Gas-Phase Pyrolysis in Organic Synthesis: New Route for Synthesis of Functionally Substituted Imidazoles

Osman M. E. El-Dusouqui[a], Mervat M. Abdelkhalik[b], Nouria A. Al-Awadi[a] and Mohamed H. Elnagdi[a]

[a]Chemistry Department, Kuwait University, P.O. Box 5969, Safat 13060, Kuwait
[b]Applied Science Department, College of Technological Studies,
Public Authority for Applied Education and Training, Kuwait
nouria@kuc01.kuniv.edu.kw

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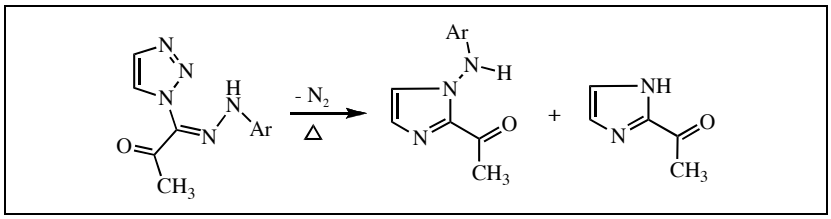

1,2,3-Triazolylpropanone was prepared and coupled with aryldiazonium salts yielding the corresponding arylhydrazones. Gas-phase pyrolysis of the hydrazono derivative produced *N*-arylamino-2-acetylimidazole as well as 2-acetylimidazole. The latter is the product of further pyrolysis of the former.

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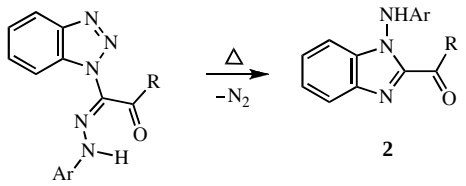
INTRODUCTION

Gas-phase pyrolyses of functionally substituted aryl-hydrazones have been shown to be an efficient route in the synthesis of otherwise not readily obtainable heteroaromatics [1-3]. In an earlier study, we were able to show that gas-phase pyrolysis of benzotriazolylaryl-hydrazono ketones **1** is a useful alternative process for the synthesis of benzimidazoles **2** (Scheme 1) [4]. In conjunction with this work, we report here results of our investigation of the gas-phase pyrolysis of 1-(1,2,3-tri-azol-1-yl)-1-arylhydrazonopropanone **3**.

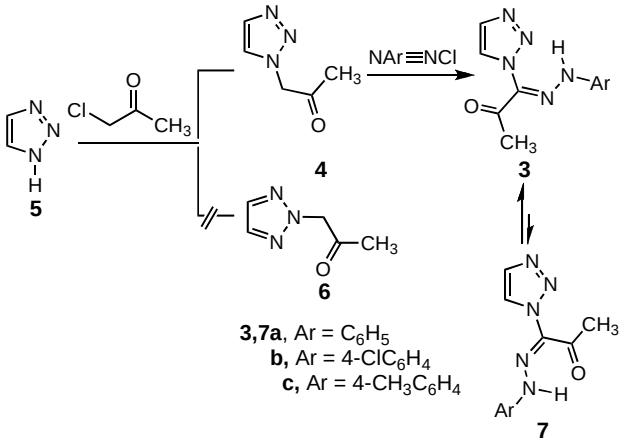
Scheme 1



RESULTS AND DISCUSSION

The novel arylhydrazones **3** were prepared *via* coupling 1-(1*H*-1,2,3-triazol-1-yl)propanone **4** with aromatic diazonium salts. Compound **4** in turn could be prepared *via* reacting 1,2,3-triazole **5** with chloropropanone. Although the symmetric 1-(1,2,3-triazol-2-yl)propanone **6** might also be expected in the reaction, only **4** was formed as established by ^{1}H NMR spectrum of the reaction product which revealed two doublets at δ = 7.77 and 7.97 ppm (*J* = 1.3 Hz). These are interpretable for 1,2,3-triazole *H*-4 and *H*-5. For alkylation product **6**, only one proton signal would be expected for the two 1,2,3-triazole ring hydrogens as both protons in this case would resonate at the same field. Arylhydrazono ketones have recently been shown to prefer *anti* conformation due to stereoelectronic factors [2,4-6], hence we suggest that likewise **3** also exists mainly in *anti*-form **3** rather than **7**.

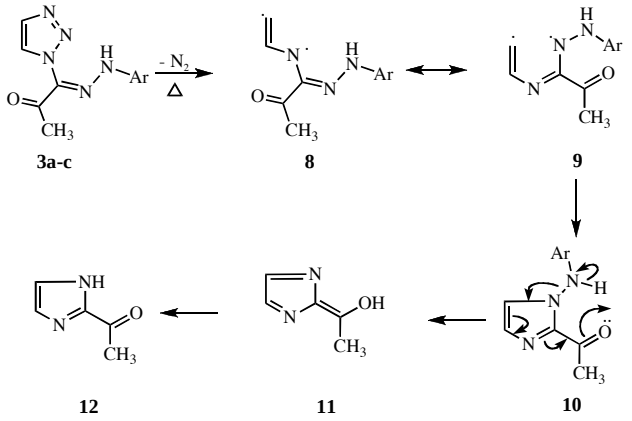
Scheme 2



Compounds **3a-c** were pyrolysed in the gas phase and the pyrolysates were separated by LCMS. Two main products were identified, also from their MS data. 2-Acetylimidazole **12** could be easily identified: mp 136-138 °C (Lit. mp 137-137.5 °C [7]); molecular mass (M+1) =111. Besides, comparison of mixed mp and of R_f value with that of an authentic specimen confirmed the identity of this product. The other products of pyrolysis are

ascertained to be (l-arylamino-2-imidazolyl)ethanone **l0a-c** of molecular masses 201 from **3a**, 235 from **3b** and 215 from **3c**. These products are believed to be formed *via* elimination of molecular nitrogen from **3a-c** leading to the biradical **8**, which is in resonance with its canonical form **9**. This biradical is directly cyclized into *N*-arylamino-acetyl imidazoles **l0a-c**. It is most likely that 2-acetyl-imidazole **12** results from further pyrolytic elimination of incipient aminoarene from *N*-arylaminoacetylimidazole **10** *via* a transition state similar to the quazi-aromatic six-membered transition state suggested earlier to account for the pyrolytic behavior of arylhydrazonoketones [7] (Scheme 3). Loss of an arylamino moiety to give the corresponding imidazole derivative and arylamine has been reported for benzimidazole **2** [4].

Scheme 3



EXPERIMENTAL

General. Melting points were determined on a Shimadzu-Gallenkamp apparatus and are uncorrected. Elemental analysis was by means of a LECO CHNS-932 Elemental Analyzer. NMR spectra were measured using a Bruker DPX 400 MHz superconducting spectrometer, and FT-IR measurements were from a Perkin Elmer 2000 FT-IR system. Mass spectrometric analysis was carried out on a VG-Autospec-Q high performance tri-sector GC/MS/MS, and the instrument for HPLC was an Agilent 1100 series LC/MSD with an API-ES/APCI ionization mode.

Synthesis.

1-(1*H*-1,2,3-triazol-1-yl)propanone 4. Compound **4** was prepared following published procedure [4] which involves reacting 1*H*-1,2,3-triazole with chloroacetone in acetone in the presence of triethylamine. Yield 62% (7.75 g); white crystals from benzene; m.p. 245°C; IR (KBr): ν/cm^{-1}: 1630 (C=O); MS: *m/z* = 125 (M$^{+\cdot}$); ^{1}H NMR (DMSO-d$_6$): δ (ppm) = 2.33 (s, 3H, CH_3), 5.50 (s, 2H, CH_2), 7.96 (d, 1H, *J* = 1.00 Hz, triazolyl-H), 8.28 (d, 1H, *J* = 1.0 Hz, triazolyl-H). *Anal.* Calcd. for $C_5H_7N_3O$ (125.13): C 47.99, H 5.64, N 33.58. Found C 48.25, H 5.60, N 33.76.

General procedure for the preparation of compounds 3a-c. Compounds **3a-c** were prepared following earlier procedures [8] which involve coupling the 1,2,3-triazol-1-yl propanone **4** with the corresponding aromatic diazonium salts.

(*Z*)-1-(2-Phenylhydrazono)-1-(1*H*-1,2,3-triazol-1-yl)propanone 3a. Yield 71% (1.62 g); brownish crystals from ethanol; m.p. 135-136 °C; IR (KBr): ν/cm^{-1}: 3135 (NH), 1672 (C=O); MS: *m/z* = 229 (M$^{+\cdot}$); ^{1}H NMR (DMSO-d$_6$): δ (ppm) = 2.56 (s, 3H, CH_3), 7.07 (t, 1H, *J* = 7.20 Hz, phenyl-H), 7.37 (t, 2H, *J* = 7.32 Hz, phenyl-H), 7.45 (d, 2H, *J* = 7.80 Hz, phenyl-H), 7.99 (d, 1H, *J* = 0.8 Hz, triazolyl-H), 8.30 (d, 1H, *J* = 0.8 Hz, triazolyl-H), 10.89 (br. s, 1H, NH). *Anal.* Calcd. for $C_{11}H_{11}N_5O$ (229.10): C 57.63, H 4.84, N 30.55. Found C 56.99, H 4.65, N 30.21.

(*Z*)-1-[2-(4-Chlorophenyl)hydrazono)]-1-(1*H*-1,2,3-triazol-1-yl)]propanone 3b. Yield 82% (2.15 g); yellow crystals from ethanol; m.p. 209 °C; IR (KBr): ν/cm^{-1}: 3210 (NH), 1667 (C=O); MS: *m/z* = 263 (M$^{+\cdot}$); ^{1}H NMR (DMSO-d$_6$): δ (ppm) = 2.56 (s, 3H, CH_3), 7.42 (d, 2H, *J* = 8.8 Hz, chlorophenyl-H), 7.46 (d, 2H, *J* = 8.8 Hz, chlorophenyl-H), 8.00 (d, 1H, *J* = 0.75 Hz, triazolyl-H), 8.30 (d, 1H, *J* = 0.75 Hz, triazolyl-H), 10.94 (br. s, 1H, NH). *Anal.* Calcd. for $C_{11}H_{10}ClN_5O$ (263.68): C 50.10, H 3.82, N 26.56. Found C 49.80, H 3.90, N 26.41.

(Z)-1-[2-(*p*-Tolylhydrazono)]-1-(1*H*-1,2,3-triazol-1-yl)]-propanone 3c. Yield 80% (1.95 g); reddish crystals from ethanol; m.p. 129 °C; IR (KBr): ν/cm^{-1}: 3231 (NH), 1671 (C=O); MS: *m/z* = 243 (M$^{+\cdot}$); ^{1}H NMR (DMSO-d$_6$): δ (ppm) = 2.27 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 7.18 (d, 2H, *J* = 8.2 Hz, tolyl-H), 7.32 (d, 2H, *J* = 8.2 Hz, tolyl-H), 7.99 (d, 1H, *J* = 0.75 Hz, triazolyl-H), 8.29 (d, 1H, *J* = 0.75 Hz, triazolyl-H), 10.83 (br. s, 1H, NH). *Anal.* Calcd. for $C_{12}H_{13}N_5O$ (243.26): C 59.25, H 5.39, N 28.79. Found C 59.40, H 5.39, N 28.35.

Gas-Phase Pyrolysis.

General Procedure for Pyrolysis of 3a-c. Each of compounds **3a-c** was introduced in the reaction tube (1.5x12 cm Pyrex), cooled in liquid nitrogen, sealed under vacuum (0.06 mbar) and placed in the pyrolyser for 900 s at a temperature verified for complete pyrolysis. The pyrolysate was then separated into its constituents by preparative TLC (MERCK, 12 PSC-Platten 20x20 cm, Silica gel 60 F_{254} 2mm) using chloroform: petroleum ether (40:60) in 80:20 ratio as eluent, and each constituent was collected, analyzed and characterized. The techniques used include ^{1}H NMR and high performance GC/MS. A full description of the reactor and attachments has been detailed in earlier publications [1,4].

1-[1-(Phenylamino)-1*H*-imidazol-2-yl]ethanone 10a. MS: *m/z* for $C_{11}H_{11}N_3O$ (201.23) = 201 (M$^{+\cdot}$), ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.64 (s, 3H, CH_3), 6.82(d, 1H, *J* = 0.9 Hz, imidazolyl -H), 6.93 (d, 1H, *J* = 0.9 Hz, imidazolyl-H), 7.49 (d, 2H, *J* = 8.05 Hz, phenyl-H), 7.55 (t, 3H, *J* = 8.05 Hz, phenyl-H), 10.40 (br. s, 1H, NH).

1-[1-(4-Chlorophenylamino)-1*H*-imidazol-2-yl]ethanone 10b. MS: *m/z* for $C_{11}H_{10}ClN_3O$ (235.67) = 235 (M$^{+\cdot}$), ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.68 (s, 3H, CH_3), 7.21 (d, 1H, *J* = 1.0 Hz, imidazolyl-H), 7.25 (d, 1H, *J* = 1.0 Hz, imidazolyl -H), 7.47 (d, 2H, *J* = 8.7 Hz, chlorophenyl-H), 7.56 (d, 2H, *J* = 8.7 Hz, chlorophenyl-H), 10.43 (br. s, 1H, NH).

1-[1-(*p*-Toluidino)-1*H*-imidazol-2-yl]ethanone 10c. MS: *m/z* for $C_{12}H_{13}N_3O$ (215.25) = 215 (M$^{+\cdot}$), ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.38 (s, 3H, CH_3), 2.70 (s, 3H, CH_3), 6.62 (d, 1H, *J* = 0.9 Hz, imidazolyl-H), 7.06 (d, 1H, *J* = 0.9 Hz, imidazolyl -H), 7.15 (d, 2H, *J* = 8.4 Hz), 7.49 (d, 2H, *J* = 8.4 Hz), 10.40 (br. s, 1H, NH).

1-(1*H*-Imidazol-2-yl)ethanone 12. m.p. 136 °C (Lit [5] mp 136-137 °C); IR (KBr): ν/cm^{-1}: 1680 (C=O); MS: *m/z* = 111

($M^{+\cdot}$+1); ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.58 (s, 3H, CH_3), 7.35 (s, 2H, imidazolyl-H), 10.30 (br. s, 1H, NH).

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