Regiospecific Synthesis of Terminal, Oxyfunctionalized Methyl Ketone Enamines *via* Catalytic Aminomercuriation of Prop-2-ynyl Esters and Ethers

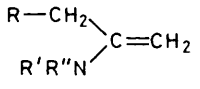
José Barluenga,* Fernando Aznar, Ramón Liz, and Carmen Postigo

Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

Catalytic aminomercuriation of 1-substituted prop-2-ynyl esters and ethers (**5**) provides a mild, simple, and regiospecific route to the terminal functionalized enamines (**6**) despite the fact that they are potentially isomerisable to their internal form; hydrolysis of (**6**) furnishes α-oxyketones (**7**).

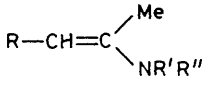
Enamines[1] derived from alkyl methyl ketones, obtained by a variety of methods, have usually been reported to exist as a mixture of isomers differing in the terminal (**1**) or internal (**2**) double bond position.[2] In fact, apart from a series of enol ether- and enol sulphide-enamines, (**3**) and (**4**), recently prepared by us *via* catalytic aminomercuriation of prop-2-ynyl ethers and sulphides,[3] only some isolated instances are known in which the location of the double bond is unambiguous [*e.g.*, (**1a**),[2c] (**2a**)[4]]. Since both electronic and steric factors[2f,5] seem to influence the regioisomer distribution, we decided to employ the more hindered 1-substituted prop-2-ynyl esters and ethers (**5**) as unsaturated substrates in catalytic aminomercuriation processes.[6]

When a 1-substituted prop-2-ynyl ester or ether (**5**) was treated with an excess of piperidine or morpholine, in the presence of mercury(II) acetate as catalyst, the corresponding β′-oxysubstituted enamine (**6**) was regiospecifically obtained, the internal isomer not being detected in the crude reaction mixture, according to the ^{1}H n.m.r. spectra (90 MHz)†



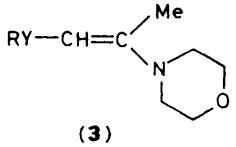
(**1**)

a R = Pr^i
R′ = R″ = Me



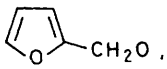
(**2**)

a R = Ph
R′R″ = $(CH_2)_2O(CH_2)_2$

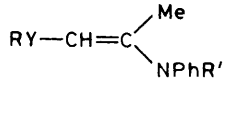


(**3**)

RY = CH_2=CH−CH_2O,



PhO, PhS



(**4**)

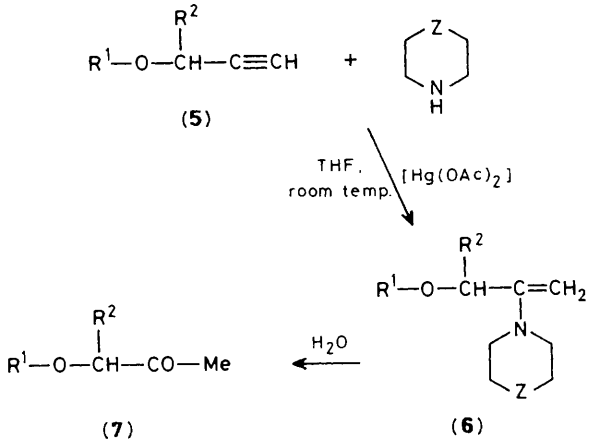
RY = MeO, CH_2=CH−CH_2O, $PhCH_2O$, PhO, PhS
R′ = Me, Et

† In some instances, *ca.* 5% of the corresponding acetamide was observed as by-product.

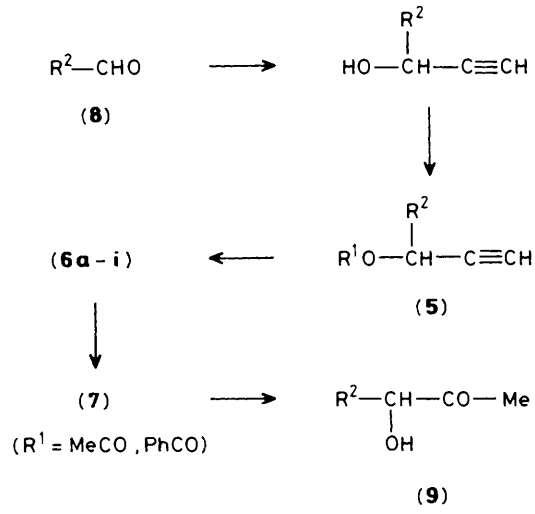
Table 1. β′-Oxyenamines (**6**).

Compound	R^1	R^2	Z	% Yield[a]	Selected n.m.r. data: δ_H (CH–C=CH_2)[b]		δ_C (CH–C=CH_2)[c]		
(6a)	MeCO	Me	CH_2	56	5.3	4.15 & 3.9	72.9	157.8	88.8
(6b)	MeCO	Me	O	61	5.35	4.3 & 4.0	68.9	156.8	88.8
(6c)	MeCO	Pr	O	66	5.3	4.25 & 4.0	72.9	156.5	90.1
(6d)	MeCO	Bu	O	64	5.3	4.3 & 4.0	73.1	156.5	90.2
(6e)	MeCO	Bu^i	O	70	5.35	4.25 & 4.0	71.2	156.8	89.9
(6f)	MeCO	C_9H_{17}[d]	O	91[e]	5.3	4.3 & 4.0	71.0	156.8	90.1
							71.8	157.2	90.9[f]
(6g)	MeCO	Ph	O	84	6.3	.25 & 4.1[g]	74.1	154.4	90.7
(6h)	PhCO	Me	CH_2	41[e]	5.55	4.25 & 3.9	70.6	157.5	89.7[h]
(6i)	PhCO	Me	O	69	5.6	4.35 & 4.0	70.2	156.7	89.4
(6j)	Et	Me	CH_2	51	*ca.* 3.4[i]	4.0 & 3.8	77.5	157.5	88.2
(6k)	Et	Me	O	60	*ca.* 3.4[i]	4.05 & 3.85	77.3	156.7	88.6

[a] Isolated yield based on starting alkyne (**5**). [b] In CCl_4 (Me_4Si); recorded on a Varian EM390 spectrometer. [c] Neat (Me_4Si + D_2O capillary). [d] (*R*)-Me_2C=CH–$(CH_2)_2$–CHMe–CH_2–. [e] Yield of the crude reaction product. [f] Duplicate signals due to the presence of diastereoisomers. [g] In $CDCl_3$. [h] In CCl_4. [i] Superimposed with the CH_2–O resonance.



Scheme 1



Scheme 2

(Scheme 1 and Table 1). The mildness of the reaction and work-up conditions, and the basicity of the reaction medium can account for the absence of undesired side-processes, such as self-condensation,[2d,2f,7] which often accompany the synthesis of methyl ketone enamines.

Comparison of compounds (**6**) with the above mentioned (**3**) shows how the stereoelectronic factors dramatically affect the isomer distribution. Doubtless, the enol ether stabilisation operating in (**3**) should be overcome by the steric hindrance associated with the non-observed tetrasubstituted internal enamine regioisomer of (**6**) in such a way that only the less substituted form (**6**) is observed, in order to guarantee the coplanarity of the N–C=C moiety.[2f] However, a reaction test carried out with mercury(II) chloride, 1-methylprop-2-ynyl acetate (**5**; R^1 = MeCO, R^2 = Me), and *N*-methylaniline (molar ratio 1 : 20 : 100) led exclusively to the corresponding tetrasubstituted enol ester-enamine, MeCOO–CMe=CMe–NMe–Ph. This result is consistent with the weaker enaminic character of the enamines derived from aromatic amines, in which the steric hindrance can be strongly relieved by rotation of the *N*-alkylanilino moiety.

In a typical run, dry mercury(II) acetate (15 mmol) was added under argon during *ca.* 5 min to a stirred solution of a prop-2-ynyl ester or ether (**5**)‡ (20 mmol) and dry piperidine or morpholine (60 mmol) in dry tetrahydrofuran (THF, 60 ml). The mixture was stirred overnight at room temperature, then filtered under argon, and the liquid phase evaporated under reduced pressure (0.05 Torr). The resulting residue was treated with dry n-hexane (3 × 20 ml), filtered under argon, and the liquid phase concentrated *in vacuo* (0.05 Torr). The crude reaction product was an essentially pure, colourless, or pale yellow liquid which can be trap-to-trap condensed or distilled *in vacuo*.§

Hydrolysis of enamines (**6**) (stirring with *ca.* a threefold excess of water at room temperature and conventional

‡ The 1-substituted prop-2-ynyl esters (**5**; R^1 = MeCO, PhCO) were prepared in a conventional manner from the corresponding alkynol,[8] acetyl or benzoyl chloride, and pyridine; the ether (**5**; R^1 = Et, R^2 = Me) was prepared as described.[9]

§ In order to avoid the heating-promoted self-condensation of enamines, the trap-to-trap condensation method (preheated oil bath temperature 90—120 °C, 0.001 Torr) is preferable.

work-up) afforded almost quantitatively the corresponding α-oxyketones (**7**). These compounds are of interest because of the presence of α-acyloxy functions in a number of naturally occurring ketones.[10] In addition, it should be pointed out that the overall process outlined in Scheme 2 represents a regiospecific conversion of the very accessible aldehydes (**8**) into the acyloins (**9**), a synthetic approach which should be taken into account in view of the fact that the regioselective α-hydroxylation of carbonyl compounds still remains a current problem in preparative organic chemistry.[11]

Received, 27th May 1986; Com. 705

References

1 For a recent review on enamines, see: P. W. Hickmott, *Tetrahedron*, 1982, **38**, 1975, 3363.

2 (a) G. Bianchetti, D. Pocar, P. Dalla Croce, and A. Vigevani, *Chem. Ber.*, 1965, **98**, 2715; (b) R. Jacquier, C. Petrus, and F. Petrus, *Bull. Soc. Chim. Fr.*, 1966, 2845; (c) W. A. White and H. Weingarten, *J. Org. Chem.*, 1967, **32**, 213; (d) D. Pocar, G. Bianchetti, and P. Ferrutti, *Gazz. Chim. Ital.*, 1967, **97**, 579; (e) G. Bianchetti, P. Ferrutti, and D. Pocar, *ibid.*, 1967, **97**, 597; (f) D. Pocar, R. Stradi, and B. Gioia, *ibid.*, 1968, **98**, 958; (g) R. Carlson, L. Nilson, C. Rappe, A. Babadjamian, and J. Metzger, *Acta Chem. Scand., Ser. B*, 1978, **32**, 85; (h) J. Barluenga, F. Aznar, R. Liz, and R. Rodes, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2732.

3 J. Barluenga, F. Aznar, and R. Liz, *Synthesis*, 1984, 304; J. Barluenga, F. Aznar, R. Liz, and M. Bayod, *J. Chem. Soc., Chem. Commun.*, 1984, 1427.

4 R. Stradi, P. Trimarco, and A. Vigevani, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1.

5 W. D. Gurowitz and M. A. Joseph, *J. Org. Chem.*, 1967, **32**, 3289; U. Edlung and G. Bergson, *Acta Chem. Scand.*, 1971, **28**, 3625.

6 J. Barluenga, F. Aznar, R. Liz, and R. Rodes, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1087.

7 P. W. Hickmott, B. J. Hopkins, and C. T. Yoxall, *J. Chem. Soc. B*, 1971, 205.

8 Prepared as described: L. Skattebøl, E. R. H. Jones, and M. C. Whiting, *Org. Synth.*, Coll. Vol. IV, John Wiley & Sons, New York, 1963, p. 792.

9 L. Brandsma, 'Preparative Acetylenic Chemistry,' Elsevier, Amsterdam, 1971, p. 172.

10 K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, 1961, **26**, 4563; P. Schreier, *J. Agric. Food Chem.*, 1980, **28**, 926; G. S. Reddy and M. V. Bhatt, *Synthesis*, 1981, 223, and references therein.

11 H.-U. Reissig, *Nachr. Chem. Tech. Lab.*, 1986, **34**, 328, and references therein.