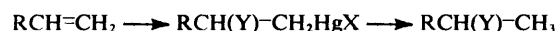


Amidomercuriation: A General Addition of Amides and Related Compounds to Olefins †

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The addition of different carboxamides and related compounds such as urethane or urea to olefins using mercury(II) nitrate followed by sodium borohydride reduction to give the corresponding *N*-substituted amides, urethanes, or ureas, respectively, is described. The monoalkylated ureas, through the same amidomercuriation–demercuration procedure, yield symmetrical and unsymmetrical *N,N'*-disubstituted ureas. This amidomercuriation–demercuration process provides a new, convenient, and general method for the Markovnikov amidation of carbon–carbon double bonds.

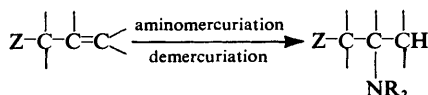
The solvomercuration–demercuration of alkenes is probably the most important synthetic method employing intermediate organomercurials. This sequence provides a general method for the Markovnikov functionalization of alkenes (Scheme 1).¹



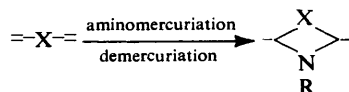
Scheme 1.

Its advantages over other procedures are: (a) extremely mild reaction conditions are involved; (b) considerable functionality is accommodated; (c) carbon skeletal rearrangements are rare; and (d) numerous nucleophiles, Y, can be employed, *e.g.* water, alcohols, hydroperoxides, carboxylic acids, amines, nitriles, and azide and nitrite ions.² Primary emphasis will be on those procedures which accomplish the above transformation *in situ*, without isolation of the intermediate organomercurials, as these are clearly the synthetically more appealing procedures. The sodium borohydride reduction in alkaline media³ is the most convenient *in situ* reducing agent. The final result of this tandem procedure is the regiospecific addition of nucleophiles to non-activated olefins.

We have also employed the aminomercuriation–demercuration (Y = R₂NH) of functionalized olefins and dienes for the synthesis of 1,2-bifunctionalized systems (Scheme 2) and nitrogen-containing heterocycles (Scheme 3), respectively.



Scheme 2. Z = R₂N,^{4a} RS,^{4a} or R³Si^{4b}



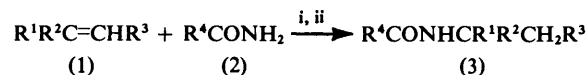
Scheme 3. X = (CH₂)₂,^{5a} (CH₂)₃,^{5b} (CH₂OCH₂),^{5c} CH₂N(R)CH₂,^{5d} or CH₂Si(Me)₂CH₂^{4b}

However, the aminomercuriation with ammonia and mercury(II) salts afforded ammonia–mercury(II) complexes^{2c,6} instead of the products of addition to the double bond, primary amines. This observation prompted us to investigate

the addition of amides to olefins using mercury(II) salts. It is apparent that the hydrolysis of the resulting *N*-alkylamides should provide the corresponding primary amines.

Results and Discussion

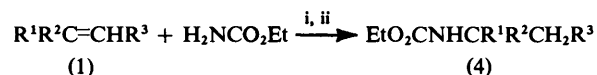
Synthesis of *N*-Substituted Carboxamides.—The reaction of the olefins (1) with the primary amides (2) using mercury(II) nitrate in methylene dichloride, followed by *in situ* demercuration with sodium borohydride in aqueous sodium hydroxide and *n*-butylamine as co-solvent, yielded the corresponding *N*-substituted amides (3) (Scheme 4 and Table 1).



Scheme 4. Reagents: i, Hg(NO₃)₂; ii, NaBH₄

The best yields of the *N*-alkyl carboxamides (3) were obtained when anhydrous mercury(II) nitrate was employed. The mercuration with *N*-substituted amides such as *N*-propylacetamide and -succinimide, under the conditions we investigated failed. This fact reduced the possibility of this reaction working with dienes. The sodium borohydride reduction in the presence of an organic amine gave the best results when the deamidomercuriation reaction was avoided.^{5a} The ready conversion of the representative olefins (1) into the corresponding Markovnikov derivatives is noticeable. Only in the mercuration of linear alkenes (hex-1-ene and oct-1-ene) with formamide were the regioisomeric amides (3o) and (3p), respectively, obtained.

Synthesis of *N*-Substituted Urethanes.—The same amidomercuriation reaction, with urethane as nucleophile and



Scheme 5. Reagents: i, Hg(NO₃)₂; ii, NaBH₄

further *in situ* demercuration with alkaline sodium borohydride leads to the *N*-substituted urethanes (4) (Scheme 5 and Table 2).

Our preliminary attempts to use urethane in the intermolecular cyclization of suitable dienic systems (Scheme 3) were successful. As an example, the amidomercuriation–demercuration of cyclo-octa-1,5-diene with urethane yielded

† Preliminary communication, J. Barluenga, C. Jiménez, C. Nájera, and M. Yus, *J. Chem. Soc., Chem. Commun.*, 1981, 670.

Table 1. *N*-Substituted carboxamides (3)

Olefin (1)			Amide (2) R ⁴	Product (3)	Yield (%) ^a		M.p. or b.p. [°C (mmHg)]	Lit. m.p. or b.p. [°C (mmHg)]	Ref.
R ¹	R ²	R ³			(3)	Hg ⁰			
H	(CH ₂) ₃		Me	(3a)	42	100	72–75 (0.1)	89–92 (0.5)	7
H	(CH ₂) ₄		Me	(3b)	92	93	101–103 ^b	103	8
H	<i>n</i> -C ₄ H ₉	H	Me	(3c)	88	92	89–92 (0.1)	106–111 (1.8)	9
H	<i>n</i> -C ₅ H ₁₁	H	Me	(3d)	81	86	90–93 (0.1)		
H	<i>n</i> -C ₆ H ₁₃	H	Me	(3e)	97	100	70–72 ^b	129–129.2 (1.5)	10
H	Ph	H	Me	(3f)	84	96	53–56 ^b	57	11
Me	Ph	H	Me	(3g)	80	95	96–99 (0.001)	97.5–98.5	12
H	PhCH ₂	H	Me	(3h)	17	100	97–100 (0.001)	180–185 (13)	13
H	(CH ₂) ₄		Ph	(3i)	85	100	146–147 ^c	153	8
H	<i>n</i> -C ₄ H ₉	H	Ph	(3j)	70	72	81–83 ^d	81–83	14
H	<i>n</i> -C ₆ H ₁₃	H	Ph	(3k)	72	75	76–78 ^d	76.5	15
H	Ph	H	Ph	(3l)	53	100	120–122 ^d	120	16
Me	Ph	H	Ph	(3m)	99	100	156–158 ^e	159	17
H	(CH ₂) ₄		H	(3n)	50	89	70–73 (0.1)	118–120 (3)	18
H	<i>n</i> -C ₄ H ₉	H	H	(3o) ^f	57	94	63–65 (0.1)	111 (12) ^g	19
H	<i>n</i> -C ₆ H ₁₃	H	H	(3p) ^h	35	88	70–73 (0.1)	102–105 (0.6) ⁱ	7
H	Ph	H	H	(3q)	35	92	90–95 (0.001)	184.5–186 (22)	20

^a Based on mercury(II) nitrate. ^b From hexane. ^c From ethanol. ^d From methanol. ^e From carbon tetrachloride. ^f Isolated as a mixture of 2-hexylformamide (29%) and 1-hexylformamide (71%). ^g B.p. of 2-hexylformamide. ^h Isolated as a mixture of 2-octylformamide (95%) and 1-octylformamide (5%). ⁱ B.p. of a mixture of regioisomeric octylformamides.

Table 2. *N*-Substituted urethanes (4)

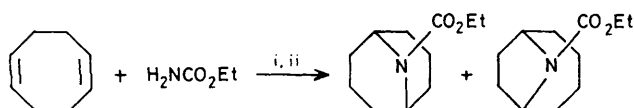
Olefin (1)			Product (4)	Yield (%) ^a		M.p. or b.p. [°C (mmHg)]	Lit. m.p. or b.p. [°C (mmHg)]	Ref.
R ¹	R ²	R ³		(4)	Hg ⁰			
H	(CH ₂) ₃		(4a)	95	98	65–70 (0.1)	125 (20)	21
H	(CH ₂) ₄		(4b)	96	99	55–57	56	22
H	(CH ₂) ₆		(4c)	25	93	75–78 (0.1)		
H	<i>n</i> -C ₄ H ₉	H	(4d)	86	93	50–53 (0.1)		
H	<i>n</i> -C ₆ H ₁₃	H	(4e)	83	100	76–78 (0.1)	80–81 (0.35)	23
H	Ph	H	(4f)	99	100	82–84 (0.001)	93–95 (0.25)	24
Me	Ph	H	(4g)	57	100	114–116 (0.1)	112–115 (0.1)	25

^a Isolated yields based on mercury(II) nitrate.

Table 3. *N*-Substituted and *N,N'*-disubstituted ureas (5) and (7)

Olefin (1) ^a		Olefin (6)		Product	Yield (%) ^b		M.p. or b.p. [°C (mmHg)]	Lit. m.p. (°C)	Ref.
R ²	R ³	R ⁴	R ⁵		(5) ^c or (7) ^c	Hg ⁰ ^b			
(CH ₂) ₃				(5a)	62	100	197–199 ^d	198–200	27
(CH ₂) ₄				(5b)	84	85	194–196 ^e	195–196	28
<i>n</i> -C ₄ H ₉	H			(5c)	83	90	114–116 ^f		
<i>n</i> -C ₆ H ₁₃	H			(5d)	76	80	121–123 ^f		
Ph	H			(5e)	91	100	136–137 ^g	137	29
(CH ₂) ₄		(CH ₂) ₄		(7a)	59	94	237–238 ^d	236–238	18
(CH ₂) ₄		Ph	H	(7b)	65	86	178–180 ^f		
<i>n</i> -C ₆ H ₁₃	H	Ph	H	(7c)	78	98	100–105 (0.001)		
Ph	H	Ph	H	(7d)	75	84	116–120 (0.001)	153 ^h	20

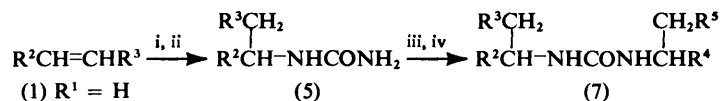
^a R¹ = H. ^b Isolated yields based on mercury(II) nitrate. ^c Isolated yields based on compound (5). ^d From acetone. ^e From carbon tetrachloride. ^f From methanol. ^g From water. ^h For *meso*-compound.

Scheme 6. Reagents: i, Hg(NO₃)₂; ii, NaBH₄

N-ethoxycarbonyl-9-azabicyclo-[3.3.1]- and -[4.2.1]-nonanes (Scheme 6).

Similar results were obtained in the sulphonamidomercuriation–demercuration of cyclo-octa-1,5-diene.²⁶

Synthesis of Substituted Ureas.—When urea was used as the nucleophile in the amidomercuriation–demercuration of alkenes, the *N*-substituted ureas (5) were obtained (Scheme 7 and Table 3). Although the urea is a double nucleophile, dialkylated compounds were never observed under the different stoichiometric conditions which we studied. The corresponding *N,N'*-disubstituted ureas (7) were prepared by a subsequent amidomercuriation–demercuration process. Thus, when the obtained monoalkylated ureas (5) were allowed to react with another olefin (6) in the presence of mercury(II) nitrate and further reduction with alkaline sodium boro-



Scheme 7. Reagents: i, $\text{H}_2\text{NCONH}_2\text{-Hg}(\text{NO}_3)_2$; ii, NaBH_4 ; iii, $\text{R}^4\text{CH}=\text{CHR}^5$ (6)- $\text{Hg}(\text{NO}_3)_2$; iv, NaBH_4

hydride then carried out, symmetrical and unsymmetrical N,N' -disubstituted ureas (7), depending on the employed olefins (1) and (6), were obtained (Scheme 7 and Table 3).

Experimental

M.p.s are uncorrected and were measured on a Büchi-Tottoli capillary melting point apparatus. I.r. spectra were determined with a Pye-Unicam Sp-1000 spectrometer. ^1H and ^{13}C N.m.r. spectra were recorded on a Varian FT-80 spectrometer, with SiMe_4 as internal standard.

Amidomercuriation-Demercuriation of Olefins. General Procedure.—To a solution of the olefin (1) (10 mmol) and the amide (2) (or urethane or urea) (50 mmol) in methylene dichloride (30 ml), anhydrous mercury(II) nitrate (Fluka; 10 mmol) was added. After being stirred for ca. 24 h under reflux, the resulting solution was cooled to 0°C and then 10% aqueous sodium hydroxide (30 ml), *n*-butylamine (10 ml), and finally a solution of sodium borohydride (10 mmol) in 10% sodium hydroxide (10 ml) were added. The mixture was extracted and the mercury(0) was precipitated and filtered off. The organic layer was saturated with sodium chloride, separated and dried (Na_2SO_4) and the solvents evaporated off. The residue was distilled *in vacuo* or recrystallized to yield products (3), (4), and (5). Data for these compounds are available as a Supplementary Publication * (SUP No. 23494, 5 pages).

***N*-Ethoxycarbonyl-9-azabicyclo-[3.3.1]- and -[4.2.1]-nonanes.**—Anhydrous mercury(II) nitrate (20 mmol) was added to a solution of cyclo-octa-1,5-diene (1.2 ml, 10 mmol) and urethane (4.5 g, 50 mmol) in methylene dichloride (30 ml). The mixture was stirred under reflux for 24 h, then cooled to 0°C , and 10% sodium hydroxide (20 ml), *n*-butylamine (10 ml) and a solution of sodium borohydride (0.76 g, 20 mmol) in 10% aqueous sodium hydroxide (10 ml) were added. After being stirred for 20 h, the solution was saturated with sodium chloride, decanted and dried. Mercury(0) was isolated (3.9 g, 98%). After the solvents had been removed the residue was distilled (71–73 $^\circ\text{C}/0.1$ mmHg) to give a mixture of *N*-ethoxycarbonyl-9-azabicyclo-[3.3.1]-³⁰ and -[4.2.1]-nonanes³¹ (1.8 g, 90%) in ca. 1 : 1 molar ratio (by g.l.c.; Bentone 34 and di-isodecyl phthalate), $\nu(\text{film})$ 1690 cm^{-1} (CO); $\delta(\text{CCl}_4\text{-D}_2\text{O}$ capillary) 1.1 (t, J 7 Hz, Me), 1.2–2.3 (m, CH_2), and 3.8–4.3 (m with q at 3.9, J 7 Hz, CH_2O and CH); $\delta(^{13}\text{C})$ ($\text{CCl}_4\text{-D}_2\text{O}$ capillary) 14.3, 14.4, 20.0, 24.0, 28.9, 29.4, 29.9, 30.9, 33.1, 34.3, 45.4, 46.3, 54.9, 55.2, 153.2, and 153.9 p.p.m.

N,N' -Disubstituted Ureas (7). General Procedure.—To a suspension of the obtained *N*-substituted urea (5) (10 mmol) and the olefin (6) (10 mmol) in methylene dichloride (30 ml), anhydrous mercury(II) nitrate (10 mmol) was added. After stirring the mixture under reflux for 24 h, the reduction was carried out as above. Data for compounds (7) are given in the Supplementary Publication (SUP No. 23494, 5 pages).

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* For details of the Supplementary Publications Scheme, see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. I*, 1981, Index issue.