Synthesis of Substituted 2-Aminopent-4-enals and 2-Amino-3-(2-furyl)propanals *via* [3,3]- and [1,3]-Sigmatropic Shifts of β-Allyloxyenamines

José Barluenga,* Fernando Aznar, Ramón Liz, and Miguel Bayod

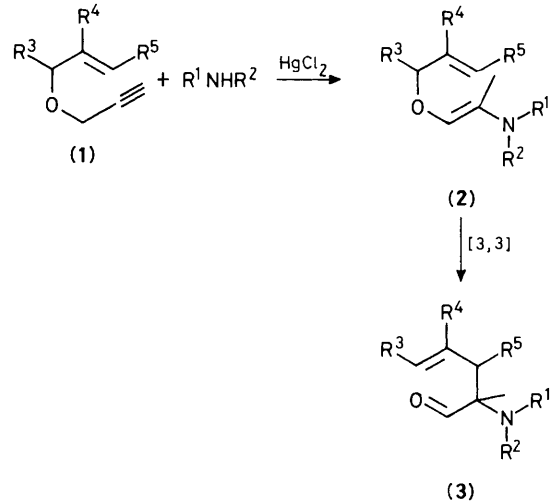
Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, 33071-Oviedo, Spain

The presence of an amino substituent at the 2-vinyl position in substituted allyl vinyl ethers facilitates low-temperature rearrangements through [3,3]- or [1,3]-sigmatropic shifts, which lead to the aminoaldehydes (**3**) and (**5**), respectively.

There have been many reports recently on attempts to improve the usefulness of the aliphatic Claisen rearrangement as a tool in organic synthesis, either by lowering the activation energy of the reaction or by increasing the functionalization of the products.[1] While investigating catalytic aminomercuriation of terminal acetylenes,[2] a facile synthesis of β-methoxy- or β-phenoxy-enamines, $ROCH{=}C(NR^1R^2)Me$ was developed [(**1**)→(**2**)].[3] If R was an allylic substituent these oxyenamines would be suitable substrates for Claisen rearrangement, with an amino group attached to the 2-vinyl position. This communication reports the low-temperature Claisen rearrangement of β-allyloxyenamines (**2**), which are almost quantitatively transformed into the 2-aminopent-4-enals (**3**) (Scheme 1), a class of compounds showing a high degree of functionalization and, to our knowledge, not previously reported in the literature [*e.g.* (**3b**), i.r. (film) $\nu_{C=O}$ 1735 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 0.95 (s, 3H), 1.6 (d, 3H), 2.1—2.65 (m, 6H), 3.45—3.8 (m, 4H), 5.2—5.5 (m, 2H), and 9.3 (s, 1H); ^{13}C n.m.r. δ (neat) 14.7 (q), 19.2 (q), 38.2 (t), 49.7 (t), 68.5 (s), 68.8 (t), 127.1 (d), 130.0 (d), and 195.2 (d); *m/z* 197 (M^+)]. Although a pair of diastereoisomers could be expected for (**3d,h**), only one diastereoisomer was detected by n.m.r. spectroscopy; similarly, only one of the two possible geometric isomers of (**3b,f**) was observed.

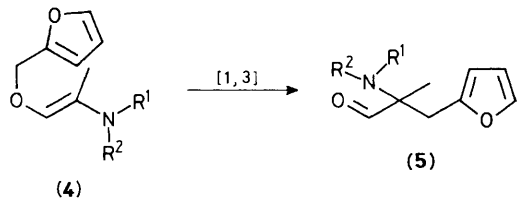
β-Allyloxyenamines (**2a—d**) derived from morpholine rearrange to the corresponding aminoaldehyde (**3a—d**) in a few hours at 40 °C,† whereas those derived from *N*-methylaniline, (**2e—h**), completely rearrange in 2—3 h at 110 °C. As expected, all the enamines (**2**) rearrange at a faster rate than allyl vinyl ether (AVE; see Table 1 for comparison). This result agrees with the predictions derived from the theoretical model proposed by Carpenter[4,5] for the aliphatic Claisen rearrangement when a π-donor substituent is present at the 2-vinyl position. Also consistently, the greater π-donor morpholinoenamines rearrange at lower temperatures than the *N*-methylanilino derivatives. Insofar as a methyl group can be considered a π-donor substituent,[6] the half-lives of (**2b**) and (**2c**) [but not (**2d**)] also agree with Carpenter's predictions.‡

The half-lives shown in Table 1 were measured using ^{13}C n.m.r. spectroscopy. A peak at *ca.* δ 52 [assigned to C-2 and C-6 of the morpholino moiety of (**2**)] gradually disappeared and a new peak at *ca.* δ 49 [assigned to the analogous nuclei of (**3**), which are expected to have similar relaxation times] appeared at the same rate. The approximate half-lives of compounds (**2**) were deduced from the reasonably time-independent first-order rate constant obtained for each transformation (**2**) → (**3**).



a; R^1, R^2 = -$[CH_2]_2O[CH_2]_2$-, R^3 = R^4 = R^5 = H
b; R^1, R^2 = -$[CH_2]_2O[CH_2]_2$-, R^3 = Me, R^4 = R^5 = H
c; R^1, R^2 = -$[CH_2]_2O[CH_2]_2$-, R^3 = H, R^4 = Me, R^5 = H
d; R^1, R^2 = -$[CH_2]_2O[CH_2]_2$-, R^3 = R^4 = H, R^5 = Me
e; R^1 = Ph, R^2 = Me, R^3 = R^4 = R^5 = H
f; R^1 = Ph, R^2 = R^3 = Me, R^4 = R^5 = H
g; R^1 = Ph, R^2 = Me, R^3 = H, R^4 = Me, R^5 = H
h; R^1 = Ph, R^2 = Me, R^3 = R^4 = H, R^5 = Me

Scheme 1



a; R^1, R^2 = -$[CH_2]_2O[CH_2]_2$-
b; R^1, R^2 = -$[CH_2]_4$-
c; R^1, R^2 = -$[CH_2]_5$-

Scheme 2

Thermal rearrangement of type (**2**) enamines when the oxyallyl moiety is part of an aromatic system gives different results. For example, β-furfuryloxyenamines (**4**), obtained in a similar way to (**2a—d**), are easily transformed at 80 °C§ into the corresponding 2-amino-3-(2-furyl)-2-methylpropanals (**5**) (Scheme 2), through a [1,3]-sigmatropic shift [*e.g.* (**5a**), i.r.

† As an exception, (**2c**) requires higher temperatures (80—90 °C).

‡ From his theoretical model, Carpenter[5] states that a π-donor substituent increases the rate of Claisen rearrangement in any 1-, 2-vinyl, and 1-allyl positions, but substitution at 2- and 3-allyl positions lowers reaction rate. However, Carpenter's studies only deal with monosubstituted allyl vinyl ethers, whereas compounds (**2b—d**) are trisubstituted ones.

§ Compound (**4b**) rearranges at such a rate that only trace amounts of it are detected in the crude reaction product resulting from the room temperature aminomercuriation of furfuryl prop-2-ynyl ether, amino-aldehyde (**5b**) being directly isolated after work-up.

Table 1. Approximate half-lives, $t_{\frac{1}{2}}$, for (**2a**—**d**) at 40 °C.

Compound	$t_{\frac{1}{2}}$ (h)
(**2a**)	29
(**2b**)	3
(**2c**)	(390)[a]
(**2d**)	8
AVE[b]	5.3×10^4 [c,d]

[a] Calculated from the readily measured half-lives at 85 °C (1.5 h) and 130 °C (5 min) using the Eyring equation. [b] Given for comparison. [c] Calculated from the activation parameters reported in ref. 4 using the Eyring equation. [d] Calculated value at 110 °C, 24.4 h.

(film) $\nu_{C=O}$ 1755 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 1.1 (s, 3H), 2.45—2.65 (m, 4H), 2.95 (s, 2H), 3.6—3.8 (m, 4H), 6.05—6.4 (m, 2H), 7.35 (br. s, 1H), and 9.5 (s, 1H); ^{13}C n.m.r. δ (neat) 15.6 (q), 32.1 (t), 48.2 (t), 67.9 (s), 68.5 (t), 109.8 (d), 111.9 (d), 148.2 (d), 152.6 (s), and 195.7 (d); *m/z* 223 (M^+)]. This is one of the few known cases of [1,3]-sigmatropic shifts of alkyl groups from heteroatoms[7] and can be understood in terms of the tendency of the furan ring to preserve its aromatic character. It is noteworthy that, although the furan ring has relatively low aromatic character, the products (**5**) resulting from a [1,3]-sigmatropic shift are the only ones observed, no trace products from the possible alternative [3,3] migration being detected by n.m.r. spectroscopy.

Typically, compounds (**2**) and (**4**) are obtained in 50—60% yield as previously reported.¶ They are then heated in an argon atmosphere at the appropriate temperature, over a period of *ca.* $10 \times t_{\frac{1}{2}}$, and the corresponding aldehyde (**3**) or (**5**) is obtained by fractional condensation at 0.001 Torr. However, in some instances the overall synthesis can be carried out in a one-pot fashion from the corresponding allyl prop-2-ynyl ether (**1**).

Received, 16th May 1984; Com. 681

References

1 F. E. Ziegler, *Acc. Chem. Res.*, 1977, **10**, 227; G. B. Bennett, *Synthesis*, 1977, 589.
2 J. Barluenga, F. Aznar, R. Liz, and R. Rodes, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2732; *ibid.*, 1983, 1087.
3 J. Barluenga, F. Aznar, and R. Liz, *Synthesis*, 1984, 304.
4 C. J. Burrows and B. K. Carpenter, *J. Am. Chem. Soc.*, 1981, **103**, 6983.
5 C. J. Burrows and B. K. Carpenter, *J. Am. Chem. Soc.*, 1981, **103**, 6984.
6 I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions,' Wiley, Chichester, 1976, p. 47.
7 R. T. Arnold and S. T. Kulenović, *J. Org. Chem.*, 1980, **45**, 891.

¶ See ref. 3. Method E/X for enamines derived from aliphatic amines and method A/W at room temperature for (**2e**—**h**); reaction time, 24 h.