Further Rearrangement of Meisenheimer Products of Allyl Aryl Amine Oxides†

Krishna C. Majumdar* and Gour H. Jana

Department of Chemistry, University of Kalyani, Kalyani 741 235, West Bengal, India

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Thyagarajan and co-workers have studied the molecular reorganization of arylpropynyl sulfoxides[1] and arylpropynylamine oxides.[2] It has been proposed that the [2s,3s] sigmatropic shift is followed by a [3s,3s] shift, enolization, ketol formation, etc., to give a five-membered ring in benzo[*b*]thiophenes and indoles in almost quantitative yields. The formation of indoles occurs readily in one step by simply stirring a solution of arylpropynylamine with 1 equiv of *m*-CPBA at room temperature. More recently,[3] this methodology has been successfully applied to form fused heterocyclic rings in different heterocycles. The initial step in the reorganization of arylpropynyl sulfoxides and arylpropynylamine oxides is a [2s,3s] sigmatropic rearrangement analogous to the [2s,3s] shift in allylarylamine oxides[4] in the case of the Meisenheimer rearrangement. Recently, we have observed a [1a,3s] sigmatropic shift during thermal rearrangement of [(aryloxy)methyl]coumarins.[5] This observation prompted us to study the Meisenheimer rearrangement of different allylic substrates and also the subsequent thermal rearrangement of the initial Meisenheimer products. Here we report the results of our investigation.

The allylic tertiary amines **3a**−**f** were prepared by the reaction of *N*-methylaniline (**1**) with appropriate allylic halides **2a**−**f** in refluxing acetone in the presence of anhydrous potassium carbonate (Scheme 1) in 65−80% yields.

Results and Discussion

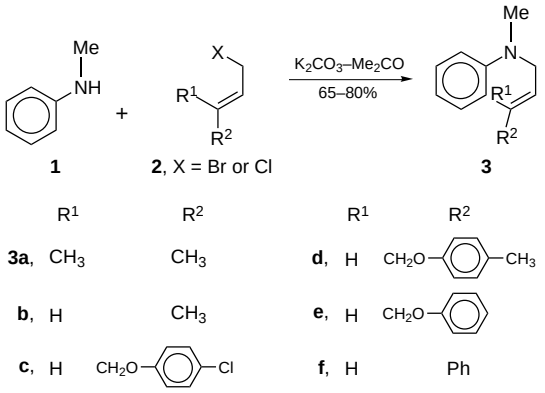
When *N*-methyl-*N*-phenyl-*N*-[1-((*E*)-3-methylbut-2-enyl)]amine (**3a**) was treated with 1 equiv of *m*-CPBA in chloroform at 0−5 °C, within 10 min formation of a highly polar *N*-oxide was observed as indicated by TLC. If this reaction mixture was kept at rt for 8−10 h a new product **5a**, characterized as *O*-[2-(2-methylbut-3-enyl)]-*N*-methyl-*N*-phenylhydroxylamine was obtained in excellent yield.

On similar treatment substrates **3b**−**e** furnished the corresponding products **5b**−**e** also in nearly quantitative yields. These products turned reddish brown on standing in air. Interestingly, a different product was isolated from the reaction of **3f** and characterized as *O*-[1-((*E*)-3-phenylprop-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (**6f**). Presumably, **6f** was produced from the rearrangement of **5f** under the reaction conditions.

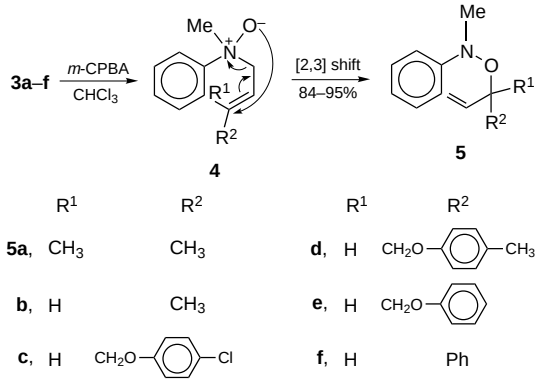
Meisenheimer product **5a** in C_6H_5Cl remained unaffected at 100 °C (3 h). However, a new product *O*-[1-((*E*)-3-methylbut-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (**6a**) was obtained in 70% yield when heated at 120−130 °C for 4 h. Further heating gradually decomposes the product to *N*-methylaniline. The reaction was also studied in *o*-dichlorobenzene, and the results were about the same. However, the same product **6a** was obtained in slightly higher yield (80%) in a shorter reaction time (2 h) in DMF at 120 °C. Similar treatment of Meisenheimer products **5b**−**e** led to products **6b**−**e** in 60−72% yields.

The formation of products **6a**−**e** from **5a**−**e** may be explained by a concerted [1,3] shift (Scheme 3). Steric effects are likely to limit the generality of [1,3] shifts,

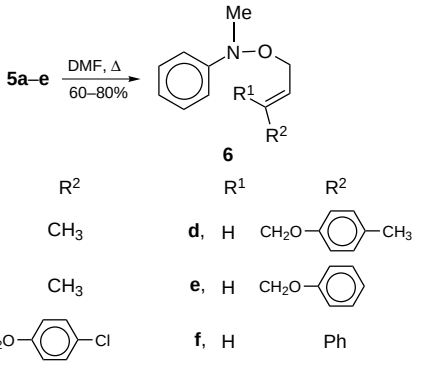
Scheme 1



Scheme 2



Scheme 3



† Dedicated to Professor B. S. Thyagarajan of the University of Texas at San Antonio on the occasion of his 65th birthday.

(1) (a) Majumdar, K. C.; Thyagarajan, B. S. *J. Chem. Soc., Chem. Commun.* **1972**, 83. (b) Majumdar, K. C.; Thyagarajan, B. S. *Int. J. Sulfur Chem., Part A* **1972**, *2*, 93.

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and examples of thermal [1,3] shifts are rare.[6] The formation of products **6a**−**e** is unaffected when a radical scavenger (e.g., hydroquinone) is added to the reaction mixture. On the other hand, the reaction also does not take place at 100 °C in the presence of a radical initiator (AIBN). As the formation of **6a**−**e** from **5a**−**e** is unaffected in the presence of a radical inhibitor as well as radical initiator it seems that migration of the less crowded neutral oxygen heteroatom to a carbon atom is facilitated through a concerted low energy transition state.

In the case of the amine oxide rearrangement of arylprop-2-ynylamine oxide, the [2, 3] sigmatropic shift (*i.e.*, Meisenheimer rearrangement) is followed by a [3,3] shift, but in the present work it is interesting to note that initial Meisenheimer rearrangement products undergo [1,3] shifts of the oxygen heteroatom to carbon on further heating.

Experimental Section

General Methods. UV absorption spectra were recorded in ethanol. IR spectra were run as thin films. ^{1}H-NMR spectra were performed at the IICB, Calcutta. Elemental analyses and mass spectra were determined at CDRI, Lucknow. Silica gel 60−120 mesh was used for chromatographic separation. Pet. ether indicates petroleum ether (60−80 °C).

General Procedure for the Preparation of Tertiary Amines 3a−f. A mixture of *N*-methylaniline (**1**) (2.14 g, 0.020 mol) and the appropriate allylic halides **2a**−**f** (0.022 mol) was refluxed in dry acetone (100 mL) in the presence of anhyd K_2CO_3 (2 g) for 4−10 h. Progress of the reaction was monitored by TLC. The reaction mixture was cooled and filtered. The solvent was removed from the filtrate in vacuo, and the crude mass was chromatographed over silica gel to provide the pure products **3a**−**f**.

***N*-Methyl-*N*-phenyl-*N*-[1-((*E*)-3-methylbut-2-enyl)]-amine (3a):** yield 85%, viscous liquid; UV λ_{max} 251 (log ϵ 3.00), 300 (log ϵ 2.54); IR (thin film) 2980, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.76 (s, 6H), 2.92 (s, 3H), 3.92 (d, J = 7 Hz, 2H), 5.26 (t, J = 7 Hz, 1H), 6.68−6.80 (m, 3H), 7.16−7.36 (m, 2H); MS *m*/*z* 175 (M$^+$). Anal. Calcd for $C_{12}H_{17}N$: C, 82.29; H, 9.71; N, 8.00. Found: C, 82.00; H, 9.48; N, 8.29.

***N*-Methyl-*N*-phenyl-*N*-[1-((*E*)-but-2-enyl)]amine (3b):** yield 81%; viscous liquid; UV λ_{max} 251 (log ϵ 2.86), 300 (log ϵ 2.24); IR (thin film) 3000, 1590 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.70 (d, J = 5 Hz, 3H), 2.90 (s, 3H), 3.84−4.08 (m, 2H), 5.34−5.60 (m, 1H), 5.64 (dt, J = 16, 5 Hz, 1H), 6.68−6.80 (m, 3H), 7.16−7.40 (m, 2H); MS *m*/*z* 161 (M$^+$). Anal. Calcd for $C_{11}H_{15}N$: C, 81.99; H, 9.32; N, 8.69. Found: C, 81.72; H, 9.00; N, 8.42.

***N*-Methyl-*N*-phenyl-*N*-[1-[(*E*)-4-(4′-chlorophenoxy)but-2-enyl]]amine (3c):** yield 80%; viscous liquid; UV λ_{max} 251 (log ϵ 3.13), 300 (log ϵ 2.42); IR (thin film) 3000, 1600, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.96 (s, 3H), 3.96−4.16 (m, 2H), 4.48−4.68 (m, 2H), 5.80 (dt, J = 16, 5 Hz, 1H), 5.92 (dt, J = 16, 5 Hz, 1H), 6.68−7.44 (m, 9H); MS *m*/*z* 287, 289 (M$^+$). Anal. Calcd for $C_{17}H_{18}ClNO$: C, 70.96; H, 6.26; N, 4.86. Found: C, 70.66; H, 6.58; N, 4.57.

***N*-Methyl-*N*-phenyl-[1-[(*E*)-4-(4′-methylphenoxy)but-2-enyl]]amine (3d):** yield 65%; viscous liquid; UV λ_{max} 251 (log ϵ 3.01), 300 (log ϵ 2.30); IR (thin film) 3020, 1590, 1280 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.30 (s, 3H), 2.96 (s, 3H), 3.92−4.12 (m, 2H), 4.48−4.72 (m, 2H), 5.76 (dt, J = 16, 5 Hz, 1H), 5.90 (dt, J = 16, 5 Hz, 1H), 6.68−7.40 (m, 9H); MS *m*/*z* 267 (M$^+$). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.89; H, 7.86; N, 5.24. Found: C, 80.59; H, 7.58; N, 5.00.

***N*-Methyl-*N*-phenyl-*N*-[1-((*E*)-4-phenoxybut-2-enyl)]-amine (3e):** yield 83%; viscous liquid; UV λ_{max} 251 (log ϵ 3.08), 300 (log ϵ 2.38); IR (thin film) 3000, 1600, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.92 (s, 3H), 3.94−4.16 (m, 2H), 4.50−4.70 (m, 2H), 5.80−5.96 (m, 2H), 6.68−7.46 (m, 10H); MS *m*/*z* 253 (M$^+$). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.63; H, 7.51; N, 5.53. Found: C, 80.90; H, 7.38; N, 5.48.

***N*-Methyl-*N*-phenyl-*N*-[1-((*E*)-3-phenylprop-2-enyl)]-amine (3f):** yield 72%; viscous liquid; UV λ_{max} 251 (log ϵ 3.05), 265 (log ϵ 2.77); IR (thin film) 3060, 1600, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.96 (s, 3H), 4.06 (d, J = 5 Hz, 2H), 6.22 (dt, J = 16, 5 Hz, 1H), 6.52 (d, J = 16 Hz, 1H), 6.60−7.60 (m, 10H); MS *m*/*z* 223 (M$^+$). Anal. Calcd for $C_{16}H_{17}N$: C, 86.09; H, 7.62; N, 6.28. Found: C, 86.40; H, 7.54; N, 6.54.

General Procedure for Oxidation and Meisenheimer Rearrangement of Tertiary Amines 3a−f. *m*-(Chloroperoxy)benzoic acid (0.010 mol, 3.44 g, 50%) in $CHCl_3$ (50 mL) was added to a well-stirred solution of the appropriate tertiary amine (0.010 mol) in $CHCl_3$ (50 mL), at 0−5 °C over a period of 20 min. The reaction mixture was stirred for 10 h longer. The reaction mixture was washed with an aqueous solution of K_2CO_3 and dried (Na_2SO_4). The solvent was removed, and the crude mass was purified by column chromatography over silica gel. Compounds **5a**−**e** and **6f** were obtained when the column was eluted with pet. ether.

***O*-[2-(2-Methylbut-3-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (5a):** yield 89%; viscous liquid; UV λ_{max} 235 (log ϵ 2.71), 279 (log ϵ 2.22); IR (thin film) 2980, 1600, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.40 (s, 6H), 3.08 (s, 3H), 5.04−5.32 (m, 2H), 5.96−6.28 (m, 1H), 6.92−7.44 (m, 5H); MS *m*/*z* 191 (M$^+$). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.39; H, 8.90; N, 7.33. Found: C, 75.62; H, 8.66; N, 7.08.

***O*-[2-(But-3-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (5b):** yield 95%; viscous liquid; UV λ_{max} 241 (log ϵ 3.13), 279 (log ϵ 2.57); IR (thin film) 3060, 1590, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.36 (d, J = 7 Hz, 3H), 3.08 (s, 3H), 4.32 (m, 1H), 5.16 (br d, J = 10 Hz, 1H), 5.24 (br d, J = 18 Hz, 1H), 5.80−6.20 (m, 1H), 6.92−7.52 (m, 5H), MS *m*/*z* 177 (M$^+$). Anal. Calcd for $C_{11}H_{15}NO$: C, 74.57; H, 8.47; N, 7.90. Found: C, 74.30; H, 8.69; N, 7.72.

***O*-[2-[1-(4′-Chlorophenoxy)but-3-enyl]]-*N*-methyl-*N*-phenylhydroxylamine (5c):** yield 91%; viscous liquid; UV λ_{max} 226 (log ϵ 3.28), 250 (log ϵ 2.30), 264 (log ϵ 3.05); IR (thin film) 3060, 1590, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.08 (s, 3H), 4.14 (d, J = 4 Hz, 2H), 4.44−4.68 (dt, J = 7, 4 Hz, 1H), 5.33 (dt, J = 10, 1.2 Hz, 1H), 5.43 (dt, J = 16, 1.2 Hz, 1H), 5.88−6.28 (m, 1H), 6.80−7.64 (m, 9H); MS *m*/*z* 303, 305 (M$^+$). Anal. Calcd for $C_{12}H_{17}ClNO_2$: C, 67.22; H, 5.93; N, 4.61. Found: C, 67.50; H, 5.76; N, 4.84.

***O*-[2-[1-(4′-Methylphenoxy)but-3-enyl]]-*N*-methyl-*N*-phenylhydroxylamine (5d):** yield 85%; viscous liquid; UV λ_{max} 226 (log ϵ 3.28), 279 (log ϵ 2.70); IR (thin film) 3000, 1600, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.28 (s, 3H), 3.12 (s, 3H), 4.16 (d, J = 4 Hz, 2H), 4.48−4.72 (dt, J = 7, 4 Hz, 1H), 5.34 (br d, J = 10 Hz, 1H), 5.43 (br d, J = 17 Hz, 1H), 5.88−6.28 (m, 1H), 6.80−7.60 (m, 9H); MS *m*/*z* 283 (M$^+$). Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.32; H, 7.42; N, 4.94. Found: C, 76.09; H, 7.29; N, 5.36.

***O*-[2-(1-Phenoxybut-3-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (5e):** yield 84%; viscous liquid; UV λ_{max} 225 (log ϵ 3.32), 250 (log ϵ 3.30), 264 (log ϵ 3.01); IR (thin film) 3000, 1600, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.04 (s, 3H), 4.10 (d, J = 4 Hz, 2H), 4.40−4.64 (dt, J = 7, 4 Hz, 1H), 5.20−5.56 (m, 2H), 5.84−6.20 (m, 1H), 6.76−7.52 (m, 10H); MS *m*/*z* 269 (M$^+$). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.84; H, 7.06; N, 5.20. Found: C, 75.62; H, 6.66; N, 5.28.

Rearrangement of Meisenheimer Products 5a−f in DMF. A mixture of **5a**−**e** (4 mmol) and DMF (3 mL) was heated on an oil bath at 120−130 °C for 30 min to 2 h. The reaction was monitored by TLC. The reaction was cooled and then subjected to column chromatography over silica gel. Compounds **6a**−**e** were obtained when the column was eluted with pet. ether. Starting material (15−20%) was recovered in each case except in the case of **5a**.

***O*-[1-(3-Methylbut-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (6a):** yield 80%; viscous liquid; UV λ_{max} 241 (log ϵ 3.28), 263 (log ϵ 2.69); IR (thin film) 2900, 1660, 1270 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.74 (d, J = 4 Hz, 6H), 3.08 (s, 3H), 4.32 (d, J = 6 Hz, 2H), 5.46 (t, J = 6 Hz, 1H), 6.88−7.44 (m, 5H); MS *m*/*z* 191 (M$^+$). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.39; H, 8.90; N, 7.33. Found: C, 75.22; H, 8.60; N, 7.10.

***O*-[1-((*E*)-But-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (6b):** yield 60%; viscous liquid; UV λ_{max} 248 (log ϵ 3.25),

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302 (log ϵ 2.69); IR (thin film) 2960, 1600, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.74 (d, J = 4 Hz, 3H), 3.08 (s, 3H), 4.25−4.52 (m, 2H), 5.52−5.76 (m, 1H), 5.90 (dt, J = 16, 5 Hz, 1H), 6.92−7.48 (m, 5H); MS m/z 177 (M^+). Anal. Calcd for $C_{11}H_{15}NO$: C, 74.57; H, 8.47; N, 7.90. Found: C, 74.80; H, 8.33; N, 7.74.

***O*-[1-[(*E*)-4-(4′-Chlorophenoxy)but-2-enyl]]-*N*-methyl-*N*-phenylhydroxylamine (6c):** yield 72%; viscous liquid; UV λ_{max} 226 (log ϵ 3.26), 278 (log ϵ 2.64); IR (thin film) 2900, 1600, 1230 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.08 (s, 3H), 4.36 (d, J = 4 Hz, 2H), 4.52 (d, J = 4 Hz, 2H), 5.96 (dt, J = 16, 4 Hz, 1H), 6.08 (dt, J = 16, 4 Hz, 1H), 6.72−7.44 (m, 9H); MS m/z 303, 305 (M^+). Anal. Calcd for $C_{17}H_{18}ClNO_2$: C, 67.22; H, 5.93; N, 4.61. Found: C, 67.08; H, 5.77; N, 4.37.

***O*-[1-[(*E*)-4-(4′-Methylphenoxy)but-2-enyl]]-*N*-methyl-*N*-phenylhydroxylamine (6d):** yield 61%; viscous liquid; UV λ_{max} 226 (log ϵ 3.25), 277 (log ϵ 2.63); IR (thin film) 3010, 1600, 1230 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 2.20 (s, 3H), 3.00 (s, 3H), 4.30 (d, J = 4 Hz, 2H), 4.42 (br s, 2H), 5.92 (dt, J = 16, 4 Hz, 1H), 6.04 (dt, J = 16, 4 Hz, 1H), 6.62−7.40 (m, 9H); MS m/z 283 (M^+). Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.32; H, 7.4; N, 4.97. Found: C, 76.10; H, 7.77; N, 4.70.

***O*-[1-((*E*)-4-Phenoxybut-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (6e):** yield 62%; viscous liquid; UV λ_{max} 230 (log ϵ 3.09), 277 (log ϵ 2.58); IR (thin film) 3010, 1600, 1230 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.08 (s, 3H), 4.42 (d, J = 4.5 Hz, 2H), 4.54 (d, J = 4.5 Hz, 2H), 5.96 (dt, J = 16, 5 Hz, 1H), 6.08 (dt, J = 16, 5 Hz, 1H), 6.72−7.48 (m, 10H); MS m/z 269 (M^+). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.84; H, 7.06; N, 5.20. Found: C, 75.62; H, 6.66; N, 5.08.

***O*-[1-((*E*)-3-Phenylprop-2-enyl)]-*N*-methyl-*N*-phenylhydroxylamine (6f):** yield 48%; viscous liquid; UV λ_{max} 265 (log ϵ 2.91); IR (thin film) 3010, 1600, 1230 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.08 (s, 3H), 4.50 (d, J = 5 Hz, 2H), 6.38 (dt, J = 16, 5 Hz, 1H), 6.68 (d, J = 16 Hz, 1H), 6.96−7.68 (m, 10H); MS m/z 239 (M^+). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.33; H, 7.11; N, 5.85. Found: C, 80.12; H, 7.00; N, 5.60.

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