Amidomercuration; a New and Regiospecific Addition of Amides to Olefins

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Summary The reaction of olefins with anhydrous mercury(II) nitrate in the presence of primary amides leads, after *in situ* alkaline sodium borohydride reduction, to the corresponding N-substituted amides; this procedure provides a new, convenient method for the Markovnikov amidation of carbon–carbon double bonds.

Among all the synthetic methods employing intermediate organomercurials, the solvomercuration–demercuration of alkenes is probably the most important.[1] Numerous nucleophiles can be regiospecifically added to olefins *via* a mercuration reaction: for example, water, alcohols, hydroperoxides, carboxylic acids, amines, nitriles, and azide and nitrite ions.[2] The subsequent *in situ* reduction, without isolation of the intermediate organomercurials, using sodium borohydride in alkaline medium[3] provides a very general method for the Markovnikov functionalization of alkenes. However, no mercuration reaction in the presence of amides as nucleophiles has yet been reported to our knowledge. Also, our initial study with mercury(II) acetate was unsuccessful.[4]

We report now the amidomercuration–demercuration of olefins using anhydrous mercury(II) nitrate. When primary amides and related compounds such as urea or the urethane (**2**; R^4 = OEt) were allowed to react with the olefins (**1**) in the presence of anhydrous mercury(II) nitrate† in methylene dichloride, followed by *in situ* demercuration with sodium borohydride in sodium hydroxide–n-butylamine‡ solution, the corresponding N-substituted amides (**3**) were obtained (Scheme and Table).

$$\underset{(\mathbf{1})}{R^1R^2C{=}CHR^3} + \underset{(\mathbf{2})}{R^4CONH_2} \xrightarrow{\text{i, ii}} \underset{(\mathbf{3})}{R^4CONHCR^1R^2CH_2R^3}$$

Scheme. i, $Hg(NO_3)_2$; ii, $NaBH_4$.

Under the conditions studied by us, the mercuration with N-substituted amides such as *N*-propyl-acetamide and -succinimide failed.

In a typical reaction, anhydrous mercury(II) nitrate (Fluka, 10 mmol) was added to a stirred solution of the olefin (10 mmol) and the amide (100 mmol) in methylene dichloride (30 ml) and the mixture was heated under reflux for 6—24 h. The reaction mixture was cooled to 0 °C and then n-butylamine (10 ml), 10% sodium hydroxide (30 ml), and a solution of sodium borohydride (10 mmol) in 10% sodium hydroxide (10 ml) were added. The precipitated mercury(0) was filtered off, the filtrate was saturated with sodium chloride, and the organic layer separated and dried with anhydrous sodium sulphate. Finally, the solvents were removed and the residue distilled *in vacuo* or recrystallized to yield the product (**3**).

Table. Synthesis of N-substituted amides (**3**) from the olefins (**1**) and the amides (**2**).

	Olefin		Amide	% Yield[a]	M.p. or b.p.,
R^1	R^2	R^3	R^4	of (**3**)[b]	T/°C (mmHg)
H	$-[CH_2]_3-$		Me	42	72—75 (0·1)
H	$-[CH_2]_4-$		Me	92	101—103[c]
H	n-C_5H_{11}	H	Me	81	90—93 (0·1)
H	n-C_6H_{13}	H	Me	97	70—72
H	$-[CH_2]_6-$		Me	44	92—95 (0·1)
H	Ph	H	Me	84	53—56[d]
Me	Ph	H	Me	80	96—99 (0·001)
H	$PhCH_2$	H	Me	17	97—100 (0·001)
H	Ph	H	Ph	53	120—122[e]
H	Ph	H	NH_2	75	136—137[f]
H	Ph	H	OEt	99	82—84 (0·001)

[a] Based on mercury(II) nitrate. Yields have not been optimized. [b] All compounds reported in this paper gave i.r. and ^1H n.m.r. spectra and combustion analyses in accord with the structures shown. [c] Lit. (Beilstein, supplement 1, **12**, 115) m.p. 103 °C. [d] Lit. (Beilstein, **12**, 1095) m.p. 57 °C. [e] Lit. (Beilstein, **12**, 1095) m.p. 120 °C. [f] Lit. (Beilstein, **12**, 1096) m.p. 137 °C.

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† The use of $Hg(NO_3)_2 \cdot H_2O$ leads to lower yields.

‡ When the reduction with $NaBH_4$ in alkaline medium was carried out in the presence of an amine, higher yields were obtained (ref. 4).

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