v-Triazolines. Part XIII (1). Reactions of α-Ketoenamines with Toluene-*p*-sulphonylazide

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Some enamines derived from α-diketones have been reacted with tosylazide yielding unstable 5-amino-*v*-triazolines, which were found to undergo cycloreversion to diazo compounds and amidines. In the case of the enamines derived from 4-aryl-2,3-butanediones, a competitive rearrangement to (*Z*)-4-aryl-4-amino-3-tosylamino-3-butene-2-ones was observed.

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Sulphonylazides have been shown to react with enamines affording *v*-triazoline intermediates, which are mainly unstable and rapidly rearrange or undergo cycloreversion according to various pathways (2). In Scheme 1, two of the observed reactions courses are shown in view of their interest in the present paper. Paths a) and b) are competitive and their dependence on the kind of R' has been investigated extensively (2,3,4). When R' is an acyl substituent, path b) becomes strongly favoured and the rearrangement according to path a) was not observed.

In order to evidence the effect, if any, of an acyl group as the R'' substituent, the reactions of some α-ketoenamines with tosylazide were investigated. Enamines **1a-e** were reacted with tosylazide in boiling ethanol until complete reaction (tlc), and the reaction products were isolated by crystallization or chromatography.

Enamine **1a** and tosylazide reacted slowly with nitrogen evolution yielding a tarry reaction mixture from which amidine **2a** was isolated in moderate yield (Scheme 2). An important amount of tosylamide was also obtained, probably formed through the thermal decomposition of the azide. The reaction of enamine **1b** with tosylazide was also accompanied by a quantitative evolution of nitrogen. From the reaction mixture, amidine **2b** and benzyl ethyl ether (**3**) were isolated.

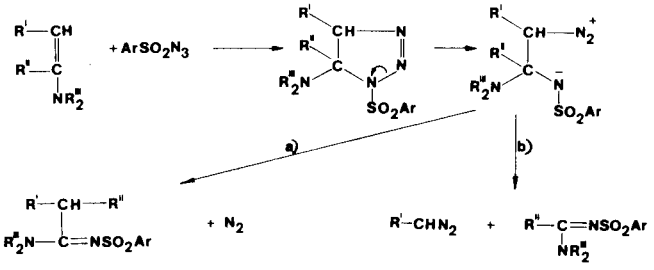
The formation of both reaction products is rationalized through path b) in Scheme 1, the ether being the reaction product of phenyl diazomethane with ethanol. This product was identified by glc and comparison with an authentical sample. The structure of amidine **2b** was demonstrated by analytical and spectral data and confirmed by acidic hydrolysis to 2-oxophenylacetic acid (**4**).

A new reaction path was identified in the reaction of tosylazide with enamine **1c** (Scheme 3). This reaction yielded two crystalline products: 1-piperidino-1-tosylimino-2-propanone (**2a**) and (*Z*)-4-phenyl-4-piperidino-3-tosylamino-3-butene-2-one (**5a**). In the mother liquor from the crystallization of the above products, benzyl ethyl ether (**3**) was identified as described previously. The structure of enamine **5a** was inferred from analytical and spectroscopic data and confirmed through X-ray analysis (5). In agreement with its structure, this enamine was easily hydrolized and deacetylated by boiling with 20% sulphuric acid yielding ω-tosylamino acetophenone (**6**).

Enamines **1d** and **1e** behaved similarly which afforded a mixture of amidine **2a** and enamines **5b** and **5c**, respectively. Owing to the formation of tarry wine-coloured by-products, the yield of **5b** was low. In all cases the expected benzylethylether was identified by glc in the reaction mixture.

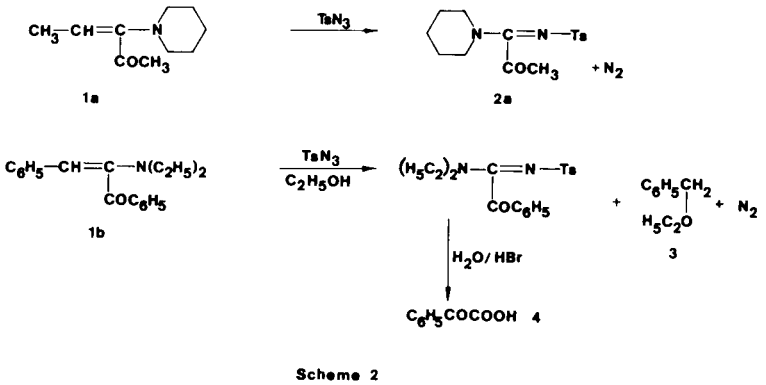
A characteristic feature of enamines **5a-c** is the exceptionally high value of the chemical shift of the signal associated with the acetyl group (1.10, 1.28 and 1.13 ppm for **5a**, **5b** and **5c**, respectively). However, this is explained by the conformation of the molecule, in which the H-bonding between the NH and CO groups obliges the methyl residue to take a position where it is strongly shielded by the aromatic ring.

The above results also showed that in the case of the

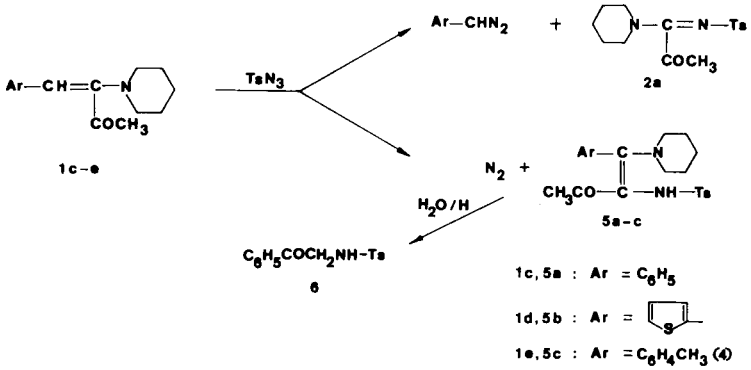


Scheme 1

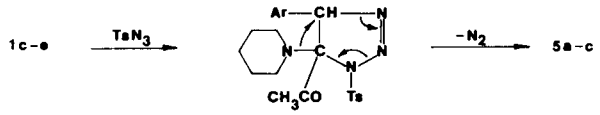
0022-152X/79/050925-03$02.25



Scheme 2



Scheme 3



Scheme 4

cycloaddition of tosylazide to α-ketoenamines, the intermediate triazoline adducts can undergo cycloreversion according to path b) in Scheme 1. However, starting from enamines **1c-e**, the new rearrangement to enamines **5a-c** is also operative. This mechanism can be rationalized as shown in Scheme 4, through a zwitterionic intermediate which rearranges with migration of the piperidine residue instead of the acetyl group. The shift of the amine residue is probably favoured by the low migrative aptitude of the acetyl group.

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were determined with a Beckman Acculab 4 spectrometer (in nujol mull or in the solvent indicated, cm^{-1}). The ^1H-nmr spectra were recorded with a Varian A-60 spectrometer for solutions in deuteriochloroform. Chemical shifts are expressed in ppm relative to TMS as internal standard. Mass spectra were obtained with a MAT 112 spectrometer operating at 70 eV, ionic current 60 μA, ion source temperature 270° by the direct inlet system.

Enamines **1a-e**.

1,3-Diphenyl-2-diethylamino-2-propene-1-one (**1b**) was prepared as described in the literature (6), m.p. 51-54°. 4-Phenyl-3-piperidino-3-butene-2-one (**1c**) was obtained by the method of Cromwell (7), m.p. 56-58°, b.p. 140-145° at 1 mm Hg; ir: 1700 (CO); nmr: 5.72 (1H, s, -CH=). 3-Piperidino-3-pentene-2-one (**1a**) was prepared according to Duhamel (8). Essentially by the same procedure were obtained 4-(2-thienyl)-3-piperidino-3-butene-2-one (**1d**), yellow oil, b.p. 120-125° at 1 mm Hg; ir: 1700 (CO); nmr: 2.27 (3H, s, CH_3), 5.22 (1H, s, -CH=) and 4-(4-methylphenyl)-3-piperidino-3-butene-2-one (**1e**), yellow oil, b.p. 130-140° at 0.8 mm Hg; ir: 1710 (CO); nmr: 2.05 (3H, s, CH_3CO), 2.31 (3H, s, CH_3), 5.52 (1H, s, -CH=).

Reaction of Tosylazide with Enamine **1a**.

Enamine **1a** (1 g., 6 mmoles) was refluxed in anhydrous ethanol (50 ml.) with tosylazide (1.12 g., 6 mmoles) for 5 hours. At the end of the reaction, the mixture was evaporated and the oily brown residue chromatographed on silica gel with ether as eluent. After a fraction containing tosylamide (m.p. 136°, 0.4 g.), the amidine **2a** was obtained (0.3 g., yield 16.3%) as a white powder, m.p. 115° (from ethanol); ir: 1720 (CO); nmr: 1.64 (6H, m, $(CH_2)_3$), 2.39 (3H, s, CH_3), 2.60 (3H, s, CH_3CO), 3.25 and 3.65 (2H + 2H, 2m, CH_2NCH_2(9)), 7.17-7.90 (4H, m, aromatic).

Anal. Calcd. for $C_{15}H_{20}N_2O_3S$: C, 58.40; H, 6.55; N, 9.10. Found: C, 58.40; H, 6.55; N, 8.90.

Reaction of Tosylazide with Enamine **1b**.

The enamine (**1b**, 2.51 g., 9 mmoles) was dissolved in anhydrous ethanol (20 ml.) and reacted with tosylazide (1.77 g., 9 mmoles) by refluxing for 3.5 hours. About 200 ml. of nitrogen were collected. The reaction mixture was concentrated under

reduced pressure at room temperature until formation of a crystalline precipitate which was filtered off and recrystallized from ethanol yielding the pure amidine **2b** (1.93 g., yield 60%) as white crystals, m.p. 103°; ir: 1680 (CO); nmr: 1.03 and 1.22 (2 x 3H, 2t, $(CH_2)CH_3$ (9)), 2.39 (3H, s, CH_3), 3.13 and 3.59 (4H, 2q, $CH_2(CH_3)$ (9)), 7.10-8.00 (9H, m, aromatic).

Anal. Calcd. for $C_{19}H_{22}N_2O_3S$: C, 63.70; H, 6.15; N, 7.80. Found: C, 63.60; H, 5.95; N, 7.85.

In the mother liquor from the filtration of amidine **2b**, benzyl methyl ether (**3**) was identified by glc through comparison with an authentic sample.

Hydrolysis of **2b**.

The amidine (0.2 g.) was refluxed with 47% hydrobromic acid (4 ml.) for 2 hours. The reaction mixture was evaporated and the residue taken up with water (5 ml.). Tosylamide (m.p. 136°) was filtered off. The filtrate was extracted with ether yielding 2-oxophenylacetic acid (**4**) which was identified as the 4-nitrophenylhydrazone, m.p. 165° (11).

Anal. Calcd. for $C_{14}H_{11}N_3O_4$: C, 58.95; H, 3.85; N, 14.75. Found: C, 58.70; H, 3.95; N, 14.40.

On heating this compound yielded benzaldehyde 4-nitrophenylhydrazone, m.p. 187°.

Reaction of Tosylazide with Enamine **1c**.

The enamine (**1c**, 2.29 g., 10 mmoles) was dissolved in anhydrous ethanol (20 ml.) and tosylazide (1.97 g., 10 mmoles) in ethanol (10 ml.) was dropped in. The reaction mixture was refluxed for 3 hours. About 240 ml. of nitrogen were collected. The reaction solution was then evaporated and the oily residue was washed with light petroleum. The washings were analyzed by glc and benzyl ethyl ether was identified comparing with an authentical sample. The solid residue was filtered, dissolved in ethyl acetate and chromatographed on a silica gel/celite column using ethyl acetate/benzene (1:1) as the eluent. The first fraction yielded amidine (**2a**) (1.23 g., 40%). From the second fraction, enamine (**5a**) was obtained as yellow crystals (from ethanol or acetonitrile), m.p. 180-181° (1.51 g., 38%); ir: 3230 (NH), 1620 (CO); nmr: 1.10 (3H, s, CH_3CO), 1.72 (6H, m, $(CH_2)_3$), 2.46 (3H, s, CH_3), 3.34 (4H, m, CH_2NCH_2), 6.95 (1H, s, NH, exchangeable), 7.15-8.00 (9H, m, aromatic); ms: 398 (32) $[M^+]$, 243 (100) $[M\text{-}Ts^{+\cdot}]$, 199 (67) $[M\text{-}Ts\text{-}AcH^{+\cdot}]$, 104 (65) $[C_6H_5CH{=}N^+]$, 91 (68) $[C_7H_7^+]$, 84 (70) $[N(CH_2)_5^+]$.

Anal. Calcd. for $C_{22}H_{26}N_2O_3S$: C, 66.35; H, 6.55; N, 7.05. Found: C, 66.65; H, 6.45; N, 7.00.

Hydrolysis of **5a**.

The enamine (0.2 g.) was refluxed for 15 minutes with 20% sulphuric acid (10 ml.). After cooling, the crude reaction mixture was extracted twice with benzene and the extract was evaporated to dryness. The solid residue was recrystallized from ethanol yielding white crystals of ω-tosylaminoacetophenone (**6**, 0.08 g., yield 55%, m.p. 115°), identical with an authentical sample (12).

Reaction of Tosylazide with Enamine **1d**.

The enamine (0.8 g., 3.4 mmoles) was reacted with tosylazide (0.67 g., 3.4 mmoles) in ethanol (40 ml.) by refluxing for 2.5 hours. After evaporation of the reaction mixture a tarry, wine-coloured residue was obtained. Through chromatography on silica gel with ether as eluent, amidine **2a** (0.2 g., yield 19.1%) was isolated, m.p. 114-115°. The second fraction yielded enamine **5b** (0.1 g., yield 7.3%) as yellow crystals (from *n*-hexane), m.p. 148-150°; ir (carbon tetrachloride): 3280 (NH), 1610 (CO); nmr: 1.28 (3H, s, CH_3CO), 1.70 (6H, m, $(CH_2)_3$), 2.41 (3H, s, CH_3), 3.32 (4H, m, CH_2NCH_2), 6.80-7.85 (8H, m, NH, exchangeable, and aromatic); ms: 404 (1.3) $[M^+]$, 249 (100) $[M\text{-}Ts^{+\cdot}]$, 205 (15) $[M\text{-}Ts\text{-}AcH^{+\cdot}]$, 110 (15) $[C_4H_3S\text{-}CH{=}N^+]$, 91 (29) $[C_7H_7^+]$, 84 (59) $[N(CH_2)_5^+]$.

Anal. Calcd. for $C_{20}H_{24}N_2O_3S_2$: C, 59.35; H, 6.00; N, 6.90. Found: C, 59.35; H, 6.00; N, 6.85.

Reaction of Tosylazide with Enamine **1e**.

The enamine (1.2 g., 5 mmoles) and tosylazide (1.0 g., 5 mmoles) were reacted as described for **1d**. The crude reaction mixture was chromatographed with methylethyl ketone:benzene (1:3), affording amidine **2a** (m.p. 115°, 0.5 g., yield 32.5%) and enamine **5c** (0.1 g., yield 48%) as yellow crystals, m.p. 170-172° (from cyclohexane); ir (carbon tetrachloride): 3280 (NH), 1605 (CO); nmr: 1.13 (3H, s, CH_3CO), 1.62 (6H, m, $(CH_2)_2$), 2.38 and 2.41 (6H, 2s, CH_3), 3.30 (4H, m, CH_2NCH_2), 6.85-7.95 (9H, m, NH, exchangeable, and aromatic); ms: 412 (0.34) $[M^+]$, 257 (99) $[M\text{-}Ts^{+\cdot}]$, 213 (20) $[M\text{-}Ts\text{-}AcH^{+\cdot}]$, 124 (9) $[MeC_6H_4CH{=}N^+]$, 91 (100) $[C_7H_7^+]$, 84 (99) $[N(CH_2)_5^+]$.

Anal. Calcd. for $C_{23}H_{28}N_2O_3S$: C, 67.00; H, 6.80; N, 6.80. Found: C, 66.65; H, 6.70; N, 7.15.

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