Catalytic Aminomercuriation of Propargyl Ethers and Thioethers: Synthesis of β-Oxy- and β-Thioenamines and Related Compounds

José BARLUENGA*, Fernando AZNAR, Ramón LIZ

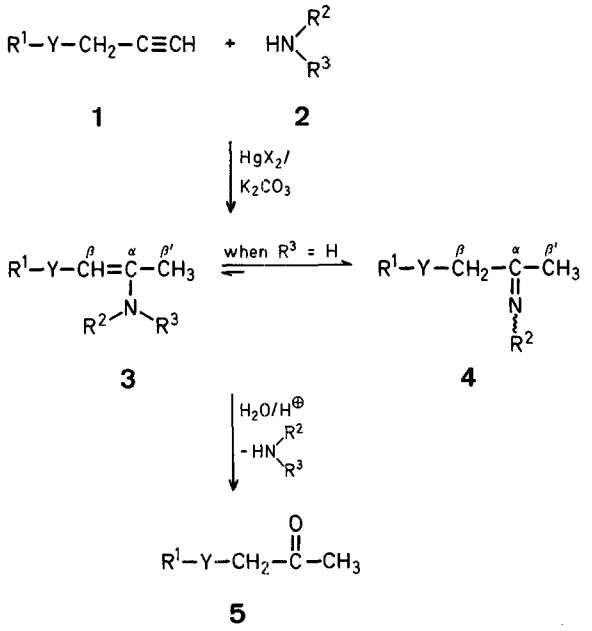
Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, Oviedo-7, Spain

Enamines[1] and, on a small scale, enol ethers[2,3,4] are two classes of compounds whose reactivity has attracted much attention. In previous work[5,6], we have described a facile synthesis of enamines via catalytic aminomercuriation of terminal alkynes. We now report an extension of this method to propargyl ethers and thioethers with a terminal triple bond and some characteristic reactions of the enamines prepared.

When the reaction of a propargyl ether or thioether **1**, a secondary amine **2**, and a catalytic amount of mercury(II) chloride or acetate is carried out at room or moderate temperature, usually in the presence of potassium carbonate, the corresponding β-alkyloxy-, β-phenoxy-, or β-phenylthioenamine **3** with the more substituted double bond is obtained (Table 1).

On the other hand, enamines derived from unsymmetrical ketones have been reported to exist as a mixture of isomers differing in the double bond position[7,8]. However, spectroscopic studies on enol ether- or enol thioether-enamines **3** only allow us to ascertain the presence of the more substituted isomer. This finding can be related with the higher degree of electron delocalisation to be expected for the isomer with the internal double bond. This result is particularly interesting in the cases of morpholino enamines **3k, l**, whose N—C=C moiety should reach coplanarity with less strain in the less substituted form[9]. Compounds **3a–g** are produced as a ~ 2 : 1 mixture of *(Z)*- and *(E)*-isomers. Stereoelectronic factors account for the predominance of the *(Z)*-stereoisomer and also that it displays the lowest field signals for H-β and C-β in the ^{1}H-N.M.R. spectra[10,11,12]. In contrast, a single stereoisomer, probably *(E)*, is present in compounds **3h–l**.

On hydrolysis with acid, compounds **3** behave as enamines and lead in all cases exclusively to the corresponding monosubstituted acetones **5**. 2-Aminopropanals derived from the enol ether or enol thioether hydrolysis could not be detected.



The above results and the known existence of some metastable secondary enamines[13] prompted us to substitute primary for secondary amines in the previously described reaction. However, only the corresponding imines **4** (Table 2) were always isolated under our reaction conditions. Compounds **4a–d** were obtained as a ~ 5 : 1 mixture of *(E)*- and *(Z)*-isomers, determined by ^{1}H-N.M.R.; compounds **4e, f** appear as a single stereoisomer, tentatively assigned as the *(E)*-isomer.

Potassium carbonate is added to avoid the acid-catalysed self-condensation processes of enamines[15,16]. Otherwise, some lowered yields in compounds **3** are usually obtained when secondary amines are employed. However, a surprising behaviour is observed in the mercury(II) chloride-catalysed reaction of propargyl ethers **6** with *N*-methylaniline **7** at room temperature, which lead to the formation of the corresponding 2,4-bis[alkoxymethyl]- or 2,4-bis[aryloxymethyl]-1,4-dimethyl-1,4-dihydroquinolines **9** (Table 3).

Table 1. Enol Ether- or Enol Thioether-enamines **3** prepared

Product No.	R^1Y	R^2	R^3	Reaction conditions: time/temp. [°C]	Reaction conditions: Method[a]	Yield[b] [%]	b.p. [°C]/[torr]	Molecular formula[c]	^{1}H-N.M.R. (CCl_4/TMS)[d,e,f] δ [ppm]	^{13}C-N.M.R. (CCl_4/TMS)[d,f] δ [ppm]: C-β	C-α	C-β'
3a	H_3CO	C_6H_5	CH_3	5 h/ r.t.	A/W	41	50°/ 0.05	$C_{11}H_{15}NO$ (177.2)	1.65 (s, 3H); 2.95 (s, 3H); 3.45, 3.55 (2s, 3H); 5.65, 6.05 (2s, 1H); 6.35–7.2 (m, 5H)	142.9, 148.1(2d)	122.2, 125.4(2s)	15.4, 11.7(2q)
3b	H_3CO	C_6H_5	C_2H_5	24 h/ r.t.	B/Y	46	58°/ 0.05	$C_{12}H_{17}NO$ (191.3)	1.15 (t, 3H); 1.65 (s, 3H); *3.35 (q, 2H);* 3.45, 3.55 (2s, 3H); 5.7, 6.0 (2s, 1H); 6.4–7.2 (m, 5H)	143.5, 149.0(2d)	119.3, 122.9(2s)	16.5, 12.7(2q)
3c	*H_3CO*	*3-H_3C—C_6H_4*	*C_2H_5*	*24 h/ 67°*	A/W	63	65°/ 0.001	*$C_{13}H_{19}NO$* (205.3)	*1.15 (t, 3H);* 1.65 (s, 3H); 2.25 (s, 3H); 3.3 (q, 2H); 3.45, 3.55 (2s, 3H); 5.65, 6.0 (2s, 1H); 6.2–7.0 (m, 4H)	*141.4,* 147.1(2d)	*118.9,* 121.8(2s)	*15.3,* 11.4(2q)
3d[i]	$C_6H_5CH_2O$	C_6H_5	CH_3	13 h/ r.t.	A/Y	60	106°/ 0.001	$C_{17}H_{19}NO$ (255.3)	1.6, 1.7 (2s, 3H); 3.0, 2.95 (2s, 3H); 4.7, 4.75 (2s, 2H); 5.85, 6.25 (2s, 1H); 6.5–7.5 (m, 10H)[g]	141.0, 146.4(2d)	122.0, 125.7(2s)	15.3, 11.7(2q)
3e[j]	C_6H_5O	C_6H_5	CH_3	20 h/ r.t.	A/X	76	90°/ 0.001	$C_{16}H_{17}NO$ (239.3)	1.75, 1.85 (2s, 3H); 3.1, 3.05 (2s, 3H); 6.25, 6.5 (2s, 1H); *6.55–7.35 (m, 10H)*	136.2, 140.1(2d)	–[h]	16.0, 12.9(2q)
3f[i]	C_6H_5O	C_6H_5	C_2H_5	21 h/ 67°	A/X	17	105°/ 0.001	$C_{17}H_{19}NO$ (253.3)	1.25 (t, 3H); 1.75, 1.85 (2s, 3H); 3.55, 3.45 (2q, 2H); 6.2, 6.5 (2s, *1H);* 6.6–7.3 (m, 10H)	135.8, 140.9(2d)	–[h]	16.9, 13.5(2q)
3g[j]	C_6H_5O	3-H_3C—C_6H_4	C_2H_5	17 h/ r.t.	A/X	62	110°/ 0.001	$C_{18}H_{21}NO$ (267.4)	1.1 (t, 3H); 1.55 (s, 3H); 2.2 (s, 3H); 3.3, 3.5 (2q, 2H); 5.7, 6.0 (2s, 1H); 6.2–7.1 (m, 9H)	135.8, 140.9(2d)	–[h]	16.9, 13.5(2q)
3h[i]	C_6H_5S	C_6H_5	CH_3	18 h/ r.t.	A/X	70	118°/ 0.001	$C_{16}H_{17}NS$ (255.4)	1.9 (s, 3H); 3.1 (s, 3H); 5.1 (s, 1H); 6.85–7.4 (m, 10H)	92.8(d)	154.2(s)	19.0(q)
3i[i]	C_6H_5S	C_6H_5	C_2H_5	22 h/ r.t.	B/X	31	123°/ 0.001	$C_{17}H_{19}NS$ (269.4)	1.2 (t, 3H); 1.9 (s, 3H); 3.65 (q, 2H); *5.15 (s, 1H);* 6.85–7.35 (m, 10H)	90.2(d)	153.3(s)	18.9 (q)
3j[i]	C_6H_5S	3-H_3C—C_6H_4	C_2H_5	16 h/ 45°	A/X	45	126°/ 0.001	$C_{18}H_{21}NS$ (283.4)	1.15 (t, 3H); 1.8 (s, 3H); 2.3 (s, 3H); 3.6 (q, 2H); 5.1 (s, 1H); 6.55–7.3 (m, 9H)	88.5 (d)	156.9(s)	17.5(q)
3k[i]	C_6H_5S	—$(CH_2)_2$—O—$(CH_2)_2$—		4 h/ 100°	D/X	55	130°/ 0.001	$C_{13}H_{17}NOS$ (235.3)	2.05 (s, 3H); 2.95 (m, 4H); 3.65 (m, 4H); 4.95 (s, 1H); 6.85–7.3 (m, 5H)	–[h]	136.7(s)	12.2(q)
3l[j]	C_6H_5O	—$(CH_2)_2$—O—$(CH_2)_2$—		16 h/ r.t.	E/X	73	101°/ 0.001	$C_{13}H_{17}NO_2$ (219.3)	1.75 (s, 3H); 2.75 (m, 4H); 3.65 (m, 4H); 6.8 (s, 1H); 6.65–7.35 (m, 5H)			

[a] See *Experimental.*
[b] Based on alkyne.
[c] All new compounds **3a–l** gave satisfactory microanalyses: C ±0.25; H ±0.19; N ±0.15.
[d] Recorded in a Varian FT-80a spectrometer with a D_2O capillary.
[e] Unresolved long-range coupling between C-β and C-β' hydrogen atoms was observed for **3a–g**.
[f] First value in duplicate signals concerns to the (*E*)-isomer.
[g] In $CDCl_3$.
[h] The corresponding carbon nucleus resonates in the range of the *aromatic carbons.*
[i] The starting alkyne is prepared according to Ref.[20].
[j] The starting alkyne is prepared according to Ref.[21].

Table 2. Imines **4** prepared

Product No.	R^1Y	R^2	Reaction conditions: time/temp. [°C]	Method[a]	Yield[b] [%]	m.p. [°C]/(solvent) or b.p. [°C]/[torr]	Molecular formula[c] or lit. data	^{1}H-N.M.R. ($CDCl_3$/TMS)[d,e] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS)[d,e] δ [ppm]: C-α	C-β	C-β′
4a[j]	C_6H_5O	C_6H_5	5 h/r.t.	A/X[f]	88	75–77° (hexane)	76–77.5° (hexane)[13]	1.9, 2.3 (2s, 3H); 4.7, 4.45 (2s, 2H); 6.55–7.45 (m, 10H)	168.3, 167.7(2s)	73.5, 66.9(2t)	16.2, 23.5(2q)
4b[j]	C_6H_5O	2-H_3C—C_6H_4	3 h/r.t.	A/X[f]	84	100°/0.001	$C_{16}H_{17}NO$ (239.3)	1.85, 2.1 (2s, 3H); 2.1, 2.35 (2s, 3H); 4.75, 4.35 (2s, 2H); 6.5–7.45 (m, 9H)	168.7, 168.1(2s)	73.8, 65.7(2t)	17.2, 24.2(2q)
4c[j]	C_6H_5O	2-H_3CO—C_6H_4	13 h/r.t.	A/X[f]	67	112°/0.001	$C_{16}H_{17}NO_2$ (255.3)	1.8, 2.3 (2s, 3H); 3.75, 3.7 (2s, 3H); 4.75, 4.4 (2s, 2H); 6.55–7.45 (m, 9H)	170.8, 170.6(2s)	74.1, 67.9(2t)	17.6, 24.2(2q)
4d[k]	C_6H_5S	C_6H_5	5 h/r.t.	A/X[f]	81	44–46° (hexane)[g]	37–39° (ethanol)[h,13]	1.8, 2.25 (2s, 3H); 3.7, 3.35 (2s, 2H); 6.25–7.55 (m, 10H)[i]			
4e[j]	C_6H_5O	n-C_4H_9	12 h/r.t.	E/X	53	56°/0.001	$C_{13}H_{19}NO$ (205.3)	0.9 (t, 3H); 1.15–1.85 (m, 4H); 1.9 (s, 3H); 3.3 (t, 2H); 4.5 (s, 2H); 6.7–7.5 (m, 5H)	166.2(s)	75.1(t)	15.0(q)
4f[j]	C_6H_5O	$C_6H_5CH_2$	1.25 h/100°	D/X	56	120°/0.001	$C_{16}H_{17}NO$ (239.3)	1.9 (s, 3H); 4.45 (s, 2H); 4.5 (s, 2H); 6.7–7.35 (m, 10H)[i]			

[a] See Experimental.
[b] Based on alkyne.
[c] All compounds **4** gave satisfactory microanalyses: C ±0.3; H ±0.15; N ±0.06.
[d] Recorded in a Varian FT-80A spectrometer with a D_2O capillary.
[e] First value in duplicate signals concerns to the (*E*)-isomer.
[f] Similar yields were reached when reactions were carried out with commercial tetrahydrofuran, air atmosphere and absence of potassium carbonate and a moist work-up (a 10 min basic sodium borohydride reduction, extraction with ether) is selected.
[g] b.p. 123°/0.001.
[h] Tautomeric equilibrium with a 10% amount of the corresponding secondary enamine.
[i] In $CDCl_3$.
[j] The starting alkyne was prepared according to Ref.[21].
[k] The starting alkyne was prepared according to Ref.[20].

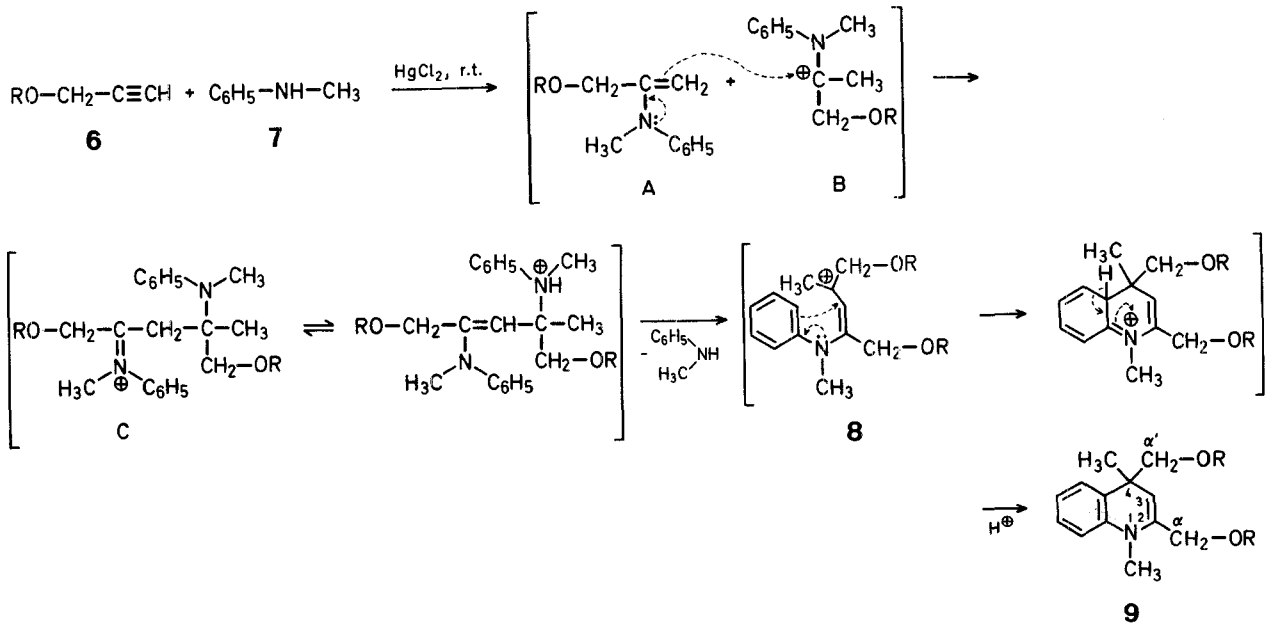


Table 3. 1,4-Dihydroquinoline Derivatives **9** prepared[a]

Product No.	R	Yield[b] [%]	Molecular formula[c]	^{1}H-N.M.R. ($CDCl_3$/TMS)[d,e] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS)[d,e] δ [ppm]			
					C-2	C-3	C-α	C-α'
9a[f]	CH_3	89	$C_{15}H_{19}NO_2$ (245.3)	1.4 (s, 3H); 2.8 (s, 3H); 3.25 (s, 3H); 3.30 (s, 3H); 3.31 (s, 2H); 4.1 (s, 2H); 5.35 (s, 1H); 6.3–7.1 (m, 4H)	119.7 (s)	109.8 (d)	77.7 (t)	71.5 (t)
9b[i]	CH_2=CH—CH_2	70	$C_{19}H_{25}NO_2$ (299.4)	1.4 (s, 3H); 2.85 (s, 3H); 3.45 (s, 2H); 3.85–4.1 (m, 4H); 4.3 (s, 2H); 4.95–6.15 (m, 7H); 6.45–7.45 (m, 4H)	121.9 (s)	111.9 (d)	76.7 (t)	71.1 (t)
9c[i]	H_3C—CH=CH—CH_2	46	$C_{21}H_{29}NO_2$ (327.5)	1.3 (s, 3H); 1.7 (m, 6H); 2.85 (s, 3H); 3.4 (s, 2H); 3.75–4.0 (m, 4H); 4.25 (s, 2H); 5.5 (s, 1H); 5.55–6.3 (m, 4H); 6.45–7.3 (m, 4H)	122.1 (s)	112.1 (d)	76.4 (t)	70.9 (t)
9d[j]	C_6H_5—CH_2	65	$C_{27}H_{29}NO_2$ (399.5)	1.35 (s, 3H); 2.85 (s, 3H); 3.45 (s, 2H); 4.3 (s, 2H); 4.45 (s, 2H); 4.5 (s, 2H); 5.5 (s, 1H); 6.5–7.5 (m, 14H)	122.0 (s)	112.2 (d)	76.7 (t)	71.4 (t)
9e[g,j]	C_6H_5	83	$C_{25}H_{25}NO_2$ (371.5)	1.5 (s, 3H); 2.9 (s, 3H); 5.6 (s, 2H)[h]; 4.8 (s, 2H); 5.6 (s, 1H); 6.5–7.3 (m, 14H)	119.4 (s)	110.4 (d)	72.2 (t)	67.3 (t)
9f[j]	3-H_3C—C_6H_4	84	$C_{27}H_{29}NO_2$ (399.5)	1.55 (s, 3H); 2.25 (s, 3H); 2.3 (s, 3H); 2.9 (s, 3H); 3.9 (s, 2H); 4.8 (s, 3H); 5.65 (s, 1H); 6.5–7.3 (m, 12H)	121.5 (s)	113.0 (d)	73.8 (t)	68.9 (t)

[a] Reactions were carried out at room temperature during 18 h. Reaction conditions C and work-up procedure Z were selected (see Experimental).
[b] Based on alkyne.
[c] All new compounds **9a–f** gave satisfactory microanalyses: C ±0.23; H ±0.13; N ±0.11.
[d] Recorded in a Varian FT-80A spectrometer.
[e] Unresolved long-range coupling between C-3 and C-α hydrogen atoms was always observed.
[f] M.S., m/e = 245 (M^+).
[g] M.S., m/e = 371 (M^+).
[h] In CCl_4 solution the α' methylene hydrogen atoms are not accidentally equivalent and this signal displays the typical pseudoquatriplet pattern.
[i] The starting alkyne is prepared according to Ref[20].
[j] The starting alkyne is prepared according to Ref.[21].

Dihydroquinolines **9** are also formed from the corresponding β-alkyloxy- or β-aryloxyenamines **3** and gaseous hydrogen chloride as shown by the conversion of **3e** to **9e**. The formation of compounds **9** can be rationalized in terms of an initial self-condensation process[15,16] of enol ether-enamines **3**, followed by an *ortho*-cyclisation of the protonated dienamine intermediate **8**[17]. Although the signals for the protons of the less substituted isomers A are not distinguishable in the ^{1}H-N.M.R. spectra of compounds **3**, trace amounts of A might be in equilibrium with **3** to allow the progress of the reaction as shown in above.

When other amines, different from *N*-methylaniline, are used in the latter reaction, none or small amounts of impure dihydroquinoline derivatives are obtained.

The formation of compounds **9b, c**, in which a carbon-carbon double bond originally present in the starting propargyl ether **6** has remained unchanged, implies that the well known stoichiometric aminomercuriation of olefins[18,19] cannot compete against the catalytic aminomercuriation of terminal acetylenes.

Preparation of Compounds 3, 4 and 9; General Procedure:
See Tables 1–3 for choice of the appropriate reaction conditions and work-up procedure.

Method A: Potassium carbonate (0.55 g, 4 mmol) and mercury(II) chloride (0.27 g, 1 mmol) are successively added, under argon, to a solution of propargyl ether or thioether **1** (20 mmol) and the dry amine **2** (100 mmol) in dry tetrahydrofuran (10 ml), and the mixture is stirred. An external water bath is used when the reaction is carried out at room temperature.

Method B: Analogous to Method A, but without potassium carbonate.

Method C: Analogous to Method A, but potassium carbonate, argon atmosphere, and tetrahydrofuran are not employed.

Method D: Potassium carbonate (1.38 g, 10 mmol) and mercury(II) chloride (1.36 g, 5 mmol) are succesively added, under argon, to a solution of propargyl ether or thioether **1** (20 mmol) and the dry amine **2** (100 mmol) in dry dioxan (30 ml), and the mixture is stirred under reflux.

Method E: Mercury(II) acetate (4.76 g, 15 mmol) is added under argon to a solution of 3-phenoxy-1-propyne (**1**; R^1-Y = C_6H_5O; 2.64 g, 20 mmol) and the dry amine **2** (60 mmol) in dry dichloromethane (50 ml) at room temperature, and the mixture is stirred.

Work-up Procedures:

Method W, (under argon): Volatile components and reaction products are successively distilled in vacuo from the crude reaction mixture.

Method X, (under argon): The volatile components are evaporated in vacuo and the crude products treated with dry ether (3 × 20 ml) and filtered. Insoluble matter is discarded and the liquid phase concentrated and distilled in vacuo.

Method Y: Aqueous 3 molar potassium hydroxide is added until basic to the resultant mixture which is then extracted with ether (3 × 20 ml), washed, and dried with sodium sulphate. Volatile components and reaction products are succesively distilled in vacuo.

Method Z, (for compounds **9**): Aqueous 3 molar potassium hydroxide is added until basic to the resultant mixture which is then extracted with ether (3 × 20 ml), washed, and dried with sodium sulphate. The volatile components are evaporated in vacuo and the crude mixture is treated with *n*-hexane (3 × 20 ml) and filtered. Insoluble matter is discarded and the liquid phase concentrated. For compounds **9a** and **9e** and additional chromatographic purification (silica gel; cyclohexane/ether, 1 : 1) is required. Compounds **9** are stable brown oils or amorphous solids which could not be crystallised.

Received: October 12, 1983

* Address for correspondence.

[1] P.W. Hickmott, *Tetrahedron* **38**, 1975, 3363 (1982).
[2] C. Earnshaw, C.J. Wallis, S.J. Warren, *J. Chem. Soc. Perkin Trans. 1* **1979**, 3099.
[3] M. Riediker, J. Schwartz, *J. Am. Chem. Soc.* **104**, 5842 (1982).
[4] J.C. Gilbert, U. Weerasooriya, *J. Org. Chem.* **48**, 448 (1983).
[5] J. Barluenga, F. Aznar, R. Liz, R. Rodes, *J. Chem. Soc. Perkin Trans. 1* **1980**, 2732.
[6] J. Barluenga, F. Aznar, R. Liz, R. Rodes, *J. Chem. Soc. Perkin Trans. 1* **1983**, 1087.
[7] W.D. Gurowitz, M.A. Joseph, *J. Org. Chem.* **32**, 3289 (1967).
[8] R. Carlson et al., *Acta Chem. Scand.* [B] **32**, 85 (1978).
[9] D. Pocar, R. Stradi, B. Gioia, *Gazetta Chim. Ital.* **98**, 958 (1968).
[10] R. Stradi, D. Pocar, *Chim. Ind.* **53**, 265 (1971).
[11] R. Stradi, D. Pocar, C. Cassio, *J. Chem. Soc. Perkin Trans. 1* **1974**, 2671.
[12] R. Stradi, P. Trimarco, A. Vigevani, *J. Chem. Soc. Perkin Trans. 1* **1978**, 1.
[13] See for example: R. Knorr, A. Weiss, P. Löw, E. Räpple, *Chem. Ber.* **113**, 2462 (1980).
[14] D.Y. Curtin, E.J. Grubbs, C.G. McCarty, *J. Org. Chem.* **28**, 2775 (1963).
[15] G. Bianchetti, P. Dalla Croce, D. Pocar, *Ist. Lomb. Sci. Lett.* [A] **99**, 259 (1965); *C.A.* **65**, 7173 (9965).
[16] P.W. Hickmott, B.J. Hopkins, C.T. Yoxall, *J. Chem. Soc.* [B] **1971**, 205.
[17] To our knowledge, this type of cyclisation is unknown in the enamine field. Hence, the overall process **3** → **9** represents the first example of the specific reactivity of compounds **3**, the extension of which is currently under investigation.
[18] J. Barluenga, C. Jiménez, C. Nájera; M. Yus, *Synthesis* **1982**, 417; and references cited therein.
[19] M.B. Gasc, A. Lattes, J.J. Perie, *Tetrahedron* **39**, 703 (1983).
[20] Cf. J.K. Kim, M.C. Caserio, *J. Org. Chem.* **44**, 1897 (1979).
[21] Cf. C.F. Allen, J.W. Gates, Jr., *Org. Synth. Coll Vol.* III, 418 (1950).