## Tandem Amidomercuration-Reductive Alkylation of Alkenes. One-Pot Sythesis of Amidic 1,4-Bifunctionalized Compounds

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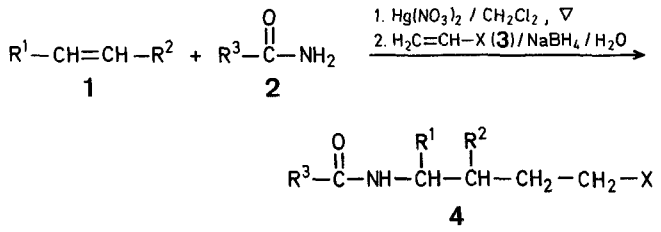
The addition of amides and related compounds to alkenes[1] in the presence of mercury(II) nitrate and subsequent reduction with sodium borohydride[2] represents a general method to prepare *N*-substituted amides. On the other hand, the reductive radical coupling between oxy- and aminomercurials with electron-poor alkenes by means of various borohydrides is known[3]. We have now studied the combination of both of these processes in a one-pot synthesis.

Various alkenes (**1**) were allowed to react with anhydrous mercury (II) nitrate and amides (**2**) of different types in boiling dichloromethane. After the mercuration reaction, reductive coupling was carried out using sodium borohydride and an electron-poor olefin (**3**) to give the bifunctionalized products **4**. Ethylene, propylene, 1-hexene, and cyclohexene were used as alkenes **1**, formamide, acetamide, methyl carbamate, and urea as nucleophilic agents **2**, and acrylonitrile, butenone, and methyl acrylate as electrophilic olefins **3** in this one-pot synthesis.




**1** **2** **4**

In nearly all cases, the intermediate acylaminoalkylmercury compounds were soluble in the reaction media. When the above-described tandem reaction was carried out with cyclohexene, the products **4i–l** consisted of more than 90% *trans* isomer (N.M.R. analysis of the crude reaction product) and after the purification, this isomer was the only isolated compound[4]. The regiochemistry of products **4b–h** derived from linear alkenes was ascertained from their N.M.R. spectra.

Bifunctionalized compounds of the type **4** have received attention because they may serve as useful building blocks in alkaloid syntheses[5].

**Methyl *N*-(1-Butyl-4-cyanobutyl)-carbamate [4f, 5-(Methoxycarbonylamino)-nonanenitrile]; Typical Procedure:**

To a solution of methyl carbamate (2.25 g, 30 mmol) and 1-hexene (1.2 ml, 10 mmol) in dichloromethane (100 ml), anhydrous mercury(II) nitrate (Fluka, 3.25 g, 10 mmol) is added. [In the preparation of products **4a**, **4b** and **4c**, the gaseous alkene is bubbled through the mixture under reflux for 8 h].

The mixture is stirred under reflux for ~ 24 h, then cooled to 0 °C and acrylonitrile (5 ml, 75 mmol) and a solution of sodium borohydride (1.9 g, 50 mmol) in water (10 ml) are quickly added. Stirring is continued for 2 h, mercury is filtered off, the liquid layers are decant-

**Table 1.** Preparation of *N*-Substituted Amides **4**

| 4 | $R^1$ | $R^2$ | $R^3$ | X | Yield[a] [%] | b.p.[b]/torr or m.p. [°C] | Molecular Formula[c] |
|---|---|---|---|---|---|---|---|
| **a** | H | H | $H_3CO$ | —CN | 29 (32)[d] | b.p. 70–73°/0.001 | $C_7H_{12}N_2O_2$ (156.2) |
| **b** | $CH_3$ | H | $CH_3$ | —CN | 30 | b.p. 75–77°/0.01 | $C_8H_{14}N_2O$ (154.2) |
| **c** | $CH_3$ | H | $H_3CO$ | —CN | 68 | b.p. 63–65°/0.001 | $C_8H_{14}N_2O_2$ (170.2) |
| **d** | *n*-$C_4H_9$ | H | $CH_3$ | —CN | 77 | b.p. 83–85°/0.01 | $C_{11}H_{20}N_2O$ (196.3) |
| **e** | *n*-$C_4H_9$ | H | $CH_3$ | —$COOCH_3$ | 50 | b.p. 73–75°/0.01 | $C_{12}H_{23}NO_3$ (229.3) |
| **f** | *n*-$C_4H_9$ | H | $H_3CO$ | —CN | 71 (62)[d] | b.p. 122–125°/0.001 | $C_{11}H_{20}N_2O_2$ (212.3) |
| **g** | *n*-$C_4H_9$ | H | $H_3CO$ | —CO—$CH_3$ | 40[d] | b.p. 80–83°/0.001 | $C_{12}H_{23}NO_3$ (229.3) |
| **h** | *n*-$C_4H_9$ | H | $H_3CO$ | —$COOCH_3$ | 61[d] | b.p. 105–110°/0.001 | $C_{12}H_{23}NO_4$ (245.3) |
| **i** | —$(CH_2)_4$— | | H | —CN | 40 | b.p. 80–82°/0.01 | $C_{10}H_{16}N_2O$ (180.25) |
| **j** | —$(CH_2)_4$— | | $CH_3$ | —CN | 44 | m.p. 160–162°[e] | $C_{11}H_{18}N_2O$ (194.3) |
| **k** | —$(CH_2)_4$— | | $H_3CO$ | —CN | 63 | m.p. 77–79°[f] | $C_{11}H_{18}N_2O_2$ (210.3) |
| **l** | —$(CH_2)_4$— | | $NH_2$ | —CN | 57 | m.p. 180–182°[g] | $C_{10}H_{17}N_3O$ (195.3) |

[a] Isolated yield based on alkene **1**.
[b] Distillation interval.
[c] The microanalyses were in good agreement with the calculated values: C, ±0.14; H, ±0.09; N, ±0.13.
[d] Yield when the mercuration step was carried out using $Hg(NO_3)_2/HgO$ (mol ratio $1/Hg(NO_3)_2/HgO = 1/0.65/0.35$).
[e] From $CCl_4$.
[f] From hexane.
[g] From acetone.

**Table 2.** Spectrometric Data of Compounds **4**

| 4 | I.R. ($CCl_4$)[a] $\nu$[$cm^{-1}$] | $^1$H-N.M.R. (solvent/$TMS_{int}$)[b] $\delta$[ppm] | $^{13}$C-N.M.R. (solvent)[b] $\delta$[ppm][c] |
|---|---|---|---|
| **a** | 3400 (NH); 2250 (CN); 1740 (CO) | ($CCl_4$): 1.6 (m, 4H, C—$CH_2$—$CH_2$—C); 2.4 (t, 2H, $J$ = 6 Hz, $CH_2$—CN); 3.15 (t, 2H, $J$ = 6 Hz, $CH_2$—N); 3.6 (s, 3H, $H_3CO$); 6.1 (br. s, 1H, NH) | ($CCl_4$): 16.4, 22.65, 28.3, 39.9, 51.7, 120.1, 157.5 |
| **b** | 3340 (NH); 2260 (CN); 1740 (CO) | ($CDCl_3$): 1.15 (d, 3H, $J$ = 6 Hz, CH—$CH_3$); 1.6 (m, 4H, CH—$CH_2$—$CH_2$); 2.0 (s, 3H, $H_3C$—CO); 2.4 (m, 2H, $CH_2$—CN); 3.95 (m, 1H, CH); 6.95 (br. s, 1H, NH)[d] | ($CCl_4$): 16.7, 20.9, 22.3, 23.0, 35.6, 44.2, 120.1, 169.9 |
| **c** | 3400 (NH); 2250 (CN); 1740 (CO) | ($CCl_4$): 1.0–2.0 (m, 7H, CH—$CH_3$ + CH—$CH_2$—$CH_2$); 2.2–2.5 (m, 2H, $CH_2$—CN); 3.5–4.0 (m with s at 3.6, 4H, CH + $H_3CO$); 5.4 (br. s, 1H, NH) | ($CCl_4$): 16.6, 21.0, 22.2, 35.7, 46.3, 51.6, 120.0, 156.9 |
| **d** | 3340 (NH); 2260 (CN); 1660 (CO) | ($CCl_4$): 0.9 (m, 3H, CH—$CH_3$); 1.1–1.85 (2m, 10H, $5CH_2$—C); 1.95 (s, 3H, $H_3C$—CO); 2.35 (m, 2H, $CH_2$—CN); 3.85 (m, 1H, CH); 6.75 (d, 1H, $J$ = 9 Hz, NH) | ($CCl_4$): 14.0, 16.6, 22.1, 22.55, 22.7, 28.2, 34.05, 34.8, 48.1, 119.6, 170.1 |
| **e** | 3380 (NH); 1770, 1700 (CO) | ($CCl_4$): 0.9 (m, 3H, $CH_3$—$CH_2$); 1.4 (m, 10H, $5CH_2$—C); 1.9 (s, 3H, $H_3C$—CO); 2.3 (t, 2H, $J$ = 6 Hz, $CH_2$—CO); 3.55–3.7 (m with s at 3.6, 4H, CH + $H_3C$—CO); 7.4 (d, 1H, $J$ = 9 Hz, NH) | ($CCl_4$): 14.0, 21.4, 22.6, 28.2, 34.5, 34.4, 34.7, 48.5, 51.1, 169.9, 173.1 |
| **f** | 3400 (NH); 2260 (CN); 1740 (CO) | ($CCl_4$): 0.9 (m, 3H, $H_3C$—$CH_2$); 1.1–1.9 (m, 10H, $5CH_2$—C); 2.4 (m, 2H, $CH_2$—CN); 3.1–3.8 (m with s at 3.6, 4H, CH + $H_3CO$); 5.6 (br. s, 1H, NH) | ($CCl_4$): 13.9, 16.5, 22.1, 22.5, 28.1, 34.3, 35.0, 50.4, 51.5, 119.6, 157.2 |
| **g** | 3360 (NH); 1740, 1710 (CO) | ($CDCl_3$): 0.9 (m, 3H, $CH_2$—$CH_3$); 1.4 (m, 10H, $5CH_2$—C); 2.2 (s, 3H, CO—$CH_3$); 2.5 (m, 2H, $CH_2$—CO); 3.5–3.9 (m with s at 3.7, 4H, CH + $H_3CO$); 5.2 (d, 1H, $J$ = 9 Hz, NH) | ($CCl_4$): 13.6, 19.6, 22.2, 27.6, 29.3, 34.3, 34.6, 42.8, 50.55, 51.3, 156.7, 193.1 |
| **h** | (film): 3400 (NH); 1750 (CO) | ($CCl_4$): 0.9 (m, 3H, $CH_2$—$CH_3$); 1.4 (m, 10H, $5CH_2$—C); 2.3 (t, 2H, $J$ = 6 Hz, $CH_2$—$CO_2$); 3.5–3.8 (m with s at 3.6, 7H, CH + $2H_3CO$); 5.2 (d, 1H, $J$ = 9 Hz, NH) | ($CCl_4$): 13.8, 21.3, 22.5, 28.1, 33.5, 34.6, 35.0, 50.6, 50.9, 51.2, 156.9, 173.3 |
| **i** | ($CHCl_3$): 3360 (NH); 2880 (CHO); 2260 (CN); 1700 (CO) | ($CDCl_3$): 0.8–2.1 (m, 10H, $5CH_2$—C); 2.1–2.6 (m, 3H, $CH_2$—CN + CH—$CH_2$); 3.2–3.8 (m, 1H, CH—N); 6.5 (d, 1H, $J$ = 9 Hz, NH); 8.2 (s, 1H, CH=O) | ($CDCl_3$): 13.2, 24.3, 27.3, 29.2, 32.4, 40.6, 49.5, 120.4, 160.5 |
| **j** | (Nujol): 3260 (NH); 2260 (CN); 1660 (CO) | ($CD_3OD$): 1.0–3.1 (m with s at 2.3, 16H, $6CH_2$—C + $H_3CO$ + CH—$CH_2$—$CH_2$—CN); 3.4–4.1 (m, 2H, CH—N + NH) | ($CD_3OD$): 14.55, 22.75, 26.4, 26.45, 29.5, 31.2, 34.25, 43.0, 53.1, 121.4, 172.6 |
| **k** | (Nujol): 3360 (NH); 2250 (CN); 1760 (CO) | ($CDCl_3$): 0.8–2.5 (m, 12H, $6CH_2$—C), 3.2 (m, 1H, CH—$CH_2$—$CH_2$—CN); 3.4–4.0 (m with s at 3.6, 4H, CH—N + $H_3CO$); 4.7 (d, 1H, $J$ = 9 Hz, NH) | ($CCl_4$): 14.15, 25.4, 28.3, 30.0, 33.8, 41.7, 51.6, 53.8, 119.5, 156.6 |
| **l** | (Nujol): 3430, 3320, 3200 (NH); 2240 (CN); 1660, 1600 (CO) | (DMSO-$d_6$): −2.4 – (−1.2) (2m, 10H, $5CH_2$—C); −0.9 (m, 2H, $CH_2$—CN); −0.55 – (+0.5) (m, 2H, 2CH); 2.0 (s, 2H, $NH_2$); 2.4 (d, 1H, $J$ = 9 Hz, NH) | (DMSO-$d_6$): 13.7, 25.3, 28.2, 30.0, 34.2, 42.4, 51.6, 121.1, 158.7 |

[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.

ed and separated. The water layer is extracted with dichloromethane (2 × 20 ml) and the combined organic phases are dried with sodium sulfate. The solvents are evaporated and the residue is distilled under reduced pressure to give **4f**; yield: 2.3 g (71%); b.p. 122–125°C/0.001 torr.

| | | | | |
|---|---|---|---|---|
| $C_{11}H_{20}N_2O_2$ | calc. | C 62.23 | H 9.50 | N 13.20 |
| (212.3) | found | 62.13 | 9.42 | 13.16 |

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For a recent example of radical coupling of acetamidomercurials[6] with acrylonitrile and methyl acrylate see: A.P. Kozikowski, J. Scripko, *Tetrahedron Lett.* **24**, 2051 (1983).

[4] The stereochemistry of compounds **4i–l** was determined on the basis of the N.M.R. data of the derivatives obtained from the reductive coupling of e.g., 2-methoxycyclohexylmercury acetate with acrylonitrile: J. Barluenga, J. López-Prado, P.J. Campos, G. Asensio, *Tetrahedron* **39**, 2863 (1983).

[5] See for instance: S. Danishefsky, E. Taniyama, R.R. Webb *Tetrahedron Lett.* **24**, 11 (1983).

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