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A NEW REARRANGEMENT OF NITRONES: ACID PROMOTED CONVERSION OF VINYLNITRONES INTO *N*-(γ-KETOALKYL)-*N*-PHENYLHYDROXYLAMINES

Giuseppe Bartoli*, Marino Petrini, Enrico Marcantoni
Dipartimento di Scienze Chimiche, via S. Agostino 1, I-62032 Camerino (Mc), Italy

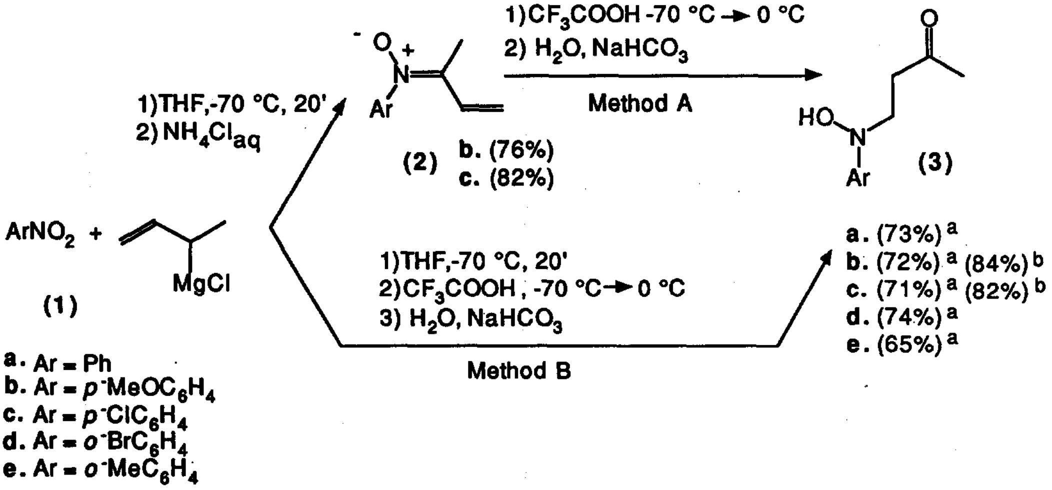
Marcella Bosco, Renato Dalpozzo
Dipartimento di Chimica Organica 'A. Mangini', viale Risorgimento 4, I-40136 Bologna, Italy

Abstract: Title compounds can be obtained from α-vinyl-α-methyl-N-phenylnitrones in the presence of anhydrous trifluoroacetic acid via *sigmatropic rearrangement of a protonated oxaziridine intermediate.*

Nitrones are known to be subject to electrophilic attack at oxygen atom. In several cases the obtained derivatives are unstable and tend to result either in hydrolysis to the parent hydroxylamine in the presence of water or in molecular skeleton rearrangement in anhydrous conditions. In fact, stable salts are obtained by treatment with hydrogen halides in anhydrous conditions[1], whereas in the presence of water an immediate hydrolysis occurs[2]. However, in particular circumstances, rearrangement to oxime *O*-ethers has been observed[3]. Moreover, whereas the reaction with alkylating reagents such as dimethyl sulphate and triethyloxonium fluoborate yields the corresponding *O*-alkylated nitrone salts[1], the reaction with acylating reagents such as acetic anhydride, acetyl chloride or phosphorus tri- or pentachloride is more complex resulting in a rearrangement to amides[1,4].

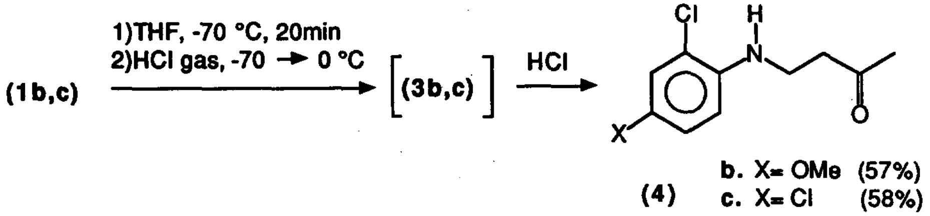
We report here that α-vinyl-α-methyl-*N*-phenyl nitrones under acidic conditions undergo an until unknown type of rearrangement to *N*-(γ-ketoalkyl)-*N*-phenylhydroxylamines (Scheme 1). In fact, when nitrones **2b,c** are treated in THF with anhydrous trifluoroacetic acid for few minutes followed by addition of water, compounds **3b,c** were isolated in 84 and 82% yield respectively (method A)[5]. Vinyl nitrones **2** can be prepared through 1,2-addition of allyl Grignard reagents to nitroarenes **1**[6]. Since recovering and purification of nitrones from reaction mixtures is generally difficult owing to their great susceptibility to hydrolysis, we devised a one-pot procedure to obtain products **3** starting from **1** (method B)[7]. Actually, this modification allows an yield improvement. In fact, overall yields of γ-ketohydroxylamines **3b,c** obtained following method A do not exceed 64 and 67% respectively. The reaction was extended to various substituted nitrobenzenes leading to compounds **3** in good yields.

Scheme 1



[a] calculated with respect to 1 following method B
[b] calculated with respect to 2 following method A

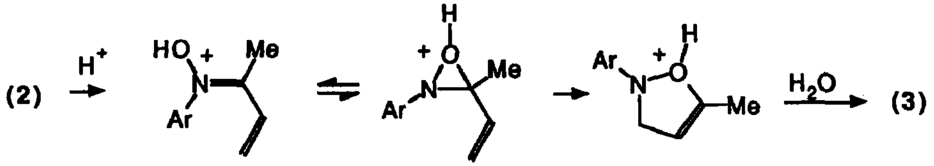
Scheme 2



Lewis acids such as $BF_3.Et_2O$ are able to perform this rearrangement although in much lower yields. On the other hand, hydrogen chloride gives the product 4[8] rised from Bamberger rearrangement of 3 (scheme 2).

Among the various possible mechanisms, the organisation of substituents in the final product suggests that the reaction proceeds through the formation of the protonated form of 2. This intermediate can cyclize to a protonated vinyloxaziridine, which in turn undergoes ring expansion to a five membered ring (scheme 3). Finally, solvolysis of the isoxazoline affords product 3. Although unsupported by experimental evidences, proposed mechanism is a logical consequence of the well-known equilibrium between nitrone salts and oxaziridines[4,9] while the subsequent ring expansion resembles a typical [1,3]-sigmatropic rearrangement of vinylcyclopropanes[10].

Scheme 3



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5. In a typical procedure nitrones **2** (5 mmol) were dissolved in dry THF (30 ml). The solution was cooled at -70 °C and then anhydrous trifluoroacetic acid (15 mmol) was added. When the temperature rised to 0 °C, the mixture was quenched, adjusted to $pH\approx8$ with a saturated solution of $NaHCO_3$, extracted with ether, dried over $MgSO_4$, concentrated and submitted to flash-chromatographic separation on a silica gel column (hexane: ethyl acetate 7/3 as eluant). Physical data for compounds **3** follow:
   3b: oil, δ_H ($CDCl_3$) 2.20 (s, 3H); 2.75 (t, 2H, $J=6.5$ Hz); 3.35 (t, 2H); 3.75 (s, 3H, OMe); 5.05 (bs, 1H, OH); 6.60-7.10 (m, 4H, arom). ν_{OH} (film) 3392 and ν_{CO} 1705 cm^{-1}; *m/z:* 193 (M^+-16) 177, 150, 136, 120, 107, 77, 65, 43.
   3c: oil, δ_H ($CDCl_3$) 2.15 (s, 3H); 2.70 (t, 2H, $J=6.5$ Hz); 3.45 (t, 2H); 4.35 (bs, 1H, OH); 6.55-7.20 (m, 4H, arom). ν_{OH} (film) 3390 and ν_{CO} 1700 cm^{-1}; *m/z:* 197, 199 (M^+-16) 180, 140, 127, 111,75, 63, 43.
   Both compounds gave satisfactory microanalyses.

6. G. Bartoli, E. Marcantoni, M. Petrini, R. Dalpozzo, *J. Org. Chem.*, **1990**, in press.

7. In a typical procedure nitrocompounds **1** (5 mmol) were dissolved in dry THF (30 ml). The solution was cooled at -70 °C and but-1-en-3-ylmagnesium chloride was added dropwise. The mixture was stirred for 20 minutes and then anhydrous trifluoroacetic acid (15 mmol) was added. When the temperature rised to 0 °C, the mixture was quenched, adjusted to $pH\approx8$ with a saturated solution of $NaHCO_3$, extracted with ether, dried over $MgSO_4$, concentrated and

submitted to flash-chromatographic separation on a silica gel column (hexane: ethyl acetate 7/3 as eluant). Physical data for compounds **3** follow:

3a: oil, δ_H ($CDCl_3$) 2.18 (s, 3H); 2.78 (t, 2H, J=6.55 Hz); 3.30 (t, 2H); 4.50 (bs, 1H, OH); 6.65-7.30 (m, 5H, arom). ν_{OH} (film) 3395 and ν_{CO} 1705 cm^{-1}; *m/z:* 163 (M^+-16), 120, 92, 77, 65, 43.

3d: oil, δ_H ($CDCl_3$) 2.15 (s, 3H); 2.85 (t, 2H, J=6.5 Hz); 3.40 (t, 2H); 4.60 (bs, 1H, OH); 6.90 (m, 4H, arom). ν_{OH} (film) 3390 and ν_{CO} 1700 cm^{-1}; *m/z:* 258, 260 (M^+), 244, 242, 189, 187, 160, 117, 90, 77, 65, 43.

3e: oil, δ_H ($CDCl_3$) 2.15 (s, 3H); 2.32 (s, 3H), 2.58 (t, 2H, J=6.55 Hz); 3.30 (t, 2H); 4.56 (bs, 1H, OH); 6.80-7.20 (m, 4H, arom). ν_{OH} (film) 3390 and ν_{CO} 1705 cm^{-1}; *m/z:* 177 (M^+-16), 168, 104, 91, 77, 65, 43.

All compounds gave satisfactory microanalyses.

8. **4b:** oil, δ_H ($CDCl_3$) 2.15 (s, 3H); 2.73 (t, 2H, J=6.55 Hz); 3.40 (t, 2H); 3.70 (s, 3H, OMe), 4.30 (bs, 1H, NH); 6.50-6.85 (m, 3H, arom). ν_{NH} (film) 3392 and n_{CO} 1705 cm^{-1}; *m/z:* 227, 229 (M^+), 184, 172, 170, 156, 154, 116, 114, 77, 65, 43.

4c: oil, δ_H ($CDCl_3$) 2.15 (s, 3H); 2.75 (t, 2H, J=6.55 Hz); 3.40 (t, 2H); 4.80 (bs, 1H, NH); 6.55-7.25 (m, 3H, arom). ν_{NH} (film) 3400 and ν_{CO} 1705 cm^{-1}; *m/z:* 231, 233, 235 (M^+), 178, 176, 174, 113, 111, 97, 75, 43.

Both compounds gave satisfactory microanalyses.

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