Alkaline Sodium Borohydride-Promoted Reductive Alkylation of β-Aminomercurials: Synthesis of 1,5-Functionalized Amines

José BARLUENGA*, Pedro J. CAMPOS, Joaquín LÓPEZ-PRADO

Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, 33071-Oviedo, Spain

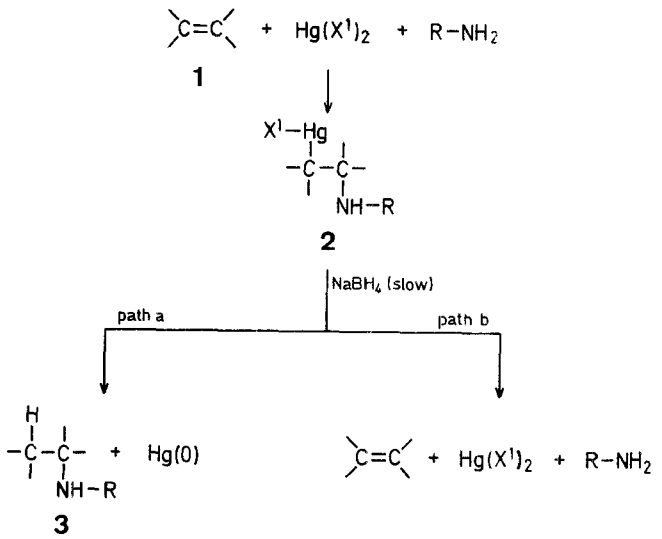
Gregorio ASENSIO

Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Valencia, 46010-Valencia, Spain

β-Aminoalkyl radicals generated by alkaline sodium borohydride reduction of aminomercurials react with electron-deficient olefins in an one pot procedure. These reactions allow direct synthesis of 5-aminonitriles and 5-aminoesters. 1,5-Diamines and aminoalcohols were also prepared by reduction of the former compounds.

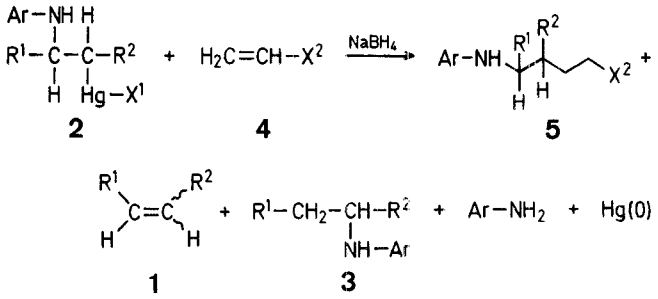
The recently introduced reductive alkylation of alkylmercurials[1] has enhanced greatly the value of organomercurials in organic synthesis. In this context the tandem oxymercuration-reductive alkylation was the first method to be explored[2]. Later it was extended to amidomercuration-reductive alkylation processes which form the basis of some new strategies designed to simplify the synthesis of natural products[3]. In a recent paper we reported an advantageous modification of the oxymercuration-reductive alkylation[4] method which allows the introduction of a wide variety of oxygen nucleophiles in the mercuration as well as the general use of sodium borohydride in the reduction step in an efficient one pot procedure.

We report now our study of the aminomercuration-reductive alkylation reaction for the simple synthesis of amines functionalized at predetermined positions. The reduction of aminomercurials is complex due to competitive deaminomercuration, often leading to poor yields. Thus, a careful selection of the reduction conditions determines the success of the process[5,6,7]. Aminomercurials show a very low solubility in 1 normal sodium hydroxide and remain in the organic phase when their reduction with sodium borohydride dissolved in 1 normal sodium hydroxide is performed in an organic-aqueous two phase medium. This fact induces slow rate reductions with deaminomercuration (Scheme A, path b). The use of an excess of amine[5] or phase transfer catalysis[7] has been employed to circumvent this difficulty.



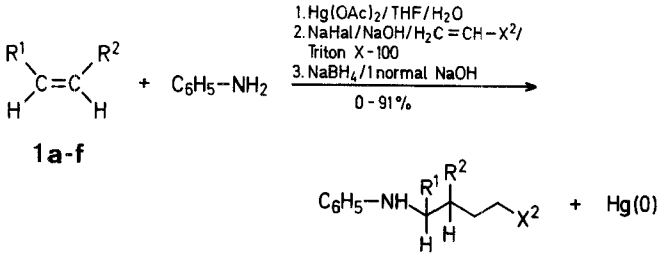
Scheme A

In the reductive alkylation of aminomercurials with sodium borohydride (Scheme **B**), both the alkylating agent (electron-deficient olefin) and the aminomercurial remain in the organic phase during the reduction. The yield of the overall process is less sensitive to the low concentration of hydride in the organic layer, showing that the fate of the intermediate alkyl radical does not depend, as in the simple reduction, on the amount of borohydride available. Since the reaction rate and yield of **3** are increased with the solubility of **2** in 1 normal sodium hydroxide, Triton X-100[8] was used as phase transfer catalyst in reactions with the more soluble aminomercurials (see Table 1) to avoid the undesirable formation of **3**.



Scheme **B**

Best yields of compounds **5** are obtained when aminomercurials **2** are reduced as chlorides (X^1 = Cl). In the practice, this was achieved by carrying out the aminomercuration-reductive alkylation in a one pot process by addition to the acetoxymercuration mixture of a ten-fold excess of sodium chloride and catalytic amounts of the surfactant, if necessary, prior to performance of the reductive-alkylation step (Scheme **C**, Method A in Table 1).



Scheme **C**

The same process in homogeneous medium of dimethylformamide/aqueous sodium hydroxide shows an increase in the reaction rate but affords compounds **5** with similar yields. It should be noted that in neutral conditions the yield of **5** drops almost to zero giving rise to the formation of decomposition products (Scheme **A**, path b).

Componds **5** possess a nitrile or ester functionality and, hence, can be readily transformed, for instance, to the corresponding primary amines or alcohols upon reduction with lithium aluminum hydride. It this way, 1,5-diamines **6** and aminoalcohols **7** substituted at predetermined positions are also easily accesible (Scheme **D**).

Table 1. Synthesis of Compounds **5**, **6**, and **7**

Entry	Starting material	R^1	R^2	X^1	X^2 in **4**	Triton X-100	Reaction time [h]	Hg (0) [%]	Product[a]	Method[b]	Yield[c] [%]
1	**1a**	C_6H_5	H	Cl	CN	No	4	90	**5a**	A	38
2	**2a**			Cl	CN	No	0.5	95	**5a**	B	37
3	**2a**			Cl	CN	No	0.5	100	**5a**	C	0
4	**1a**			OAc	CN	No	4	90	**5a**	D	23
5	**1a**			Br	CN	No	4	90	**5a**	A	8
6	**1a**			J	CN	No	4	90	**5a**	A	4
7	**1a**			Cl	$COOC_2H_5$	No	4	75	**5b**	A	31
8	**1b**	$C_6H_5CH_2$	H	Cl	CN	No	4	80	**5c**	A	36
9	**1b**			Cl	$COOC_2H_5$	No	4	75	**5d**	A	30
10	**1c**	C_4H_9	H	Cl	CN	No	4	80	**5e**	A	39
11	**1c**			Cl	$COOC_2H_5$	No	4	80	**5f**	A	31
12	**1d**	$-(CH_2)_3-$		Cl	CN	Yes	1	85	*trans*-**5g**	A	44
13	**1d**			Cl	$COOC_2H_5$	Yes	1	90	*trans*-**5h**	A	35
14	**1e**	$-(CH_2)_4-$		Cl	CN	Yes	1	70	**5i**[d]	A	47
15	**1e**			Cl	CN	No	1	70	**5i**[d]	A	13
16	**1e**			Cl	CN	Yes	1	70	**5i**[d]	A[e]	39
17	**1e**			Cl	$COOC_2H_5$	Yes	1	85	**5j**[d]	A	39
18	**1f**	$-(CH_2)_5-$		Cl	CN	Yes	1	70	*trans*-**5k**	A	30
19	**5a**								**6a**	E	85
20	**5b**								**7a**	E	80
21	**5c**								**6b**	E	86
22	**5d**								**7b**	E	80
23	**5e**								**6c**	E	91
24	**5f**								**7c**	E	85
25	**5g**								**6d**	E	89
26	**5h**								**7d**	E	86
27	**5i**[d]								**6e**[d]	E	87
28	**5j**[d]								**7e**[d]	E	85

[a] All compounds gave satisfactory microanalysis: C ±0.40, H ±0.15, N ±0.15.
[b] For reaction conditions see experimental.
[c] Based on starting material.
[d] 1:3 *cis-trans* mixture.
[e] A 3:1 excess of sodium chloride was used.

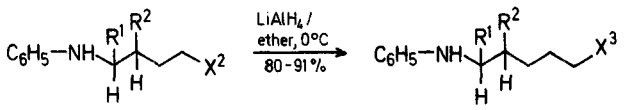
Table 2. Spectrometric Data of Compounds **5**, **6**, and **7**

Product	I.R.[a] ν[cm^{-1}]	^{1}H-N.M.R. (solvent/TMS$_{int}$)[b] δ[ppm]	^{13}C-N.M.R. (solvent)[b] δ[ppm][c]
5a	(Nujol): 3380 (NH); 2200 (CN)	($CDCl_3$): 1.6–2.2 (m, 4H, C—CH_2—CH_2—C); 2.3 (t, 2H, J = 6 Hz, CH_2—CN); 4.0 (br. s, 1H, NH); 4.3 (t, 1H, J = 6 Hz, CH—N); 6.3–7.3 (m, 10H, H_{arom})	($CDCl_3$): 16.3; 21.8; 36.4; 56.5; 112.9; 116.9; 119.3; 126.0; 126.8; 128.3; 128.7; 142.8; 146.8
5b	(film): 3420 (NH); 1740 (CO)	(CCl_4): 0.65–2.15 (m, 9H, C—CH_2—CH_2—CH_2—C, C—CH_3); 3.9 (q, 2H, J = 7 Hz, O—CH_2); 4.1 (br. s, 1H, NH); 4.1 (m, 1H, CH—N); 6.2–7.35 (m, 10H, H_{arom})	(CCl_4): 13.3; 20.8; 32.8; 36.0; 56.9; 59.9; 112.0; 116.2; 125.5; 125.9; 127.6; 128.1; 143.2; 146.7; 171.8
5c	(film): 3380 (NH); 2200 (CN)	($CDCl_3$): 1.5–1.9 (m, 4H, C—CH_2—CH_2—C); 2.3 (m, 2H, CH_2—CN); 2.85 (m, 2H, C—CH_2—C_{arom}); 3.4 (m, 1H, CH—N); 3.6 (br. s, 1H, NH); 6.4–7.3 (m, 10H, H_{arom})	($CDCl_3$): 16.6; 22.0; 32.7; 40.1; 52.9; 113.0; 117.0; 119.3; 126.1; 128.1; 129.1; 129.1; 137.6; 147.0
5d	(film): 3420 (NH); 1735 (CO)	(CCl_4): 0.9–1.6 (m, 7H, C—CH_2—CH_2—C, C—CH_3); 2.1 (t, 2H, J = 6 Hz, CH_2—COO); 2.6 (m, 2H, C—CH_2—C_{arom}); 3.4 (br. s, 1H, NH); 3.4 (m, 1H, CH—N); 3.9 (q, 2H, J = 7 Hz, O—CH_2); 6.3 (m, 10H, H_{arom})	(CCl_4): 13.4; 20.6; 32.4; 32.9; 39.3; 52.6; 58.9; 112.4; 116.3; 125.3; 127.4; 128.4; 128.6; 137.5; 146.6; 171.5
5e	(film): 3380 (NH); 2200 (CN)	($CDCl_3$): 0.6–1.8 (m, 13H, CH_3—CH_2—CH_2—CH_2—C, C—CH_2—CH_2—C); 2.15 (m, 2H, CH_2—CN); 3.2 (m, 1H, CH—N); 3.2 (br. s, 1H, NH); 6.2–7.2 (m, 5H, H_{arom})	($CDCl_3$): 13.8; 17.0; 21.8; 22.5; 27.8; 33.8; 34.7; 52.0; 112.6; 116.7; 119.4; 129.1; 147.6
5f	(film): 3400 (NH); 1730 (CO)	(CCl_4): 0.7–1.7 (m, 16H, CH_3—CH_2—CH_2—CH_2—C, C—CH_2—CH_2—C, CH_3—C); 2.1 (m, 2H, CH_2—COO); 3.2 (m, 1H, CH—N); 3.3 (br. s, 1H, NH); 3.95 (q, 2H, J = 7 Hz, O—CH_2); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 13.2; 13.4; 20.4; 21.9; 27.3; 33.1; 33.4; 33.8; 51.6; 58.8; 112.0; 115.6; 128.2; 147.2; 171.5
trans-**5g**	(film): 3370 (NH); 2190 (CN)	($CDCl_3$): 1.1–2.4 (m, 11H, C—CH_2—CH_2—CH_2—CH—CH_2—CH_2—CN); 3.3 (m, 1H, CH—N); 3.45 (br. s, 1H, NH); 6.5–7.2 (m, 5H, H_{arom})	($CDCl_3$): 15.4; 22.0; 29.4; 29.5; 32.3; 45.4; 59.4; 112.7; 116.5; 119.5; 128.7; 147.6
trans-**5h**	(film): 3420 (NH); 1745 (CO)	(CCl_4): 1.0–2.3 (m, 14H, C—CH_2—CH_2—CH_2—CH—CH_2—CH_2—COO, CH_3—C); 3.2 (m, 1H, CH—N); 3.6 (br. s, 1H, NH); 3.95 (q, 2H, J = 7 Hz, O—CH_2); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 13.3; 21.8; 28.6; 29.6; 32.0; 32.0; 45.4; 59.0; 59.4; 112.2; 115.7; 128.1; 147.4; 171.9
cis-**5i**[d]	(film): 3370 (NH); 2190 (CN)	($CDCl_3$): 0.9–2.45 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—CN); 3.55 (m, 1H, CH—N); 3.3 (br. s, 1H, NH); 6.5–7.2 (m, 5H, H_{arom})	($CDCl_3$): 13.8; 20.6; 23.2; 23.3; 26.0; 27.7; 37.4; 49.6; 112.2; 115.9; 119.4; 128.5; 146.8
trans-**5i**[d]	(film): 3370 (NH); 2190 (CN)	($CDCl_3$): 0.9–2.45 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—CN); 2.9 (m, 1H, CH—N); 3.3 (br. s, 1H, NH); 6.5–7.2 (m, 5H, H_{arom})	($CDCl_3$): 13.8; 24.4; 24.6; 28.0; 30.0; 32.5; 41.7; 55.1; 112.2; 115.9; 119.6; 128.5; 147.2
cis-**5i**[d]	(film): 3420 (NH); 1745 (CO)	(CCl_4): 0.9–2.2 (m, 16H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—COO, CH_3—C); 3.4 (m, 1H, CH—N); 3.5 (br. s, 1H, NH); 3.9 (q, 2H, J = 7 Hz, O—CH_2); 6.5–7.1 (m, 5H, H_{arom})	(CCl_4): 13.4; 21.0; 23.2; 25.1; 26.5; 28.1; 31.0; 37.9; 50.3; 58.9; 112.2; 115.7; 128.2; 146.8; 171.9
trans-**5j**[d]	(film): 3420 (NH); 2200 (CO)	(CCl_4): 0.9–2.2 (m, 16H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—COO, CH_3—C); 2.8 (m, 1H, CH—N); 3.5 (br. s, 1H, NH); 3.95 (q, 2H, J = 7 Hz, O—CH_2); 6.5–7.1 (m, 5H, H_{arom})	(CCl_4): 13.4; 24.3; 24.9; 27.2; 30.4; 30.7; 32.4; 42.0; 55.3; 58.9; 112.0; 115.5; 128.2; 147.2; 172.2
trans-**5k**	(film): 3370 (NH); 2200 (CN)	($CDCl_3$): 1.1–2.4 (m, 15H, C—CH_2—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—CN); 3.0 (m, 1H, CH—N); 3.4 (br. s, 1H, NH); 6.2–7.15 (m, 5H, H_{arom})	($CDCl_3$): 15.1; 23.8; 26.1; 29.2; 29.3; 30.3; 31.5; 44.7; 57.6; 112.9; 116.6; 119.8; 128.9; 147.0

Table 2. (Continued)

Product	I.R.[a] ν[cm^{-1}]	^{1}H-N.M.R. (solvent/TMS$_{int}$)[b] δ[ppm]	^{13}C-N.M.R. (solvent)[b] δ[ppm][c]
6a	(film): 3420–3280 (NH and NH_2)	($CDCl_3$): 1.1–1.9 (m, 6H, C—CH_2—CH_2—CH_2—C); 2.6 (m, 2H, CH_2—N); 2.9–3.8 (br. s, 3H, NH, NH_2); 4.2 (m, 1H, CH—N); 6.4–7.35 (m, 10H, H_{arom})	($CDCl_3$): 23.1; 31.9; 38.0; 40.9; 57.6; 112.8; 116.5; 125.9; 126.4; 128.1; 143.8; 147.1
6b	(film): 3380–3280 (NH and NH_2)	($CDCl_3$): 0.9–1.6 (m, 6H, C—CH_2—CH_2—CH_2—C); 2.65–2.95 (m, 4H, C—CH_2—C_{arom}, CH_2—N); 3.5 (m, 1H, CH—N); 4.6 (br. s, 3H, NH, NH_2); 6.25–7.25 (m, 10H, H_{arom})	($CDCl_3$): 22.5; 32.7; 32.9; 39.3; 41.0; 52.6; 112.2; 116.0; 125.3; 127.3; 128.4; 128.6; 137.5; 146.7
6c	(film): 3420–3300 (NH and NH_2)	($CDCl_3$): 0.6–2.0 (m, 15H, CH_3—CH_2—CH_2—CH_2—C, C—CH_2—CH_2—CH_2—C); 2.65 (m, 2H, CH_2—N); 2.95 (br. s, 2H, NH_2); 3.3 (m, 1H, CH—N); 3.6 (br. s, 1H, NH); 6.4–7.2 (m, 5H, H_{arom})	($CDCl_3$): 13.7; 22.4; 22.8; 27.8; 32.1; 34.3; 34.3; 41.2; 52.3; 112.4; 116.0; 128.8; 147.8
trans-**6d**	(nujol): 3445–3300 (NH and NH_2)	($CDCl_3$): 0.8–2.3 (m, 11H, C—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 2.65 (m, 2H, CH_2—N); 2.8–3.1 (br. s, 2H, NH_2); 3.25 (m, 1H, CH—N); 3.7 (br. s, 1H, NH); 6.4–7.25 (m, 5H, H_{arom})	($CDCl_3$): 22.0; 29.8; 30.8; 31.1; 32.1; 41.2; 46.2; 59.4; 112.2; 115.8; 128.3; 147.6
cis-**6d**[d]	(film): 3400–3260 (NH and NH_2)	($CDCl_3$): 0.9–2.2 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 2.5 (m, 2H, CH_2—N); 2.9–3.2 (br. s, 3H, NH, NH_2); 3.45[e] (m, 1H, CH—N); 6.3–7.2 (m, 5H, H_{arom})	($CDCl_3$): 20.6; 23.1; 26.3; 26.9; 28.1; 30.4; 37.6; 42.5; 50.1; 112.2; 115.4; 128.4; 146.8
trans-**6d**[d]	(film): 3400–3260 (NH and NH_2)	($CDCl_3$): 0.9–2.2 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 2.5 (m, 2H, CH_2—N); 2.9 (m, 1H, CH—N); 2.9–3.2 (br. s, 3H, NH, NH_2); 6.3–7.2 (m, 5H, H_{arom})	($CDCl_3$): 24.5; 24.9; 29.1; 29.7; 30.4; 32.6; 41.4; 42.5; 55.3; 120.0; 115.4; 128.4; 147.7
7a	(film): 3460–3300 (NH and OH)	(CCl_4): 1.1–1.7 (m, 6H, C—CH_2—CH_2—CH_2—C); 3.35 (m, 2H, CH_2—O); 3.5 (br. s, 2H, NH, OH); 4.1 (t, 1H, J = 6 Hz, CH—N); 6.2–7.2 (m, 10H, H_{arom})	(CCl_4): 21.7; 31.4; 37.6; 57.3; 61.0; 112.5; 116.3; 125.3; 125.9; 127.6; 128.1; 143.3; 146.6
7b	(film): 3480–3300 (NH and OH)	(CCl_4): 1.3 (m, 6H, C—CH_2—CH_2—CH_2—C); 2.6 (m, 2H, CH_2—C_{arom}); 3.1–3.55 (m, 5H, CH—N, CH_2—O, NH, OH); 6.3–7.1 (m, 10H, H_{arom})	(CCl_4): 21.5; 31.6; 32.8; 39.2; 52.7; 61.1; 112.4; 116.2; 125.2; 127.3; 128.4; 128.6; 137.5; 146.7
7c	(film): 3460–3300 (NH and OH)	(CCl_4): 0.7–1.7 (m, 15H, CH_3—CH_2—CH_2—CH_2—C, C—CH_2—CH_2—CH_2—C); 3.15 (m, 1H, CH—N); 3.35 (m, 2H, CH_2—O); 4.0 (br. s, NH, OH); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 13.3; 21.3; 22.0; 27.3; 31.8; 33.7; 33.7; 52.2; 61.0; 112.3; 116.0; 128.2; 146.9
trans-**7d**	(film): 3460–3300 (NH and OH)	(CCl_4): 0.9–2.0 (m, 11H, C—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 3.1 (m, 1H, CH—N); 3.35 (m, 2H, CH_2—O); 3.8 (br. s, 2H, NH, OH); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 21.9; 29.7; 29.8; 30.3; 32.0; 45.7; 59.6; 61.2; 112.5; 116.1; 128.1; 147.2
cis-**7e**[d]	(film): 3480–3300 (NH and OH)	(CCl_4): 0.9–2.1 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 2.95 (m, 1H, CH—N); 3.35 (m, 2H, CH_2—O); 3.65 (br. s, 2H, NH, OH); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 21.2; 23.3; 26.0; 26.9; 28.1; 29.4; 38.3; 50.7; 61.4; 112.3; 115.8; 128.2; 146.7
trans-**7e**[d]	(film): 3480–3300 (NH and OH)	(CCl_4): 0.9–2.1 (m, 13H, C—CH_2—CH_2—CH_2—CH_2—CH—CH_2—CH_2—C); 2.75 (m, 1H, CH—N); 3.35 (m, 2H, CH_2—O); 3.65 (br. s, 2H, NH, OH); 6.3–7.1 (m, 5H, H_{arom})	(CCl_4): 24.5; 25.0; 28.0; 28.7; 30.5; 32.5; 42.2; 55.5; 61.4; 112.1; 115.6; 128.2; 147.2

[a] Recorded with a Pye Unicam SP-1025 I.R. spectrometer.
[b] Recorded with a Varian FT-80 spectrometer using a D_2O capillary when CCl_4 was the solvent.
[c] Referred to the solvent.
[d] Date are from *cis-trans* isomers mixture.
[e] Uncertain assignement.



5a-j **6a-c** ($X^3 = NH_2$) **7a-c** ($X^3 = OH$)

Scheme **D**

The stereochemistry of the products derived from cyclic olefins was determined by N.O.E. experiments at 200 MHz[9]. Compounds **5g**, **5h**, and **5k** derived from cyclopentene (**1d**) and cycloheptene (**1f**) showed the structure *trans*. Conversely, **5i** and **5j** were found to be mixtures of *cis*/*trans* isomers in a ~1:3 molar ratio.

The tandem aminomercuration-reductive alkylation allows the synthesis of 1,5-functionalized amines in a process involving C—C bond formation through free radicals. Although this reaction only occurs between an electron-rich and an electron-deficient olefin, this limitation is in some manner overcome by the transformation of the electron withdrawing group to an electron donor by simple reduction.

One Pot Synthesis of 5-Aminonitriles and 5-Aminoesters 5 in Heterogeneous Medium; General Procedure for Method A:
A mixture of mercury(II) acetate (3.19 g, 10 mmol) in tetrahydrofuran (30 ml) and water (10 ml) is treated with aniline (0.93 g, 10 mmol). After 5–10 min of stirring, a white suspension is formed and then olefin **1** (10 mmol) is added. When the solution has turned colorless, 2 normal aqueous sodium hydroxide (20 ml), sodium halide (X = Cl, Br, J; 100 mmol), Triton X-100[8] (0.5 g) (see Table 1) and freshly distilled electron-deficient olefin **4** (100 mmol) are added. To this heterogeneous mixture, sodium borohydride (0.38 g, 10 mmol) dissolved in 1 normal aqueous sodium hydroxide (5 ml) is added dropwise. After 1–4 h at room temperature, elemental mercury is filtered off and the resulting solution extracted with dichloromethane (2 × 25 ml), the extract is washed with water (20 ml), and dried with anhydrous sodium sulfate. The solvent is removed under reduced pressure and the oily residue is purified by column chromatography on silica gel and toluene as eluent. Yields of compounds **5** are summarized in Table 1; spectral data are collected in Table 2.

Synthesis of Aminomercurial 2a:
A solution of mercury(II) acetate (3.19 g, 10 mmol) in tetradydrofuran (30 ml) and water (10 ml) is treated with aniline (0.93 g, 10 mmol). After 5–10 min of stirring, a white suspension is formed and then styrene (1.04 g, 10 mmol) is added. The colorless solution is poured into a mixture of sodium chloride (2.93 g, 50 mmol) in water (50 ml) with formation of a white precipitate. Tetrahydrofuran is evaporated under reduced pressure and water decanted. The semisolid product is recrystallized from methanol to give **2a**; yield: 3.55 g, (82%); m.p. 106–108°C.

$C_{14}H_{14}ClHgN$	calc.	N 3.24	Hg 46.40
(432.3)	found	3.15	45.33

I.R. (Nujol): $\nu = 3400\ cm^{-1}$ (NH).

^{1}H-N.M.R. (DMSO-d_6): $\delta = 2.00$ (d, 2H, J = 6 Hz, CH_2Hg); 3.24 (br.s, 1H, NH); 4.60 (m, 1H, CHN); 6.0–7.3 ppm (m, 10 H_{arom}).

^{13}C-N.M.R. (DMSO-*d*): $\delta = 41.3$; 50.3; 113.0; 115.8; 125.6; 126.5; 128.5; 128.6; 147.4; 147.5 ppm.

Reductive Alkylation in Homogeneous Basic Medium; Method B:
To a solution of mercurial **2a** (4.32 g, 10 mmol) in dimethylformamide (40 ml) and 1 normal aqueous sodium hydroxide (10 ml) is added freshly distilled acrylonitrile (3.3 ml, 100 mmol). The mixture is cooled at 0°C and then sodium borohyride (0.38 g, 10 mmol) dissolved in 1 normal aqueous sodium hydroxide (5 ml) is dropwise added. After 0.5 h elemental mercury is filtered off and the solution treated with 1 normal sodium hydroxide (20 ml) and extracted with ether (3 × 20 ml). Compound **5a** is isolated according to the procedure above described; yield: 37%.

Reductive Alkylation in Homogeneous, Neutral Medium; Method C:
The procedure is the same as that described above in B but excluding the 1 normal sodium hydroxide addition and with sodium borohydride dissolved in dimethylformamide (5 ml).

Synthesis of 5a; Method D:
The procedure is the same as that described above in A but excluding the addition of the sodium halide and Triton X-100.

Reduction of Compounds 5; General Procedure for Method E:
To a suspension of lithium aluminum hydride (0.19 g, 5 mmol) in dry ether (10 ml) is added dropwise a solution of compound **5** (5 mmol) in dry ether (5 ml) at 0°C. After 30 min of stirring, the excess of lithium aluminum hydride is destroyed by careful addition of a few drops of water. The mixture is hydrolyzed with 1 normal aqueous sodium hydroxide (20 ml), extracted with ether (3 × 20 ml), and the organic layer dried with anhydrous sodium sulfate. The solvent is removed under vacuum and the residue is purified by column chromatography on silica gel using methanol/diethylamine (10:1) as eluent. Yields of compounds **6** and **7** are summarized in Table 1; spectral data are collected in Table 2.

This work was supported in part by Comisión Asesora de Investigación Científica y Técnica (CAICYT).

Received: March 28, 1985

[1] Giese, B., Meister, J. *Chem. Ber.* **1977**, *110*, 2588.
[2] Giese, B., Heuck, K. *Chem. Ber.* **1979**, *112*, 3759.
Giese, B., Heuck, K. *Tetrahedron Lett.* **1980**, *21*, 1829.
Giese, B., Lüning, U. *Synthesis* **1982**, 735.
[3] Danishefsky, S., Taniyama, E., Weeb II, R.R. *Tetrahedron Lett.* **1983**, *24*, 11.
Danishefsky, S., Tanijama, E. *Tetrahedron Lett.* **1983**, *24*, 15.
Kozikowski, A.P., Scripko, J. *Tetrahedron Lett.* **1983**, *24*, 2015.
Harding, K.E., Burks, S.R. *J. Org. Chem.* **1984**, *49*, 40.
Carruthers, W., Williams, M.J., Cox, M.T. *J. Chem. Soc. Chem. Commun.* **1984**, 1235.
Barluenga, J., Ferrera, L., Nájera, C., Yus, M. *Synthesis* **1984**, 831.
[4] Barluenga, J., López-Prado, J., Campos, P.J., Asensio, G. *Tetrahedron* **1983**, *39*, 2863.
[5] Barluenga, J., Pérez-Prieto, J., Bayón, A., Asensio, G. *Tetrahedron* **1984**, *40*, 1199.
[6] Griffith, R.C., Gentile, R.G., Davidson, T.A., Scott, F.L. *J. Org. Chem.* **1979**, *44*, 3580.
[7] Etemar-Moghadam, G., Benhamon, M.C., Speziale, V., Lattes, A., Bielawska, A. *Nouv. J. Chim.* **1980**, *4*, 727.
[8] Non-ionic surfactant (Merck, trademark of Rohm & Hass Co.)
[9] Performed with a Bruker WP 80 SY spectrometer by Dr. Francisco Sánchez (Universidad Autónoma, Barcelona, Spain).