O); High Resolution MS (175℃, 70 eV) Calcd. for $C_{15}H_{23}NO_2Si(M^+)$: 277.1498. Found: 277.1516 (0.4%), Calcd for $C_{14}H_{20}NO_2Si(M^+$-$CH_3)$: 262.1263 Found: 262.1240 (49.1%).

N,N,N′,N′-Tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (9). Diphenic acid (50.0 g, 0.21 mol) was dissolved in $SOCl_2$ (100 m*l*) and benzene (300 m*l*) was added. The solution was refluxed overnight, then the solvents were evaporated under reduced pressure. The residue was dissolved in dry benzene (150 m*l*), and the solvent was evaporated. An additional benzene (150 m*l*) was added and evaporated again. The residue was dissolved in THF (400 m*l*) and the solution was cooled to 0℃. A mixture of Et_2NH (124.2 m*l*, 1.2 mol) and THF (150 m*l*) was added slowly *via* a 500 m*l* pressure equalizing dropping funnel. The mixture was stirred for 5 h at room temperature then poured into dilute HCl. The organic phase was separated and the aqueous phase was extracted with ether (2×100 m*l*). The combined organic phases were dried with brine, then with anhydrous $MgSO_4$. The product was purified by flash chromatography (7.5×28 cm, CH_2Cl_2 and then 1/1 EtOAc/CH_2Cl_2). Fractions corresponding to product were combined and the solvent was evaporated at reduced pressure. The residue was crystallized from ether to give 66.5 g (91.4%) of crystalline **9**: mp. 141-143℃; ^{1}H-NMR ($CDCl_3$) δ 0.99 (t, 6H, J=7.0 Hz, 2×CH_2CH_3), 1.01 (t, 6H, J=7.0 Hz, 2×CH_2CH_3), 3.06-3.74 (m, 8H, CH_2CH_3), 7.34 (s, 8H, Ar-*H*).

N,N,N′,N′-Tetraethyl-3-trimethylsilyl-[1,1′-biphenyl]-2,2′ dicarboxamide (10). Compound **9** (12.0 g, 34.1 mmol) was dissolved in THF (100 m*l*), and this solution was added to a −78℃ mixture of THF (150 m*l*), TMEDA (5.2 m*l*, 34.5 mmol), and 1.2 M s-BuLi (34.1 m*l*, 40.9 mmol). The resulting solution was stirred for 40 min at −78℃ then quenched with TMSCl (5.0 m*l*, 39.4 mmol). The mixture was allowed to warm to room temperature for 2 h then water (10 m*l*) was added. After stirring for an additional 30 min, brine (50 m*l*) and ether (100 m*l*) were added. The organic phase was separated. The aqueous phase was extracted with ether (100 m*l*) and the combined organic phases were dried with anhydrous $MgSO_4$. The solvent was evaporated. The residue was purified by dry column chromatography (2″×60 cm, 2% EtOAc in CH_2Cl_2) to give 6.4 g (44%) of white fluffy solid **10** after crystallization from pentane: mp. 110-113℃;

IR (KBr): 3020, 2970, 2900, 1640, 1480, 1440, 1321, 1300, 860, 843, 785, 760; ^{1}H-NMR ($CDCl_3$) δ 0.28 (s, 9H, Si-CH_3), 0.65 (t, 3H, J=7.0 Hz, CH_2CH_3), 0.90 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.15 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.22 (t, 3H, J=7.0 Hz, CH_2-CH_3), 2.75-3.90 (m. of q., 8H, J=7.0 Hz, CH_2CH_3), 7.03-7.55 (m 7H, Ar-*H*); MS m/e (relative intensity) 424 (100, M^+), 409 (47.6, M^+-CH_3), 352 (14.3, M^+-NEt_2), 351 (29.9, M^+-TMS), 324 (20.9, M^+-$CONEt_2$); Anal. Calcd. for $C_{25}H_{36}N_2O_2Si$: C, 70.71; H, 8.54; N, 6.60. Found: C, 70.89; H, 8.67; N, 6.66.

N,N,N′,N′-Tetraethyl-3-3′-bis(trimethylsilyl)-[1,1′-biphenyl]-2,2′-dicarboxamide (11). Compound **9** (4.0 g, 11.4 mmol) and TMEDA (7.1 m*l*, 47.0 mmol) were dissolved in THF (300 m*l*) and the solution was cooled to −78℃. A 1.3 M solution of s-BuLi in cyclohexane (36.0 m*l*, 46.8 mmol) was added over 10 min and the mixture was stirred for 1 h. The reaction was quenched with 5 ml (39.4 mmol) of TMSCl. After stirring for an additional 15 min at −78℃ the mixture was allowed to room temperature for 1 h. Water (10 m*l*) was added and the whole mixture was concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 (100 m*l*) and water (100 m*l*). The organic phase was dried with brine, and then with anhydrous $MgSO_4$. The filtered organic phase was concentrated and the residue was crystallized from pentane to give **11** (5.1 g, 90%): mp. 121.5-122.3℃; IR (KBr) 3000, 1640, 1480, 1300, 1260, 1120, 842, 780, 760; ^{1}H-NMR ($CDCl_3$) δ 0.26 (s, 18H, Si-CH_3), 0.60-1.20 (b.s, 12H, CH_2CH_3), 2.80-3.80 (m, 8H, CH_2CH_3), 7.23-7.30 (m, 4H, Ar-*H*), 7.53 (d, 2H, J=8.8 Hz, Ar-*H*); MS m/e (relative intensity) 496 (13.5, M^+), 481 (12.0, M^+-CH_3), 424 (7.6, M^+-NEt_2), 423 (16.7, M^+-TMS); Anal. Calcd. for $C_{28}H_{44}N_2O_2Si_2$: C, 67.69; H, 8.93; N, 5.64. Found: C, 67.90; H, 9.01; N, 5.69.

N,N,N′,N′-Tetraethyl-3,3′-dimethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (12). Procedure described for the preparation of **11** was followed except that the reaction was quenched with 6.0 g (42 mmol) of CH_3I. The product was crystallized from a mixture of CH_2Cl_2 and hexane (4.0 g, 92.6%): mp. 125-127℃; IR (KBr): 3000, 2900, 1630, 1435, 1295; ^{1}H-NMR ($CDCl_3$) δ 1.00 (t, 12H, J=7.3 Hz, CH_2CH_3), 2.31 (s, 6H, Ar-CH_3), 3.00-3.70 (m, 8H, CH_2CH_3), 7.15-7.22 (m, 6H, Ar-*H*); MS m/e (relative intensity) 380 (2.8, M^+); Anal. Calcd. for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36. Found: C, 75.49; H, 8.77; N, 7.22.

3,3′-Bis(methoxymethyl)-N,N,N′,N′-tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (13). Procedure described for the preparation of **11** was followed with the following variations: The reaction was quenched with MOMBr (5.0 m*l*, 61.3 mmol). The excess MOMBr was destroyed with 5 m*l* of 7 M aq. NH_4OH. The product was crystallized from pentane as a white powder (4.4 g, 88%): mp. 98.5-99.5℃; IR (KBr) 3010, 1960, 2910, 1640, 1450, 1300, 1120, 790; ^{1}H-NMR ($CDCl_3$) δ 0.99 (t, 12H, J=6.7 Hz, CH_2CH_3), 3.13-3.64 (m of q, 8H, CH_2CH_3), 3.39 (s, 6H, OCH_3), 4.43 (d, 2H, J=3.5 Hz, Ar-CH_2O), 7.31 (d, 4H, J=5.3 Hz, Ar-*H*), 7.47 (t, 2H, J=4.6 Hz, Ar-*H*); MS m/e (relative intensity) 440 (17.5, M^+), 425 (18.1, M^+-CH_3); Anal. Calcd. for $C_{26}H_{36}N_2O_4$: C, 70.88; H, 8.24; N, 6.36. Found: C, 70.83; H, 8.31; N, 6.40.

3,3′-Diiodo-N,N,N′,N′-tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (14). Procedure described for the preparation of **11** was followed with the following variations: The reaction was quenched with a solution of I_2 (15 g, 59 mmol) and THF (50 m*l*). The excess I_2 was destroyed with saturated aq. Na_2SO_3 solution. The mixture was dried with brine (2× 200 m*l*) and then with anhydrous $MgSO_4$. The solvent was evaporated and the residue was subjected to column chromatography (silica gel, 5×30 cm, CH_2Cl_2 then 10% EtOAc in CH_2Cl_2). The fractions corresponding to product were concentrated to give 4.82 g (70.2%) of **14** as a white powder. A small sample was recrystallized from a mixture of CH_2Cl_2 and hexane for elemental analysis: mp. 152-154℃; IR (KBr) 3000, 2975, 1645, 1475, 1390, 1310, 770; ^{1}H-NMR ($CDCl_3$) δ 0.99-1.20 (m, 12H, CH_3), 3.05-3.60 (m, 8H, CH_2), 7.01 (t, 2 H, J=8.0 Hz, Ar-*H*), 7.39 (s, 2H, Ar-*H*), 7.81 (d, 2H, J=8.0 Hz, Ar-*H*); MS m/e (relative intensity) 604 (48.4, M^+), 532 (34, M^+-NEt_2), 477 (55.9, M^+-I); Anal. Calcd. for $C_{22}H_{26}I_2N_2O_2$: C, 43.73; H, 4.34; N, 4.64. Found: C, 43.84; H, 4.34; N, 4.65.

3,3′-Bis(bromomethyl)-N,N,N′,N′-tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (15) Compound **13** (7.0 g, 15.9 mmol) was dissolved in CH_2Cl_2 (150 m*l*) and the solution was cooled to −78℃. BBr_3 (12.0 m*l*, 126.9 mmol) was added and the solution was stirred overnight at room temperature. Upon addition of the BBr_3 a white precipitate formed. This precipitate redissolved as the solution warmed up to give a pale yellow solution. As the tempertature of the reaction approached 25℃, a new precipitate formed. The excess reagent was quenched with 2 N HCl (5 m*l*), and the solution was filtered through a medium fritted funnel. The filtrate was washed with water, brine, and then dried with anhydrous $MgSO_4$. The solution was concentrated, and the product was purified by dry column chromatography (2″×50 cm, 5% EtOAc in CH_2Cl_2, the mixture was loaded on two columns). The product was obtained in 53.8% (4.6 g) yield after crystallization from a mixture of CH_2Cl_2 and EtOAc: mp. 154.0-154.5 ℃; IR (KBr): 3000, 2700, 1625, 1400; ^{1}H NMR ($CDCl_3$) δ 1.05 (t, 12H, J=7.1 Hz, CH_2CH_3), 3.19-3.66 (m. of q, 8H, J=7.1 Hz, CH_2CH_3), 4.52 (q, 4H, Ar-CH_2Br), 7.32 (d, 4H, J=4.6 Hz, Ar-*H*), 7.50 (t, 2H, J=4.6 Hz, Ar-*H*); MS m/e (relative intensity) 538 (0.7, M^+); Anal. Calcd. for $C_{24}H_{30}Br_2N_2O_2$: C, 53.55; H, 5.62; N, 5.20; Br, 29.69. Found: C, 53.58; H, 5.69; N, 5.12; Br, 29.75.

3-Bromo-N,N,N′,N′-tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (16) Compound **10** (5.0 g, 11.8 mmol) was dissolved in CH_2Cl_2 (200 m*l*) and Br_2 (2.3 g, 14.4 mmol) was added. The mixture was refluxed for 5 h and the excess Br_2 was destroyed with aq. $NaHSO_3$ solution. The mixture was concentrated, and the residue was partitioned between CH_2Cl_2 (150 m*l*) and water (100 m*l*). The organic phase was dried with brine, then with anhydrous $MgSO_4$. The solution was concentrated, and the product was purified by dry column chromatography (2″×40 cm, 5% then 10% EtOAc in CH_2Cl_2, the mixture was loaded on two columns) to give 2.5 g (49.2%) of **16** after recrystallization from a mixture of CH_2Cl_2 and hexane: mp. 130-133℃; IR (KBr) 3000, 2900, 1640, 1445, 1290, 770; ^{1}H-NMR ($CDCl_3$) δ 0.9-1.2 (m. of t, 12H, CH_3), 3.0-3.9 (m. of q, 8H, CH_2), 7.1-7.6 (m, 7H, Ar-*H*); MS m/e (relative intensity) 432 (18.6, M^+, ^{81}Br), 430 (18.7, M^+, ^{79}Br), 351 (11.8, M^+-Br); Anal. Calcd. for $C_{22}H_{27}BrN_2O_2$: C, 61.26; H, 6.31; N, 6.49. Found: C, 61.19; H, 6.30; N, 6.45.

3-Iodo-N,N,N′,N′-tetraethyl-[1,1′-biphenyl]-2,2′-dicarboxamide (17). Compound **10** (5 g, 11.8 mmol) and ICl (2.0 g, 12.0 mmol) were dissolved in CCl_4 (50 m*l*), and the solution was refluxed for 4 h. The mixture was cooled to 25℃ and saturated aq. $NaHSO_3$ (10 m*l*) was added. After

stirring for 30 min the reaction mixture was washed with water (2×50 m*l*). The separated aqueous layers were extracted with CH_2Cl_2 (20 m*l*). The combined organic phases were dried with brine, and then with anhydrous $MgSO_4$. The solution was concentrated under reduced pressure and the product was crystallized from hexane in 80.3% yield (4.53 g): mp. 130-132℃; IR (KBr) 3000, 2900, 1633, 1448, 1295, 1120, 760; ^{1}H-NMR ($CDCl_3$) δ 0.88-1.17 (m. of t, 12H, J=7.0 Hz, CH_2CH_3), 2.95-3.77 (m. of q, 8H, J=7.0 Hz, CH_2CH_3), 6.97-7.79 (m, 7H, Ar-*H*); MS m/e (relative intensity) 478 (44.6, M^+), 278 (20.6, M^+-$CONEt_2$); Anal. Calcd. for $C_{22}H_{27}IN_2O_2$: C, 55.24; H, 5.69; N, 5.86. Found: C, 55.22; H, 5.65; N, 5.84.

[2,2′-Bis[(diethylamino)carbonyl][1,1′-biphenyl]-3-yl]-boronic acid (18). Compound **10** (4 g, 9.4 mmol) was dissolved in CH_2Cl_2 (150 m*l*) and the solution was cooled to −78℃. BBr_3 (5.36 m*l*, 56.6 mmol) was added over 10 min. The mixture was stirred at room temperature for two days then 6 N HCl (20 m*l*) was cautiously added over 20 min. The whole mixture was stirred overnight. Brine (100 m*l*) was added, and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (100 m*l*), and the combined organic phases were washed with brine. The organic phase was washed with 2 N NaOH (2×100 m*l*), and the combined aqueous phases were washed with 150 m*l* of ether. The aqueous phase was acidified to pH 4 with 6 N HCl. The product was extracted with CH_2Cl_2 (150 m*l*, twice). The combined organic extracts were washed with brine and filtered through phase-separating filter paper. The solution was concentrated at reduced pressure and the residue was dissolved in ether (150 m*l*). The product was crystallized from the solution as a white powder (1.54 g, 40%): mp. 184-185℃; IR (KBr) 3540, 3250, 3000, 2970, 1640, 1425, 1380, 1300, 790; ^{1}H-NMR ($CDCl_3$) δ 0.73-1.24 (m. of t, 12H, CH_2CH_3), 3.35 (bs., 8H, CH_2CH_3), 6.30 (s, 2H, $B(OH)_2$, exchange with D_2O), 7.17-7.91 (m, 7H, Ar-*H*); MS m/e (relative intensity) 396 (2.3, M^+, the highest peak); Anal. Calcd. for $C_{22}H_{29}BN_2O_4$: C, 66.68; H, 7.38. Found: C, 66.64; H, 7.50.

2-Iodo-N-N-diethylbenzamide (19). The compound 2-iodobenzoic acid (25 g, 100.8 mmol), thionyl chloride (15 m*l*, 205.6 mmol), and benzene (150 m*l*) were refluxed for 5 h. The solution was concentrated at reduced pressure and the residue was dissolved in benzene (150 m*l*). The solvent was evaporated and the residue was dissolved in benzene (150 m*l*) again. The solvent was evaporated and the residue was dissolved in THF (100 m*l*). In a second 1-L round-bottom flask, Et_2NH (30 m*l*, 290 mmol) was dissolved in THF (400 m*l*) and the solution was cooled to 0℃. The acid chloride solution was added to the cooled amine solution *via* a dropping funnel for 15 min with vigorous stirring. The mixture was allowed to warm to room temperature for 3 h. Then the precipitate was removed by filtration. The filtrate was washed successively with 2 N HCl (2×200 m*l*), saturated aq. K_2CO_3 (150 m*l*), and brine. The solution was dried with anhydrous $MgSO_4$, filtered, then concentrated at reduced pressure. The product was dried at 3 torr for 24 h with magnetic stirring to give **19** (27.0 g, 88.5%, oil): ^{1}H-NMR ($CDCl_3$) δ 1.07 (t, 3H, J=7.5 Hz, CH_3), 1.29 (t, 3H, J=7.5 Hz, CH_3), 3.11-4.00 (m, 4H, CH_2), 7.05-7.82 (m, 4H, Ar-*H*); ^{13}C-NMR (500 MHz, $CDCl_3$) δ 12.42, 13.86 (CH_3); 38.79, 42.67 (CH_2); 92.67, 126.68, 128.12, 129.79, 138.90, 142.68 (aromatic C); 169.71 (C=O); High Resolution MS (130℃, 70 eV) Calcd for $C_{11}H_{14}INO$ (M^+): 303.0122 Found: 303.0130 (79.0%).

[2-(Diethylamino)carbonyl]phenylboronic acid (20). Compound **19** (20.0 g, 66 mmol) was dissolved in THF (250 m*l*) in 500-m*l* round-bottom flask, and the solution was cooled to −78℃. n-BuLi (29.0 m*l*, 72.5 mmol, 2.5 M in hexane) was added over 15 min. The solution was stirred for an additional 15 min and then cannulated into a −78℃ mixture of trimethyl borate (32 m*l*, 282 mmol) and THF (150 m*l*). The mixture was allowed to warm to room temperature for 2 h then 2 N HCl (20 m*l*) was added. After an additional stirring for 2 h, brine (50 m*l*) and ether (200 m*l*) were added, and the organic phase was separated. The aqueous phase was extracted with ether (2×100 m*l*). The combined organic phases were dried with brine and then with anhydrous $MgSO_4$. The solvent was evaporated at reduced pressure, and the residue was dissolved in minimum amount of THF. As ether was added slowly, the product crystallized. The first crop (6.3 g) was collected by filtration. Several additional crops were obtained by concentrating the filtrate at reduced pressure to give 11.7 g (80.3%) of **20**. (A small portion was converted to ester with ethylene glycol in refluxing benzene only for high resolution MS.): mp. 207-208℃; IR (KBr) 3400, 3010, 2900, 1642, 1460, 1400, 1310; ^{1}H NMR (CD_3OD) δ 1.39 (t, 3H, J=7.3 Hz CH_3), 1.49 (t, 3H, J=7.3 Hz, CH_3), 3.79 (q, 2H, J=7.3 Hz, CH_2), 4.00 (q, 2H, J=7.3 Hz, CH_2), 4.84 (s, $B(OH)_2$), 7.46 (t of d, 1H, J_o=7.0 Hz, J_m=2.0 Hz, Ar-*H*), 7.59 (t, 1H, J_o=8.0 Hz, Ar-*H*), 7.64 (d, 1H, J_o=7.0 Hz, Ar-*H*), 7.87 (d, 1H, J_o=8.0 Hz, Ar-*H*); ^{13}C NMR (500 MHz) δ 12.79, 13.88 (CH_3); 54.69, 47.39 (CH_2); 126.54, 127.41, 129.23, 130.98, 133.84 (aromatic C); 172.73 (C=O); High Resolution MS (75℃, 70 eV) Calcd for $C_{13}H_{18}BNO_3$ (ester, M^+); 247.1380, Found; 247.1360 (21.9).

N,N,N′N′,N″,N″-Hexaethyl-[1,1′: 3′,1″: 3″,1‴-terphenyl]-2,2′,2″-tricarboxamide (21). From compounds **4** and **20**: Compound **4** (2.15 g, 5.0 mmol) and tetrakis (triphenylphosphine) palladium (0) (8.9 mg, 0.08 mol %) were dissolved in and EtOH (10 m*l*) were added. The mixture was refluxed overnight and cooled to room temperature. The organic phase was separated and the aqueous phase was extracted with ether (2×20 m*l*). The combined organic phases were dried with brine and then with anhydrous $MgSO_4$. The solvent was evaporated, and the crude mixture was purified by dry column chromatography (silica gel, 2″×50 cm, 10-30% EtOAc in CH_2Cl_2). The product **21** was obtained in 40.2% yield (1.06 g) after crystallization from a mixture of CH_2Cl_2 and hexane.

From compounds **17** and **20**: The procedure described above was used except for the following variations. Compounds **17** (4.0 g, 8.4 mmol), **20** (2.4 g, 10.87 mmol) and toluene (100 m*l*) were used as starting materials. After the solution was refluxed for 20 h, an additional 20 mg of palladium (0) catalyst was added. The mixture was refluxed for an additional 12 h. The product was obtained in 40.8% yield (1.81 g): mp. 151-155℃: IR (KBr) 3000, 2900, 1625, 1435, 1285, 1080, 760; ^{1}H-NMR ($CDCl_3$) δ 0.61 (t, 3H, J=7.0 Hz, CH_2CH_3), 0.87 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.05 (bs, 12H, CH_2CH_3), 3.00-3.95 (m, 12H, CH_2CH_3), 7.33 (s, 11 H^+, Ar-*H*); MS (230℃, 70 eV) m/e (relative intensity) 527 (33.2, M^+), 427 (27.2, M^+-$CONEt_2$); Anal. Calcd for $C_{33}H_{41}N_3O_3$: C, 75.11; H, 7.83; N, 7.96. Found: C, 75.21; H, 7.74; N, 7.96.

3,3″-Bis (bromomethyl)-N,N,N′,N′,N″,N″-hexaethyl-

[1,1′: 3′,1″-terphenyl]-2,2′,2″-tricarboxamide (27). A 1.4 M solution of s-BuLi (21.9 m*l*, 30.6 mmol) and TMEDA (4.6 m*l*, 30.4 mmol) were dissolved in THF (100 m*l*) in a 300-m*l* round-bottom flask. The solution was cooled to −78 ℃. To this solution a mixture of **21** (2.0 g, 3.8 mmol) and THF (50 m*l*) was added over 5 min, and the mixture was stirred for 30 min. The reaction was quenched with MOMBr (3.5 m*l*, 42.8 mmol) then warmed to room temperature. After stirring 2 h the excess MOMBr was destroyed with 7.0 M aq. NH_4OH (1 m*l*). The solvent was evaporated and the residue was partitioned between 2 N HCl (100 m*l*) and CH_2Cl_2 (100 m*l*). The organic phase was separated and washed with water, brine, and drine, and dried with anhydrous $MgSO_4$. The solution was concentrated, and the residue was filtered through silica gel (3×15 cm, 1/1 EtOAc/CH_2Cl_2). The disubstituted product **25** cannot be separated from the monosubstituted compound **22** (ΔR_f=0.0 by 1/1 EtOAc/CH_2Cl_2 on silica gel). The mixture [MS (200℃, 70 eV): 615 (12.6%, M^+ of **25**), 570 (17.9%, M^+ of **22**] was subjected to the next step directly. The mixture was dissolved in CH_2Cl_2 (100 m*l*) and the solution was cooled to 0℃. BBr_3(7 m*l*) was added over 5 min, and the mixture was stirred 12 h. The solution was quenched with 2 N HCl (5 m*l*), and the mixture was filtered through a fine fritted glass funnel. The filtrant was washed with CH_2Cl_2 (100 m*l*). The filterate was washed with water, brine, and dried with anhydrous $MgSO_4$. The solution was concentrated and the residue was purified by a dry column chromatography (2″×80 cm, 20% then 30% EtOAc in CH_2Cl_2). The compound **27** (0.18 g, 6.6% for two steps) was obtained as an off-white solides. A small sample was recrystallized from a mixture of CH_2Cl_2 and EtOH for elemental analysis; mp. 173-175℃; IR (KBr): 3000, 2900, 1625, 1450, 1290; ^{1}H-NMR ($CDCl_3$) δ 0.69 (t, 3H, *J*=7.0 Hz, CH_2CH_3), 0.86 (t, 3H, *J*=7.0 Hz, CH_2CH_3), 1.12 (bs, 12H, CH_2CH_3), 3.13-3.59 (m, 12H, CH_2CH_3), 4.50 (m, 4H, benzylic *H*), 7.12-7.60 (m, 9H, Ar-*H*); MS m/e (relative intensity) 713 (6.8, M^+), 634 (52.3, M^+-Br, ^{81}Br), 632 (49.5, M^+-Br, ^{79}Br); Anal. Calcd. for $C_{35}H_{43}Br_2N_3O_3$: C, 58.91; H, 6.07; Br, 22.40; N, 5.89. Found: C, 59.06; H, 6.06; Br, 22.41; N, 5.77.

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