Aminomercuration-Demercuration of α,β-Unsaturated Esters; Synthesis of *N*-Aryl-β-aminocarboxylic Esters

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The preparation of β-amino acid derivatives is frequently complicated by the tendency of the reaction product to decompose to a α,β-unsaturated system[1]. β-Amino esters have been obtained by addition of amines to α,β-unsaturated esters[2,3]; however, this method is disadvantageous when aromatic amines are used since their low basicity only allows the addition reaction to take place in the presence of acid catalysts and at relatively high temperatures[2]. A second disadvantage is the reversible character of the addition process under the reaction conditions employed[4] which explains the utility of amines as catalysts in the *cis-trans*-isomerization of electrophilic olefins[5].

The aminomercuration-demercuration of unsaturated compounds constitutes an interesting method of amination of olefins and is specially useful for the synthesis of nitrogen-containing heterocycles[6]. It is also known that the methoxymercuration of acrylic esters gives mainly α-mercurated products and, in some instances, those resulting from β-mercuration[7]. These observations suggest that the arylaminomercuration-demercuration of α,β-unsaturated esters might serve as a convenient source of β-amino esters.

When different α,β-unsaturated esters **1** were allowed to react with aromatic amines **2**[8] in the presence of mercury(II) acetate in tetrahydrofuran, the corresponding α-mercurated β-amino esters **3** were obtained (Table 1).

The structure of **3** is supported by the formation of β-amino esters **4** ($R^1 = R^2 = H$) by sodium borohydride reduction in alkaline media[9]. It also correlates with the expected product resulting from the amine attack to the most electron-deficient carbon atom in the intermediate mercurinium ion[10].

Reduction and deaminomercuration are always competitive processes in the treatment of aminomercurials with sodium borohydride. In this study, we have found that, when a conjugate or hyperconjugate olefin (R^1 and $R^2 \neq H$) is produced by the deaminomercuration pathway, only this type of reaction occurs and, hence, the starting reagents **1** and **2** are regenerated[1] (mercurials **3e-h**; see Table 2). However, the reduction pathway greatly predominates when $R^1 = R^2 = H$, and β-amino esters **4** are obtained in good yield[11].

The use of weakly basic anilines does not lead to the expected β-amino esters **4**. For instance, the mercuration of methyl acrylate (**1**; $R^1 = R^2 = H$, $R^3 = CH_3$) with *p*-nitroaniline (**2**; Ar = 4-O_2N—C_6H_4, $R^4 = H$) does not proceed, at least in the reaction conditions explored [different mercury(II) salts and temperatures]; the mercuration with methyl *p*-aminobenzoate takes place with good yield to give **3i** but the reduction fails and only the deaminomercuration compounds **1** and **2** are produced in the reduction process.

I.R. and ^{1}H-N.M.R. spectra were recorded on a Pye-Unicam SP-1000 and a Varian EM-390 instrument, respectively.

Methyl 2-Acetoxymercurio-3-phenylaminopropanoate (3a): Typical Procedure:

To a well stirred solution of aniline (12.0 ml, 125 mmol) in tetrahydrofuran (50 ml), methyl acrylate (2.7 ml, 25 mmol) and mercury(II) acetate (8.0 g, 25 mmol) are added. After 5 h, the solvent is removed under re-

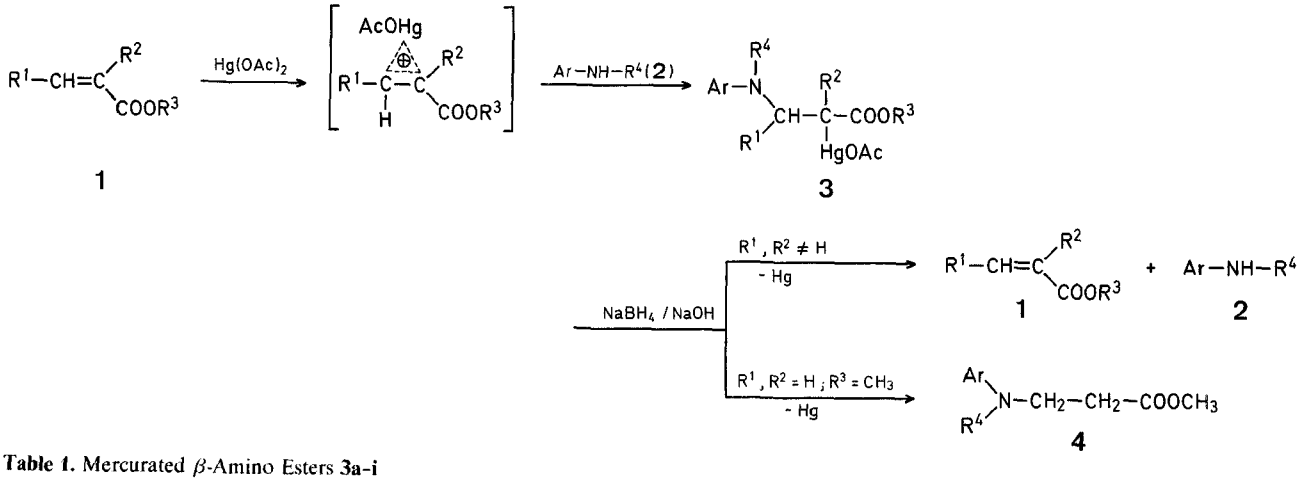

Table 1. Mercurated β-Amino Esters **3a-i**

Product	R^1	R^2	R^3	R^4	Ar	Reaction time [h]	m.p. [°C][a]	Yield [%][b]	Molecular formula[c]	
3a	H	H	CH_3	H	C_6H_5	5	oil	96	$C_{12}H_{15}HgNO_4$	(437.8)
3b	H	H	CH_3	H	4-Cl—C_6H_4	21	126–129°	94	$C_{12}H_{14}ClHgNO_4$	(472.3)
3c	H	H	CH_3	H	4-H_3C—C_6H_4	20	135–138° (dec.)	94	$C_{13}H_{17}HgNO_4$	(451.9)
3d	H	H	CH_3	CH_3	C_6H_5	15	oil	90	$C_{13}H_{17}HgNO_4$	(451.9)
3e[d]	H	CH_3	CH_3	H	C_6H_5	5	140° (dec.)	78	$C_{13}H_{17}HgNO_4$	(451.9)
3f	*cis*-$COOCH_3$	H	CH_3	H	C_6H_5	1	136–138°	90	$C_{14}H_{17}HgNO_6$	(495.9)
3g	*trans*-$COOC_2H_5$	H	C_2H_5	H	C_6H_5	1	140–142°	74	$C_{16}H_{21}HgNO_6$	(523.9)
3h	C_6H_5	H	CH_3	H	C_6H_5	50	144–145°	89	$C_{18}H_{19}HgNO_4$	(513.9)
3i	H	H	CH_3	H	4-H_3COOC—C_6H_4	20	260–263° (dec.)	78	$C_{14}H_{17}HgNO_6$	(495.9)

[a] Not corrected; compounds could not be recrystallized.
[b] Yield based on **1**.
[c] Satisfactory microanalyses obtained: N ±0.18, Hg ±0.36.
[d] Structure of **3e** is only tentative since the α-amino-β-mercurated compound cannot ruled out.

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Table 2. *N*-Aryl-β-amino Esters **4a–d** from Mercurials **3** (R^1, R^2 = H, R^3 = CH_3)

Product	R^4	Ar	Yield [%][a]	b.p. [°C]/ 0.001 torr	m.p. [°C][b] (Lit. m.p.) (hexane/$CHCl_3$)	Molecular formula[c]
4a	H	C_6H_5	47	108–110°	37–38° (37.5–38.5°)[13]	$C_{10}H_{13}NO_2$ (179.2)
4b	H	4-Cl—C_6H_4	37	128–130°	56–57°	$C_{10}H_{12}ClNO_2$ (213.7)
4c	H	4-H_3C—C_6H_4	39	119–123°	59–61° (60–61°)[14]	$C_{11}H_{15}NO_2$ (193.2)
4d	CH_3	C_6H_5	45	70–74°	—	$C_{11}H_{15}NO_2$ (193.2)

[a] Yield based on **3**.
[b] Not corrected.
[c] Satisfactory microanalyses obtained: C ±0.12, H ±0.08, N ±0.07.

duced pressure (15 and then 0.001 torr) to afford a brown oil; yield: 10.5 g (96%).

$C_{12}H_{15}HgNO_4$	calc.	N 3.20	Hg 45.82
(437.8)	found	3.16	45.75

I.R. (film): ν = 3400, 3020, 2980, 1710, 1610, 1600, 1500, 1440, 1380, 1200, 770, 700 cm^{-1}. The I.R. spectra of **3b–h** are similar.

Methyl 3-Phenylaminopropanoate (4a); Typical Procedure:
To a well stirred solution of methyl 2-acetoxymercurio-3-phenylaminopropanoate (**3a**; 21.9 g, 50 mmol) in aniline (24 ml, 250 mmol), tetrahydrofuran (100 ml), and 0.5 normal aqueous sodium hydroxide solution (50 ml), a solution of sodium borohydride (3.8 g, 100 mmol) in 2.5 normal aqueous sodium hydroxide solution (20 ml) is added. After 15 h, the reaction mixture is extracted with ether (3 × 30 ml), the organic layer is washed with water (50 ml), and dried with anhydrous sodium sulfate. Mercury(0) is obtained; yield: 8.4 g (84%). Solvents are removed under reduced pressure (15 and then 0.001 torr) and the resulting oily residue is distilled at 108–110 °C/0.001 torr to give a yellow oil [yield: 4.0 g (56%)] that is recrystallized from hexane/chloroform; m.p. 37–38 °C.

$C_{10}H_{13}NO_2$	calc.	C 67.02	H 7.31	N 7.81
(179.2)	found	67.14	7.38	7.74

I.R. (nujol): ν = 3400 (NH); 3020, 1600, 1500, 770, 700 (Ar); 1730 (C=O); 1210 cm^{-1} (C—O).

^{1}H-N.M.R. (CCl_4): δ = 2.45 (t, 2H, J = 6 Hz); 3.35 (t, 2H, J = 6 Hz); 3.65 (s, 3H); 3.95 (br. s, 1H); 6.9 ppm (m, 5H).

The I.R. and ^{1}H-N.M.R. spectra of compounds **4b–d** are similar and in accord with the structures given.

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[1] W. A. Bonner, A. J. Castro, *Essentials of Modern Organic Chemistry*, Reinhold Publishing Corporation, New York, 1965, Chap. 16–17.
[2] K. L. Mallik, M. N. Das, *Z. Phys. Chem. (Frankfurt)* **25**, 205 (1960).
[3] A. Vystrčil, S. Hudeček, *Chem. Listy* **44**, 262 (1950); *C. A.* **45**, 5626 (1951).
[4] S. T. McDowell, C. J. M. Stirling, *J. Chem. Soc.* [B] **1967**, 343.
[5] Z. Rappoport, C. Degani, S. Patai, *J. Chem. Soc.* **1963**, 4513.
[6] J. Barluenga, C. Nájera, M. Yus, *Synthesis* **1979**, 896, and references cited therein.
[7] A. J. Bloodworth, R. J. Bunce, *J. Chem. Soc. Chem. Commun.* **1970**, 753.
[8] Use of primary aliphatic amines lead to amine-mercury(II)salt complexes instead of giving addition products: J. Barluenga, C. Nájera, M. Yus, *An. Quim.* **75**, 341 (1979).
Secondary aliphatic amines slowly add to olefins to afford frequently mixtures of reaction products: A. Lattes, *Afinidad* **29**, 153 (1972).
[9] H. C. Brown, P. Geoghegan Jr., *J. Am. Chem. Soc.* **89**, 1522 (1967).
[10] On the mechanism of the solvomercuration of olefins see: G. Olah, P. R. Clifford, *J. Am. Chem. Soc.* **93**, 1261, 2320 (1971).
[11] Reaction with other reducing agents, such as metals in solution[12] (lithium/aniline) led to lower yields in compounds **4**. Under these conditions, amino derivatives from **1** ($R^1 \neq H$, $R^2 \neq H$) were not obtained.
[12] J. Barluenga, A. Ara, G. Asensio, *Synthesis* **1975**, 116.
[13] W. S. Johnson, E. L. Woroch, B. G. Buell, *J. Am. Chem. Soc.* **71**, 1901 (1949).
[14] P. L. Southwick, R. T. Crouch, *J. Am. Chem. Soc.* **75**, 3413 (1953).