

Studies in 3-oxy-assisted 3-aza Cope rearrangements†

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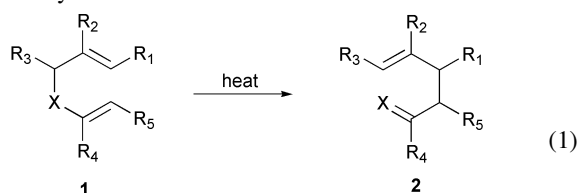
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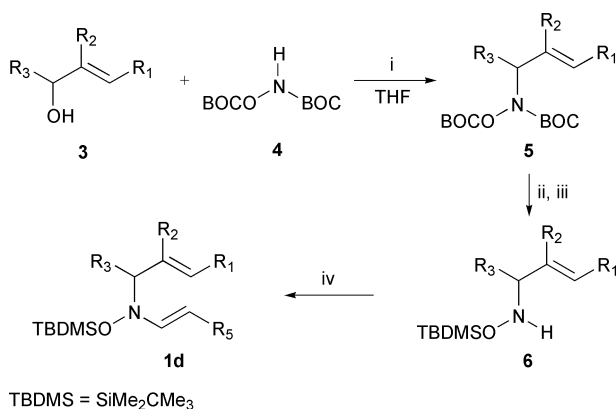
On thermolysis appropriately substituted *N*-silyloxy-*N*-allyl enamines undergo smooth 3,3-sigmatropic rearrangements to the corresponding *N*-silyloxy imino ethers.

Cope rearrangement is an important reaction in organic synthesis. This pericyclic process involving 1,5-hexadienes generally proceeds under drastic conditions (*i.e.* high temperatures and prolonged reaction times) and in poor to modest yield¹ [eqn. (1); **1a** to **2a**]. The 3-aza analogue of the above reaction involving uncharged molecules, first reported by Hill,² also requires high temperatures for the rearrangements to occur [eqn. (1); **1b** to **2b**]. Although the presence of an ether functionality

a) X = CH₂ b) X = NR c) X = CHOR d) X = NOSiMe₂CMe₃

at C-3 [eqn. (1); **1c** to **2c**] in the all carbon framework has been found to improve the overall efficiency of the process,³ the effect of such a substituent in the 3-aza version is so far not reported. We disclose in this communication the first experimental realisation with the latter type of functionality which consists of thermolysis of a number of *N*-silyloxy-*N*-allyl enamines [eqn. (1); **1d** to **2d**] and show that the corresponding 3,3-sigmatropic rearrangement products, the oxime-ethers **2d**, are obtained in good to excellent yields.

O-Silyl-*N*-allyl hydroxylamines were secured as follows: the appropriate allyl alcohol **3** and *N,O*-bis-*tert*-butoxycarbonyl hydroxylamine (**4**) were condensed by Mitsunobu's method⁴ to give the corresponding *N*-allyl-*O*-acyl hydroxamic acid **5** (Scheme 1). Removal⁵ of the protecting groups from these

TBDMS = SiMe₂CMe₃

Scheme 1 Reagents and conditions: i, diisopropylazodicarboxylate, PPh₃; THF, rt; ii, CF₃CO₂H (4 eq.), CH₂Cl₂, rt; iii, TBDMSOCl, imidazole, DMF, rt; iv, HC≡CR₅ (1 eq.), CH₃CN or CH₂Cl₂, rt.

substances provided the corresponding hydroxylamines. *O*-Silylation⁶ of the latter furnished the title compounds **6**. They underwent nucleophilic addition smoothly⁷ to ethynyl-*p*-tolylsulfone and methyl propiolate to provide the *N*-silyloxy-*N*-allyl enamines **1d** required for our study (Scheme 1, Table 1).‡

Table 1 Michael addition products **1d** from *O*-silyl hydroxylamines **6**

#	Allyl alcohol 3	<i>O</i> -Silyl hydroxylamine 6 yield ^a (%)	1,4-Addition product 1d ^b	Yield ^a (%)
1	R ₁ = R ₂ = R ₃ = H	63	R ₅ = SO ₂ Tol	70
2	R ₁ = R ₃ = H; R ₂ = Me	60	R ₅ = SO ₂ Tol	72
3	R ₂ = R ₃ = H; R ₁ = Me	58	R ₅ = SO ₂ Tol	76
4	R ₁ = R ₂ = H; R ₃ = Me	24	R ₅ = SO ₂ Tol	78
5	R ₁ = R ₃ = H; R ₂ = Ph	62	R ₅ = SO ₂ Tol	77
6	R ₂ = R ₃ = H; R ₁ = Ph	87	R ₅ = SO ₂ Tol	75
7	R ₁ = R ₂ = R ₃ = H	63	R ₅ = CO ₂ Me	70

^a Isolated yields. ^b R₄ = H, Tol = *p*-MeSO₂C₆H₄

The thermal rearrangements of the above substances were conducted in *o*-dichlorobenzene under reflux (188 °C) (*ca.* 0.03 M) and the results are collected in Table 2.‡

Examination of the Table shows that the reactions occur in consistently good yield to provide the oxime ethers **2d** as a mixture of the *syn* and *anti* isomers. Under virtually identical experimental conditions the cyclohexyl enamines **1b** (R = cyclohexyl; R₁ = R₂ = R₃ = R₄ = H; R₅ = SO₂Tol or R₁ = R₂ = R₃ = R₄ = H; R₅ = CO₂Me) showed no tendency to undergo the *aza*-Cope reaction, underlining the importance of the silyloxy group in promoting the rearrangement.

The occurrence of 1,3-shifts in these reactions is excluded because of the presence of the characteristic 2H multiplet due to H₂C=CH group in the ¹H NMR spectra of the products **2d** (Table 2; entries 3 and 6) centred at *ca.* δ 5.0 ppm and the absence of the same in that of **2d** (entry 4). In those reactions, wherein two stereogenic centres are created in the products (Table 2; entries 3 and 6), high diastereoselection was observed. The oxime pair, in each case, contained one predominant diastereomer (> 80% by ¹H NMR analysis).

Table 2 Rearrangement of *N*-silyloxy enamines **1d** to oxime ethers **2d**

#	Enamine 1d	Reaction Time (min)	Oxime ether 2d yield ^a (%)	Ratio <i>syn</i> : <i>anti</i> ^b
1	R ₁ = R ₂ = R ₃ = H; R ₅ = SO ₂ Tol	80	82	63:37
2	R ₁ = R ₃ = H; R ₂ = Me; R ₅ = SO ₂ Tol	70	81	82:18
3	R ₂ = R ₃ = H; R ₁ = Me; R ₅ = SO ₂ Tol	165	79	50:50
4	R ₁ = R ₂ = H; R ₃ = Me; R ₅ = SO ₂ Tol	25	80	50:50
5	R ₁ = R ₃ = H; R ₂ = Ph; R ₅ = SO ₂ Tol	15	80	99:1
6	R ₂ = R ₃ = H; R ₁ = Ph; R ₅ = SO ₂ Tol	240	78	37:63
7	R ₁ = R ₂ = R ₃ = H; R ₅ = CO ₂ Me	60	80	60:40

^a Isolated yields. ^b By ¹H NMR (see, ref. 8).

† Dedicated with respect to the late Professor T. R. Govindachari.

In conclusion, the first examples of 3-silyloxy-assisted 3-aza Cope reactions are reported. They are shown to occur in good to excellent yields.

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Notes and references

‡ All addition products **1d** were deduced (^1H NMR) to possess the *trans* arrangement of the olefinic bond bearing the electron withdrawing group R_5 .

§ Typical experimental procedure: *trans*-1-*N*-allyl-*N*-(*tert*-butyldimethylsilyloxy)amino-2-(*p*-tolylsulfonyl)ethylene (**1d**, Table 2, entry 1) (25 mg), in *o*-dichlorobenzene (2 mL), was heated under reflux until all the starting material had been consumed (80 min) (tlc control, silica, Et_2O :*n*-hexane 1:3, as eluent). Evaporation of the solvent under reduced pressure, followed by purification of the residue by ptlc, gave the product, a viscous oil (20.5 mg, 82% yield), as a mixture of *syn* and *anti* oxime-ethers (**2d**, Table 2, entry 1). Selected spectroscopic data: IR (neat) 1642, 1597, 1325, 1252,

1151 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.42 and 2.43 (3H, two s), 4.90–5.15 (2H, m), 6.82 and 7.36 (1H, two d).

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