Detritylation of *N*-Tritylamines via a Naphthalene-Catalyzed Lithiation Process

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Received 23 February 2004

Dedicated to the memory of Prof. Roberto Fernández de Calella

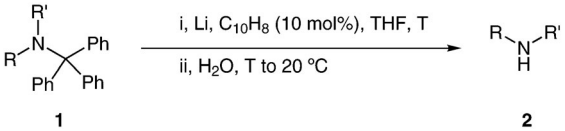
Abstract: The reaction of aliphatic and aromatic secondary and tertiary *N*-tritylamines **1** with lithium powder and a catalytic amount of naphthalene led to reductive detritylation, affording the corresponding amines **2** in good to excellent yields. The trityl group could selectively be removed in the presence of an allyl or a benzyl group. The detritylation process could successfully be extended to several hydroxy, alkoxy and amino functionalized *N*-tritylamines. The chemoselectivity between the trityl–nitrogen and the trityl–oxygen bond cleavages was also studied. This methodology represents an efficient deprotection of *N*-tritylamines under nonacidic reaction conditions.

Key words: tritylamine, lithium, lithiation, detritylation, reductive cleavage

The trityl (triphenylmethyl) group has been used to protect a variety of amines,[1] especially amino acids in the synthesis of peptides[2] and cephalosporins.[3] The role of the trityl group is to create steric hindrance around the nitrogen atom, which reduces the nucleophilicity of the latter. Due to this steric hindrance, the tritylation of the amino functionality of α-amino esters prevents epimerization at the adjacent asymmetric carbon atom and protects the ester from hydrolysis.[1] This protecting group can easily be removed by acid hydrolysis,[1c] but the undesired elimination of tritylamine has been observed in some cases.[4] Alternative detritylation procedures are palladium catalyzed hydrogenolysis,[1c] reduction with sodium in liquid ammonia,[1c] treatment with mercury salts and sodium borohydride[5] and reductive cleavage using triethylsilane[6] or low-valent titanium reagents.[7] Recently, a one-pot reductive transformation of *N*-trityl amines into the corresponding *tert*-butylcarbamates using polymethylhydrosiloxane under palladium catalysis has been reported.[8]

In the last few years, we have been using an arene-catalyzed lithiation[9,10] to prepare organolithium compounds under very mild reaction conditions. The use of an excess of lithium powder and a catalytic amount of an arene [mainly naphthalene or 4,4′-di-*tert*-butylbiphenyl (DTBB)] allowed us to generate simple organolithium compounds starting from nonhalogenated materials,[11] and functionalized organolithium compounds[12] by chlorine–lithium exchange or by ring opening of heterocycles.[13] Using this lithiation methodology, we have been able to achieve the reductive cleavage of carbon–nitrogen bonds in different substrates.[14] We have recently described the reductive detritylation of trityl ethers by a naphthalene catalyzed lithiation process.[15] In this paper, we report the application of this lithiation methodology to the removal of the trityl group in several *N*-tritylamines, which leads to the corresponding deprotected amines under mild reaction conditions.

According to our previous experience in the reductive cleavage of trityl ethers,[15] we first tried to perform the detrytilation of dioctyl(trityl)amine (**1a**) (Table 1, entry 1) at –78 °C. When a solution of **1a** in THF was added to a green suspension of an excess of lithium powder and a catalytic amount of naphthalene (1:0.2 molar ratio) in the same solvent at –78 °C, the reaction mixture took a red color, which could be indicative of the formation of the trityl radical[16] and/or the trityl anion.[17] When the reaction was complete (TLC monitoring), the hydrolysis with water at the same temperature gave a mixture of dioctylamine and triphenylmethane (Equation 1, Table 1, entry 1). The formation of the latter could be explained by protonation of the generated triphenylmethyllithium in the final hydrolysis step. The yield of dioctylamine was 61%, according to a quantitative GC analysis. In order to find the optimum reaction conditions, we performed the reaction at different temperatures (–78, –30 and 0 °C, Table 1, entries 1–3). The highest yield (90%) of dioctylamine was obtained at 0 °C (Table 1, entry 3). 4,4′-Di-*tert*-butylbiphenyl (DTBB) was also tried as an electron carrier, but the yield of dioctylamine was lower than in the naphthalene catalyzed detritylation reaction under the same conditions (compare entries 3 and 4 in Table 1).



1 2

Equation 1

Several other tertiary *N*-tritylamines **1b**–**e** were subjected to the above-mentioned detritylation process under the optimum reaction conditions (naphthalene-catalyzed lithiation at 0 °C) and the results are indicated in Table 1

SYNTHESIS 2004, No. 8, pp 1274–1280
Advanced online publication: 04.05.2004
DOI: 10.1055/s-2004-822358; Art ID: Z03504SS

(entries 5–8). Cyclic amine **1b** gave the expected detritylation product in 91% yield (Table 1, entry 5). The aromatic amine **1c** gave a 94% yield of *N*-methylaniline (Table 1, entry 6). The trityl group could be chemoselectively removed in the presence of an allyl or a benzyl group, which are also prone to undergo reductive cleavage by reaction with lithium.[14] The naphthalene-catalyzed lithiation of substrates **1d** and **1e** afforded the corresponding detritylated amines **2d** and **2e** in 62 and 84% yield, respectively (Table 1, entries 7 and 8).

Table 1 Reductive Detritylation of *N*-Tritylamines **1** by a Naphthalene-Catalyzed Lithiation Process

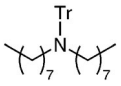
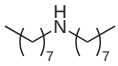
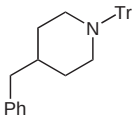
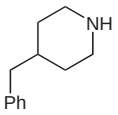
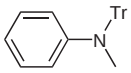
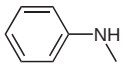
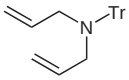
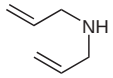
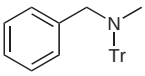
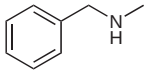
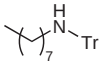
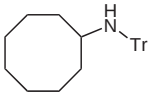
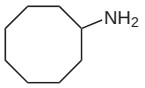
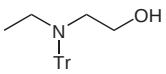
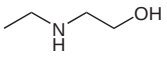
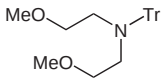
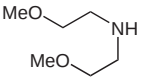
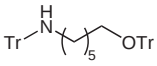
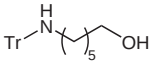
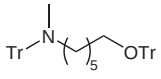
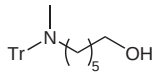
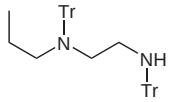
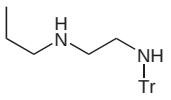
Entry	Substrate	Temp (°C)	Time (h)	Product	Yield (%)[a]
1	 **1a**	–78	4.0	 **2a**	61
2	**1a**	–30	2.0	**2a**	84
3	**1a**	0	3.5	**2a**	90 (86%)[b]
4	**1a**	0	2.0	**2a**	79[c]
5	 **1b**	0	1.0	 **2b**	91
6	 **1c**	0	1.0	 **2c**	94
7	 **1d**	0	6.0	 **2d**	62
8	 **1e**	0	1.0	 **2e**	84
9[d]	 **1f**	0	2.0	 **2f**	78 (37%)[e]
10[d]	 **1g**	0	1.0	 **2g**	87
11[f]	 **1h**	0	4.5	 **2h**	41
12	 **1i**	0	2.0	 **2i**	90
13[f]	 **1j**	0	4.0	 **2j**	80

Table 1 Reductive Detritylation of *N*-Tritylamines **1** by a Naphthalene-Catalyzed Lithiation Process (continued)

Entry	Substrate	Temp (°C)	Time (h)	Product	Yield (%)[a]
14	 **1k**	–78	2.5	 **2k**	92[g]
15[f]	 **1l**	0	4.5	 **2l**	87[g]

[a] Yield determined by quantitative GC, using commercially available amine **2** and *n*-dodecane (internal standard) in the determination of response factors.
[b] Isolated yield after column chromatography (basic aluminum oxide, hexane–EtOAc) based on the starting material **1a** is given in parentheses.
[c] DTBB was used as electron carrier instead of naphthalene.
[d] Compounds **1f** and **1g** were deprotonated with *n*-BuLi and treated with TMSCl before performing the naphthalene-catalyzed lithiation step.
[e] Isolated yield after acid-base extraction is given in parentheses.
[f] Compounds **1h**, **1j** and **1l** were deprotonated with *n*-BuLi before performing the naphthalene-catalyzed lithiation step.
[g] Isolated yield after column chromatography (basic aluminum oxide, hexane–EtOAc) based on the starting material **1**.

Interestingly, our methodology could also be applied to the deprotection of *N*-tritylated primary amines by a slight modification of the general procedure. These substrates possess a proton acidic enough to decompose the naphthalene radical-anion and/or dianion involved in our lithiation reaction. As expected, the lithium amides derived from amines **1f** and **1g** (Table 1, entries 9 and 10; generated by reaction of the amines with *n*-butyllithium) did not react in the lithiation step, the starting tritylated amines being recovered unchanged after hydrolysis. However, when amines **1f** and **1g** were deprotonated with *n*-butyllithium and treated with trimethylsilyl chloride before submitting them to the naphthalene-catalyzed lithiation step, the expected primary amines **2f** and **2g** were obtained after hydrolysis in 78 and 87% yields, respectively (Table 1, entries 9 and 10 and footnote d). The silyl group on nitrogen was also removed during the workup.

The detritylation procedure could successfully be extended to several hydroxy, alkoxy and amino functionalized *N*-tritylamines (Table 1, entries 11–15). *N*-Tritylated amino alcohol **1h** was previously treated with *n*-butyllithium in order to remove the acidic proton of the hydroxy group. The lithiation of the generated lithium alkoxide gave the expected deprotected amino alcohol **2h** in moderate yield (Table 1, entry 11 and footnote f). Complete detritylation of amino alkoxide **1i** was achieved after 2 h, affording secondary amine **2i** in 90% yield (Table 1, entry 12).

Since we have recently achieved the naphthalene-catalyzed reductive cleavage of trityl ethers,[15] we decided to investigate the chemoselectivity of the detritylation process in molecules having both a *N*-trityl and an *O*-trityl group. Thus, compound **1k** was submitted to the naphthalene-catalyzed lithiation reaction at –78 °C (Table 1, entry 14). As expected, product **2k**, resulting from the reductive cleavage of the trityl ether, was selectively obtained in 92% yield. The product of monodetritylation of the nitrogen atom was not detected in the crude reaction mixture.

On the other hand, deprotonation with *n*-butyllithium effectively protected the nitrogen atom from detritylation. The lithiation of the lithium amide derived from **1j** at 0 °C selectively gave the *N*-tritylated amino alcohol **2j** in 80% yield (Table 1, entry 13 and footnote f).

The selectivity of the reductive cleavage of a ditritylated diamine, **1l** (Table 1, entry 15), was also studied. Compound **1l** holds two different amino groups, one of them being secondary and the other one tertiary. According to the result obtained in the lithiation of amino alcohol **1j**, we thought that deprotonation of **1l** with *n*-butyllithium would prevent removal or the trityl group from the secondary amino moiety. As expected, the lithiation of the lithium amide derived from **1l** led, after hydrolysis, to monodetritylated diamine **2l** as the only reaction product in 87% yield (Table 1, entry 15 and footnote f).

In all cases, triphenylmethane was obtained (>90%) as a by-product, resulting from hydrolysis of the triphenylmethyllithium generated during the process, but it could easily be separated from the desired detritylation products by column chromatography.

The starting *N*-tritylamines **1** were prepared by reaction of the corresponding amines with trityl chloride in the presence of triethylamine and a catalytic amount of 4-(dimethylamino)pyridine.

In summary, in this paper we have presented a very efficient method for the removal of the trityl group in *N*-tritylamines via a naphthalene-catalyzed lithiation process. The methodology has proved to be useful for the deprotection of *N*-tritylated primary and secondary amines, including allylic, benzylic and functionalized substrates. Chemoselectivity of *O*-trityl versus *N*-trityl bond cleavage has been observed. Removal of the trityl group from a tertiary amine was selectively achieved in the presence of a *N*-trityl secondary amino moiety. This method represents a good alternative to the commonly used detrityla-

tion procedures for amines, which use acidic reaction conditions.

FT-IR spectra were obtained on a Nicolet Impact 400D spectrophotometer using NaCl plates (for oils) or KBr pellets (for solid compounds). NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS (0.00 ppm, ^{1}H) and $CDCl_3$ (77.0 ppm, ^{13}C) as internal standards; chemical shifts are given in δ (ppm) and coupling constants (*J*) in Hz. ^{13}C NMR assignments were made on the basis of DEPT experiments. Mass spectra (EI) were obtained at 70 eV on a Shimadzu QP-5000 spectrometer, giving fragment ions in *m*/*z* with relative intensities (%) in parentheses. High-resolution mass spectra and elemental analysis were performed by the Technical Services at the University of Alicante. TLC was carried out on Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection was done by UV_{254} light and staining with phosphomolybdic acid (5 g of phosphomolybdic acid in 120 mL of absolute EtOH); R_f values are given under these conditions. Column chromatography was performed using silica gel 60 (35–70 mesh) or basic aluminum oxide (50–160 μm particle size). When mentioned, deactivated silica gel means that it was treated with 5% Et_3N in hexane and the column was eluted with the same solvent mixture until the coming eluent was basic according to pH paper. All reagents used for the synthesis of *N*-tritylamines **1**, naphthalene and trimethylsilyl chloride were commercially available (Acros, Aldrich) and were used without further purification. Li powder was prepared according to the procedure described in Ref.[18] Commercially available *n*-BuLi was titrated with a 1 M solution of *sec*-butyl alcohol in xylene using 1,10-phenanthroline as indicator.[19] Commercially available anhyd THF (99.9%, H_2O content ≤ 0.006%, Acros) was used as solvent in all the lithiation reactions.

N-Tritylamines 1a–j, 1l, 2j and 2l; General Procedure

A solution of the corresponding amine **2** (10.0 mmol) in CH_2Cl_2 (5 mL) was added to a solution of trityl chloride (3.1 g, 11.0 mmol), Et_3N (2.5 mL, 17.6 mmol) and 4-(dimethylamino)pyridine (92 mg, 0.4 mmol) in CH_2Cl_2 (10 mL) at r.t. and the mixture was stirred overnight. The reaction was then quenched with H_2O (5 mL) and extracted with EtOAc (3 × 15 mL) and the combined organic phases were washed with brine (5 mL) and dried (Na_2SO_4). After evaporation of the solvents (15 Torr), the resulting residue was purified by column chromatography (deactivated silica gel, hexane–EtOAc) affording the expected tritylamines **1**. For the preparation of the double tritylated compound **1j**, the amounts of all the reagents and solvent used were doubled, except for the starting amino alcohol 6-aminohexanol, from which 10.0 mmol was utilized. The synthesis of compound **1l** was performed in a two-step sequence: after stirring overnight the mixture of reagents in the proportions indicated above, the same amounts of trityl chloride, Et_3N and 4-(dimethylamino)pyridine were added and the reaction was stirred overnight again. Monotritylated amino alcohol **2j** and diamine **2l** were obtained as by-products in the reactions performed to synthesize ditritylated compounds **1j** and **1l**, respectively, and they could be separated from the latter by column chromatography [deactivated silica gel, hexane–EtOAc (for **2j**) and basic aluminum oxide, hexane–EtOAc (for **2l**)]. The corresponding physical, spectroscopic and analytical data for tritylamines **1a**–**1j**, **1l**, **2j** and **2l** follow.

N,*N*-Dioctyltritylamine (1a)

Colorless oil; yield: 85%; R_f 0.24 (hexane).

IR (neat): 3084, 3057, 3031, 1595, 1488 (HC=C), 1211 cm^{-1} (CN).

^{1}H NMR: δ = 0.87 (t, 6 H, *J* = 6.8 Hz, 2 CH_3), 1.04–1.38, 1.39–1.58 [2 m, 20 H and 4 H, respectively, 2 Me(C*H*$_2$)$_6$], 2.27 (t, 4 H, *J* = 7.8 Hz, 2 CH_2N), 7.07–7.35, 7.38–7.56 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 14.1 (2 C, 2 CH_3), 22.65 (2 C), 27.9 (2 C), 29.25 (2 C), 29.55 (2 C), 30.5 (2 C), 31.8 (2 C) [2 Me(*C*H$_2$)$_6$], 53.45 (2 C, 2 CH_2N), 79.1 (CN), 125.7 (3 C), 127.3 (6 C), 129.4 (6 C), 144.45 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 483 (M$^+$, <1), 294 (14), 288 (11), 254 (12), 244 (86), 243 (100), 228 (12), 211 (17), 166 (12), 165 (85), 105 (20).

HRMS: *m*/*z* calcd for $C_{35}H_{49}N$, 483.3865; found, 483.3867.

4-Benzyl-*N*-tritylpiperidine (1b)[20]

White solid; yield: 86%; mp 194 °C; R_f 0.20 (hexane).

IR (KBr): 3080, 3057, 3023, 1595, 1491 (HC=C), 1216 cm^{-1} (CN).

^{1}H NMR: δ = 1.15–1.83 (m, 7 H, 2 C*H*HN, 2 CH_2CN and C*H*CH$_2$), 2.55 (d, 2 H, C*H*$_2$Ph), 2.91–3.16 (m, 2 H, 2 C*H*HN), 6.96–7.58 (m, 20 H, ArH).

^{13}C NMR: δ = 33.0 (2 C, 2 *C*H$_2$CN), 38.5 (*C*HCH$_2$), 43.5 (*C*H$_2$Ph), 48.55 (2 C, 2 CH_2N), 77.35 (CN), 125.35, 125.75 (3 C), 127.3 (6 C), 128.05 (2 C), 129.0 (6 C), 129.25 (2 C), 140.4, 140.85 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 419 (M$^+$ + 2, <1), 418 (M$^+$ + 1, 1), 417 (M$^+$, 4), 340 (11), 244 (50), 243 (100), 165 (59), 91 (11).

N-Methyl-*N*-tritylaniline (1c)

White solid; yield: 77%; mp 95 °C; R_f 0.47 (hexane–EtOAc, 9:1).

IR (KBr): 3085, 3051, 3031, 1594, 1498 (HC=C), 1194 cm^{-1} (CN).

^{1}H NMR: δ = 3.05 (s, 3 H, CH_3), 6.55–6.77, 6.88–7.01, 7.08–7.33, 7.36–7.51 (4 m, 3 H, 2 H, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 40.95 (CH_3), 77.35 (CN), 117.95, 120.2 (2 C), 126.4 (3 C), 127.7 (8 C), 130.5 (6 C), 144.05 (3 C), 149.9 (ArC).

MS (DIP): *m*/*z* (%) = 349 (M$^+$, <1), 244 (43), 243 (100), 228 (13), 166 (12), 165 (85).

HRMS: *m*/*z* calcd for $C_{26}H_{23}N$, 349.1830; found, 349.1826.

N,*N*-Diallyltritylamine (1d)

White solid; yield: 86%; mp 93° C; R_f 0.28 (hexane).

IR (KBr): 3079, 3055, 3029, 3017, 1635, 1603, 1594, 1487 (HC=C), 1212 cm^{-1} (CN).

^{1}H NMR: δ = 3.05 (d, 4 H, *J* = 6.1 Hz, 2 CH_2N), 4.87–5.05 (m, 4 H, 2 C*H*$_2$=C), 5.78–5.99 (m, 2 H, 2 C*H*=CH$_2$), 7.07–7.34, 7.45–7.63 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 56.2 (2 C, 2 CH_2N], 78.55 (CN), 115.25 (2 C, 2 *C*H$_2$=C), 125.95 (3 C), 127.5 (6 C), 129.3 (6 C), 143.85 (3 C, ArC), 138.65 (2 C, 2 *C*H=CH$_2$).

MS (DIP): *m*/*z* (%) = 340 (M$^+$ + 1, <1), 339 (M$^+$, 1), 244 (45), 243 (100), 228 (10), 166 (10), 165 (71).

HRMS: *m*/*z* calcd for $C_{25}H_{25}N$, 339.1987; found, 339.1973.

Anal. Calcd for $C_{25}H_{25}N$: C, 88.45; H, 7.42; N, 4.13. Found: C, 88.16; H, 7.42; N, 4.45.

N-Benzyl-*N*-methyltritylamine (1e)

White solid; yield: 90%; mp 106–107 °C; R_f 0.14 (hexane).

IR (KBr): 3082, 3052, 1594, 1487 (HC = C), 1199 cm^{-1} (CN).

^{1}H NMR: δ = 1.96 (s, 3 H, CH_3), 3.40 (s, 2 H, CH_2), 7.07–7.42, 7.47–7.68 (2 m, 12 H and 8 H, respectively, ArH).

^{13}C NMR: δ = 37.15 (CH_3), 56.45 (CH_2), 77.6 (CN), 126.0 (3 C), 126.55, 127.5 (6 C), 128.0 (2 C), 128.35 (2 C), 129.4 (6 C), 140.15 (3 C), 142.9 (ArC).

MS (DIP): *m*/*z* (%) = 363 (M$^+$, 1), 244 (59), 243 (100), 166 (12), 165 (87), 91 (30).

HRMS: *m*/*z* calcd for $C_{27}H_{25}N$, 363.1987; found, 363.1972.

***N*-Octyltritylamine (1f)[21]**
White solid; yield: 86%; mp 93 °C; R_f 0.88 (hexane).

IR (KBr): 3332 (NH), 3082, 3057, 3029, 1596, 1489 (HC=C), 1209 cm^{-1} (CN).

^1H NMR: δ = 0.87 (t, 3 H, *J* = 6.7 Hz, CH_3), 1.11–1.36, 1.39–1.66 [2 m, 10 H and 3 H, respectively, Me(CH_2)$_6$ and NH], 2.11 (t, *J* = 6.8 Hz, CH_2N), 7.11–7.36, 7.40–7.57 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 14.1 (CH_3), 22.65, 27.35, 29.25, 29.6, 30.85, 31.85 [Me(CH_2)$_6$], 43.55 (CH_2N), 70.85 (CN), 126.1 (3 C), 127.7 (6 C), 128.65 (6 C), 146.35 (3 C, ArC).

MS: *m*/*z* (%) = 371 (M^+, <1), 294 (18), 244 (19), 243 (69), 242 (22), 241 (25), 239 (16), 166 (18), 165 (100).

***N*-Cyclooctyltritylamine (1g)[20]**
White solid; yield: 97%; mp 55 °C; R_f 0.23 (hexane).

IR (KBr): 3319 (NH), 3087, 3052, 3016, 1594, 1488 (HC=C), 1210 cm^{-1} (CN).

^1H NMR: δ = 1.05–1.65 [m, 15 H, (CH_2)$_7$ and NH], 2.46–2.62 (m, 1 H, CHN), 7.05–7.35, 7.49–7.65 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 24.2 (2 C), 26.05, 27.05 (2 C), 34.65 (2 C) [(CH_2)$_7$], 52.2 (CHN), 71.6 (CN), 126.0 (3 C), 127.6 (6 C), 128.85 (6 C), 147.35 (3 C, ArC).

MS: *m*/*z* (%) = 369 (M^+, <1), 244 (21), 243 (100), 165 (52).

2-(*N*-Ethyltritylamino)ethanol (1h)
White solid; yield: 60%; mp 82 °C; R_f 0.08 (hexane–EtOAc, 9:1).

IR (KBr): 3477 (OH), 3083, 3058, 3028, 1594, 1487 (HC=C), 1209 (CN), 1064 cm^{-1} (CO).

^1H NMR: δ = 1.09 (t, 3 H, *J* = 7.2 Hz, CH_3), 2.41 (q, 2 H, *J* = 7.2 Hz, MeCH_2N), 2.56 (t, 2 H, *J* = 6.6 Hz, CH_2CH_2N), 2.90 (br s, 1 H, OH), 3.78 (t, 2 H, *J* = 6.6 Hz, CH_2O), 7.09–7.37, 7.45–7.58 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 15.8 (CH_3), 47.5 (CH_2Me), 54.6 (CH_2CO), 61.9 (CO), 78.85 (CN), 126.0 (3 C), 127.5 (6 C), 129.3 (6 C), 143.75 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 331 (M^+, <1), 244 (32), 243 (100), 165 (51).

HRMS: *m*/*z* calcd for $C_{23}H_{25}NO$, 331.1936; found, 331.1897.

***N*,*N*-Bis(2-methoxyethyl)tritylamine (1i)**
White solid; yield: 37%; mp 100 °C; R_f 0.30 (hexane–EtOAc, 4:1).

IR (KBr): 3085, 3051, 3032, 1594, 1498 (HC=C), 1195 (CN), 1035 cm^{-1} (CO).

^1H NMR: δ = 2.53 (t, 4 H, *J* = 7.2 Hz, 2 CH_2N), 3.29 (s, 6 H, 2 CH_3), 3.53 (t, 4 H, *J* = 7.2 Hz, 2 CH_2O), 7.07–7.35, 7.42–7.59 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 52.9 (2 C, 2 CH_2N), 58.75 (2 C, 2 CH_3), 72.65 (2 C, 2 CH_2O), 78.65 (CN), 126.0 (3 C), 127.5 (6 C), 129.3 (6 C), 143.65 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 375 (M^+, <1), 244 (63), 243 (100), 228 (12), 166 (12), 165 (85).

HRMS: *m*/*z* calcd for $C_{25}H_{29}NO_2$, 375.2198; found, 375.2219.

***N*-(6-Trityloxyhexyl)tritylamine (1j)**
White solid; yield: 70%; mp 138 °C; R_f 0.11 (hexane).

IR (KBr): 3440 (NH), 3084, 3057, 3018, 1596, 1488 (HC=C), 1210 (CN), 1065 cm^{-1} (CO).

^1H NMR: δ = 1.07–1.71 [m, 9 H, (CH_2)$_4$CO and NH], 1.97–2.17 (m, 2 H, CH_2N), 3.00 (t, 2 H, *J* = 6.5 Hz, CH_2O), 7.10–7.33, 7.36–7.56 (2 m, 18 H and 12 H, respectively, ArH).

^{13}C NMR: δ = 26.2, 27.15, 29.95, 30.95 [(CH_2)$_4$CO], 43.45 (CH_2N), 63.45 (CH_2O), 70.8 (CN), 86.2 (CO), 126.1 (3 C), 126.75 (3 C), 127.65 (6 C), 127.7 (6 C), 128.65 (12 C), 144.45 (3 C), 146.3 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 601 (M^+, <1), 358 (10), 258 (34), 244 (50), 243 (100), 165 (46).

HRMS: *m*/*z* calcd for $C_{44}H_{43}NO$, 601.3345; found, 601.3317.

Anal. Calcd for $C_{44}H_{43}NO$: C, 87.81; H, 7.20; N, 2.33. Found: C, 87.64; H, 7.39; N, 2.84.

***N*-Propyl-*N*,*N*′-ditritylethane-1,2-diamine (1l)**
White solid; yield: 63%; mp 125 °C; R_f 0.30 (hexane–EtOAc, 9:1).

IR (KBr): 3333 (NH), 3082, 3052, 3017, 1594, 1489 (HC=C), 1207 cm^{-1} (CN).

^1H NMR: δ = 0.44 (t, 3 H, *J* = 7.2 Hz, CH_3), 0.96–1.13 (m, 2 H, CH_2Me), 1.78 (br s, 1 H, NH), 1.95–2.10 (m, 2 H, CH_2CH_2Me), 2.30 (t, 2 H, *J* = 7.0 Hz, CH_2CH_2NH), 2.42–2.58 (m, 2 H, CH_2NH), 7.08–7.36, 7.39–7.61 (2 m, 18 H and 12 H, respectively, ArH).

^{13}C NMR: δ = 11.9 (CH_3), 23.4 (CH_2Me), 43.65, 53.95, 55.65 (3 CH_2N), 70.85 (CNH), 78.85 (CN), 125.8 (3 C), 126.15 (3 C), 127.35 (6 C), 127.75 (6 C), 128.6 (6 C), 129.4 (6 C), 144.1 (3 C), 146.15 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 343 (M^+ – 243, <1), 292 (18), 244 (24), 243 (100), 183 (20), 182 (51), 167 (26), 165 (43), 127 (14), 105 (12), 104 (13), 97 (13), 88 (23), 85 (18), 83 (14), 77 (11), 71 (24), 70 (12), 69 (16), 57 (40), 55 (20), 43 (25), 41 (14).

HRMS: *m*/*z* calcd for $C_{43}H_{42}N_2$, 586.3348; found, 586.3367.

6-Tritylamino-1-hexanol (2j)[22]
White solid; yield: 70%; mp 85 °C; R_f 0.45 (hexane–EtOAc, 9:1).

IR (KBr): 3292 (OH and NH), 3081, 3058, 3029, 1594, 1489 (HC=C), 1213 (CN), 1080 cm^{-1} (CO).

^1H NMR: δ = 1.18–1.63 [m, 9 H, (CH_2)$_4$CO and OH], 1.99–2.21 (m, 2 H, CH_2N), 3.54–3.69 (m, 2 H, CH_2O), 7.13–7.37, 7.40–7.58 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 25.7, 27.1, 30.8, 32.65 [(CH_2)$_4$CO], 43.45 (CH_2N), 62.9 (CH_2O), 70.8 (CN), 126.1 (3 C), 127.7 (6 C), 128.6 (6 C), 146.25 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 360 (M^+ + 1, <1), 359 (M^+, 2), 283 (19), 282 (89), 258 (28), 244 (23), 243 (100), 165 (35).

***N*-Propyl-*N*′-tritylethane-1,2-diamine (2l)**
Colorless oil; yield: 25%; R_f = 0.45 (hexane–EtOAc, 4:1).

IR (KBr): 3311 (NH), 3083, 3057, 3029, 1596, 1489 (HC=C), 1209 cm^{-1} (CN).

^1H NMR: δ = 0.90 (t, 3 H, *J* = 7.8 Hz, CH_3), 1.39–1.58 (m, 2 H, CH_2Me), 1.78 (br s, 2 H, 2 NH), 2.28, 2.72 (2 t, 2 H each, *J* = 6.0 Hz each, NCH_2CH_2N), 2.49 (t, 2 H, *J* = 7.3 Hz, CH_2CH_2Me), 7.10–7.35, 7.42–7.60 (2 m, 9 H and 6 H, respectively, ArH).

^{13}C NMR: δ = 11.75 (CH_3), 23.15 (CH_2Me), 43.05, 50.1, 51.6 (3 CH_2N), 70.7 (CN), 126.2 (3 C), 127.75 (6 C), 128.65 (6 C), 146.1 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 344 (M^+, <1), 258 (34), 244 (50), 243 (100), 165 (46).

HRMS: *m*/*z* calcd for $C_{24}H_{28}N_2$, 344.2252; found, 344.2282.

N-Methyl-N-(6-trityloxyhexyl)tritylamine (1k)

n-BuLi (1.6 mL of a 1.6 M solution of *n*-BuLi in hexane, 2.5 mmol) was added dropwise to a solution of tritylamine **1j** (898 mg, 2.5 mmol) in THF (10 mL) at 0 °C. After 10 min, MeI (0.16 mL, 2.5 mmol) was added at 0 °C and the reaction mixture was stirred for 12 h at r.t. The reaction was then quenched with H_2O (5 mL) and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with brine (5 mL) and dried (Na_2SO_4). After evaporation of the solvents (15 Torr), the resulting residue was purified by column chromatography (basic aluminum oxide, hexane–EtOAc) to afford the expected compound **1k** in 58% yield; colorless oil; yield: 58%; R_f 0.61 (hexane–EtOAc, 9:1).

IR (neat): 3084, 3057, 3031, 1596, 1489 (HC = C), 1216 (CN), 1079 cm^{-1} (CO).

^1H NMR: δ = 1.05–1.67 [m, 8 H, $(CH_2)_4CO$], 1.88–2.13 (m, 5 H, CH_2N and CH_3), 3.01 (t, 2 H, *J* = 6.4 Hz, CH_2O), 7.05–7.34, 7.36–7.55 (2 m, 18 H and 12 H, respectively, ArH).

^{13}C NMR: δ = 26.3, 27.3, 28.2, 30.0 [$(CH_2)_4CO$], 37.1 (Me), 52.5 (CH_2N), 63.5 (CH_2O), 76.15 (CN), 86.2 (CO), 125.7 (3 C), 126.75 (3 C), 127.65 (6 C), 127.85 (6 C), 127.9 (6 C), 128.65 (6 C), 144.45 (3 C), 146.8 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 615 (M^+, <1), 258 (14), 257 (66), 244 (20), 243 (100), 165 (26), 44 (13).

HRMS: *m*/*z* calcd for $C_{45}H_{45}NO$, 615.3501; found, 615.3497.

Reductive Cleavage of Tritylamines 1a–e and 1h–l via Naphthalene-Catalyzed Lithiation; Dioctylamine (2a); Typical Procedure

A solution of tritylamine **1a** (1.0 mmol) in THF (2 mL) was added dropwise to a green suspension of Li powder (70 mg, 10.0 mmol) and naphthalene (26 mg, 0.2 mmol) in THF (5 mL), under Ar at 0 ºC. The reaction mixture turned to a dark red color after the addition of a few drops of the solution of **1a**. After stirring at the same temperature for the time indicated in Table 1, H_2O (5 mL) was carefully added, the cooling bath was removed and the reaction mixture was stirred till it reached r.t. The mixture was extracted with EtOAc (3 × 15 mL) and the combined organic phases were washed with brine (5 mL), and then dried (Na_2SO_4). After evaporation of the solvents (15 Torr), the resulting residue was purified by column chromatography (basic aluminum oxide, hexane–EtOAc) to give dioctylamine (**2a)** in 86% yield.

Compounds **1h**, **1j** and **1l** were deprotonated with *n*-BuLi (0.69 mL of a 1.6 M solution in hexane, 1.1 mmol) at 0 °C before submitting them to the reductive cleavage step.

All reactions whose yields were determined by quantitative GC (see Table 1) were hydrolyzed with MeOH (5 mL) instead of H_2O. Commercially available amines **2a**–**e**, **2h** and **2i**, amine **2j** (prepared by us, see above), and *n*-dodecane (internal standard) were used in the determination of response factors. Compounds **2a**–**e**, **2h** and **2i** (commercially available) and **2j** and **2l** (prepared by us, see above) were characterized by comparison of their physical and spectroscopic data with authentic samples. The corresponding physical, spectroscopic and analytical data for compound **2k** follow.

6-(N-Methyl-N-tritylamino)hexan-1-ol (2k)

Colorless oil; yield: 92%; R_f 0.12 (hexane–EtOAc, 9:1).

IR (neat): 3355 (OH), 3087, 3057, 3029, 1596, 1490 (HC=C), 1203 (CN), 1033 cm^{-1} (CO).

^1H NMR: δ = 1.12–1.70 [m, 9 H, $(CH_2)_4CO$ and OH], 1.91–2.12 (m, 5 H, CH_2N and CH_3), 3.54–3.73 (m, 2 H, CH_2O), 7.02–7.60 (m, 15 H, ArH).

^{13}C NMR: δ = 25.85, 27.2, 28.25, 32.7 [$(CH_2)_4CO$], 37.1 (CH_3), 52.5 (CH_2N), 63.0 (CO), 77.95 (CN), 125.75 (3 C), 127.3 (6 C), 127.9 (6 C), 144.45 (3 C, ArC).

MS (DIP): *m*/*z* (%) = 373 (M^+, <1), 258 (13), 257 (59), 244 (21), 243 (100), 165 (31).

HRMS: *m*/*z* calcd for $C_{26}H_{31}NO$, 373.2406; found, 373.2408.

Reductive Cleavage of Tritylated Primary Amines 1f and 1g by a Naphthalene-Catalyzed Lithiation; Octylamine (2f); Typical Procedure

To a solution of **1f** (186 mg, 0.5 mmol) in THF (2 mL), under Ar at 0 ºC, was added dropwise *n*-BuLi until a red color developed in the reaction mixture (0.45 mL of a 1.6 M solution of *n*-BuLi in hexane, 0.7 mmol). After stirring for 10 min, Me_3SiCl was added until the red color vanished (0.15 mL, 1.2 mmol). The mixture was stirred for 10 min and then transferred dropwise via syringe to a green suspension of Li powder (50 mg, 7.2 mmol) and naphthalene (26 mg, 0.2 mmol) in THF (5 mL), under Ar at 0 ºC. The mixture turned to a dark red color. After stirring at the same temperature for the time indicated in Table 1, H_2O (5 mL) was carefully added, the cooling bath was removed and the mixture was stirred until it reached r.t. The mixture was acidified with 2 M HCl (5 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were discarded. The aqueous phase was basified with 2 M NaOH (5 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were dried (Na_2SO_4). Evaporation of the solvents afforded a 37% yield of pure octylamine **2f**. Cyclooctylamine was prepared from the trityl derivative **2g** in the same way.

For the reactions whose yields were determined by quantitative GC (see Table 1, entries 9 and 10), they were hydrolyzed with MeOH (5 mL) instead of H_2O. Commercially available amines **2f** and **2g**, and *n*-dodecane (internal standard) were used in the determination of response factors. Compounds **2f** and **2g** (commercially available) were characterized by comparison of their physical and spectroscopic data with authentic samples.

Acknowledgment

This work was financially supported by the DGES from the Spanish Ministerio de Educación, Cultura y Deporte (MECD) (project no. BQU2001-0538). C. B. thanks the Department of Organic Chemistry of the University of Alicante for a fellowship.

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