SYNTHESIS OF MESOMERIC BETAINES, [1,2,4]TRIAZOLO[2,3-a]-PYRIDINIUMIDES, VIA BACK-DONATED 1,6-CYCLIZATION

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Abstract - The reaction of [1,2,4]triazolium salts (4a,b) with polarized alkenes (1a,b, 2a) in the presence of K₂CO₃ in CHCl₃-EtOH gave the corresponding triazolium N-allylides (5a-c). Thermolyses of the N-allylides (5a-c) afforded the 7-imino[1,2,4]triazolo[2,3-a]pyridiniumide derivatives (6a,b) and the 7-oxo-[1,2,4]triazolo[2,3-a]pyridiniumide derivative (7a). Similar treatment of the salts (4a,b) with alkenes (1c, 2b) directly yielded mesomeric betaines (7b,c), while the reaction of the salt (4b) with alkene (2c) gave the pyrrolo[2,1-f][1,2,4]triazine derivative (8).

As part of our continuing interest in the thermolyses of azolium N-allylides and N-vinylimino ylides,¹-³ we reported a synthesis of [1,2,4]triazolo[4,3-a]pyridiniumides by the back-donated 1,6-cyclization of N-allylides which were prepared by the reaction of 1-benzyl-4-carbethoxymethyltriazolium salt with alkenes.³e

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Scheme 1

![Scheme 1](image-url)
We describe here a new study on the 1-phenacyl- or 1-carbethoxymethyl-4-benzyltriazolium salt systems (4a,b). The polarized alklenes (1a-c, 2a-c)\textsuperscript{4,6} used in the present work are shown in Scheme 1.

The starting materials, triazolium salts (4a,b) were prepared from the reaction of benzyl bromide with 1-phenacyltriazole (3a) or 1-carbethoxymethyltriazole (3b).\textsuperscript{7} The reaction of the crude salts (4a,b) with alkenes (1a,b, 2a) in the presence of K\textsubscript{2}CO\textsubscript{3} in CHCl\textsubscript{3}-EtOH gave the triazolium N-allylide derivatives (5a-c). Thermolysis of 5a in refluxing xylene afforded the desired mesomeric betaine, 7-imino[1,2,4]-triazolo[2,3-a]pyridiniumide derivative (6a). In a similar manner the mesomeric betaines, [1,2,4]triazolo[2,3-a]pyridiniumide derivatives (6b, 7a) were obtained by thermolyses of 5b,c in refluxing xylene.

In addition, the reaction of the salts (4a,b) with alkenes (1c, 2b) in the presence of K\textsubscript{2}CO\textsubscript{3} directly gave the back-donated 1,6-cyclization products (7b,c). On the other hand, treatment of 4b with 2,2-bis(methylthio)-1-nitroethylene (2c) afforded pyrrolo[2,1-f][1,2,4]triazine derivative (8) (Scheme 2).

In our previous paper,\textsuperscript{3} we described that a reasonable mechanism for the formation of the back-donated 1,6-cyclization product (7a) involves the resonance structure (5b'), as outlined in Scheme 3. As pointed out
by Acheson and Elmore\textsuperscript{2b} and Meth-Cohn,\textsuperscript{1e} the formation of \textbf{8} may be rationalized as outlined in Scheme 4. Thus, 1,5-dipolar cyclization of \textbf{9’} gives \textbf{11} resulting from the cleavage of \textbf{10} and the product \textbf{(8)} arises from \textbf{11}.

![Scheme 3](image)

![Scheme 4](image)

In conclusion the triazolium \textit{N}-allylide (\textbf{5}) which had two electron-withdrawing groups at the 3-position of the allylde group participated in back-donated 1,6-cyclization to produce the mesomeric betaines (\textbf{6, 7}). The high efficiency of the back-donated 1,6-cyclization, due to the resonance structure (\textbf{5b’}), in thermolysis of the \textit{N}-allylde of the resulting mesomeric betaine, [1,2,4]triazolo[2,3-\textit{a}]pyridiniumide, presents interesting synthetic possibilities.

**EXPERIMENTAL**

Melting points were determined with a Mitamura Mel-Temp and are uncorrected. IR spectra were recorded in KBr pellets on an IR 810 (JASCO) spectrophotometer. UV spectra were recorded on a UV-310 (Shimadzu) spectrophotometer. \textsuperscript{1}H-NMR spectra were obtained on a Gemini 300 (VARIAN) spectrometer with tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million (\textit{\delta}). Elemental
analyses (C,H,N) of all compounds described here were performed on a Yanagimoto MT-2 CHN recorder.

**The preparation of 5a,b,c, 7b,c, and 8**

A mixture of 3a,b (4 mmol) and benzyl bromide (0.68 g, 4 mmol) in acetone (50 mL) was stirred at room temperature for a week, after which the solvent was evaporated under reduced pressure. A mixture of the crude salts (4a,b), alkenes (1a,b,c, 2a,b,c) (4 mmol), and K₂CO₃ (1.21 g, 8 mmol) in CHCl₃-EtOH (1:1, 30 mL) was stirred at rt for a week and the mixture was then poured into ice-water (100 mL). The mixture was extracted with CHCl₃ (4x30 mL) and the combined extracts were washed with water, dried (Na₂SO₄), and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel.

From a benzene-CHCl₃ (1:1) fraction, compounds (5a, 7b,c) and the oily products (5b,c) were obtained. From a benzene-CHCl₃ (20:1) fraction, compound (8) was obtained.

5a: mp 219-221 °C (EtOH-CHCl₃) (0.42 g, 30 %). IR (KBr) cm⁻¹: 2200 (CN), 2190 (CN), 1620 (CO). UV (EtOH) λmax (log ε) nm: 243 (3.89), 357 (4.66). H-NMR (DMSO-d₆): 5.61 (2H, s, CH₂Ar), 7.18 (1H, s, CH=), 7.43-7.47 (10H, m, Ar-H), 9.42 (1H, s, C₅-H), 10.42 (1H, s, C₅-H). Anal. Calcd for C₂₁H₁₅N₅O: C, 71.38; H, 4.28; N, 19.82. Found: C, 71.01; H, 4.39; N, 19.69.

7b: mp 276-278 °C (EtOH-CHCl₃) (0.34 g, 23 %). IR (KBr) cm⁻¹: 1650 (CO), 1625 (CO). UV (EtOH) λmax (log ε) nm: 232 (3.53), 337 (3.60). H-NMR (DMSO-d₆): 6.05 (2H, s, CH₂Ar), 7.38-7.53 (5H, m, Ar-H), 8.15 (1H, s, C₂-H), 9.44 (1H, s, C₅-H). Anal. Calcd for C₂₀H₁₄N₄O₄: C, 64.17; H, 3.77; N, 14.97. Found: C, 64.13; H, 3.87; N, 14.65.

7c: mp 193-196 °C (EtOH-CHCl₃) (0.41 g, 28 %). IR (KBr) cm⁻¹: 2220 (CN), 1730 (CO), 1560 (CO). UV (EtOH) λmax (log ε) nm: 205 (4.42), 325 (4.17). H-NMR (CDCl₃): 1.41 (3H, t, J = 7 Hz, CH₂CH₃), 2.58 (3H, s, SCH₃), 4.48 (2H, q, J =7 Hz, CH₂CH₃), 6.05 (2H, s, CH₂Ar), 7.37-7.53 (5H, m, Ar-H), 8.28 (1H, s, C₅-H). Anal. Calcd for C₁₈H₁₆N₄O₃S: C, 58.68; H, 4.38; N, 15.21. Found: C, 58.67; H, 4.40; N, 15.18.

8: mp 175-178 °C (MeOH-CH₂Cl₂) (0.56 g, 44 %). IR (KBr) cm⁻¹: 1690 (CO). UV (EtOH) λmax (log ε) nm: 280 (4.36). H-NMR (CDCl₃): 2.63 (3H, s, SCH₃), 5.05 (2H, s, CH₂Ar), 7.36 (5H, s, Ar-H), 7.61 (1H, s, C₂-H), 8.05 (1H, s, C₆-H). Anal. Calcd for C₁₄H₁₂N₄O₃S: C, 53.16; H, 3.82; N, 17.71. Found: C, 53.05; H, 3.85; N, 17.64.
The preparation of 6a,b, and 7a

A solution of 5a (1.41 g, 4 mmol) and the crude N-allylides (5b,c) in xylene (60 mL) was refluxed for 24 h, after which the solvent was evaporated under reduced pressure and the residue was poured into ice-water (100 mL). The mixture was extracted with CHCl₃ (4x30 mL) and the combined extracts were washed with water and dried (Na₂SO₄). Concentration of the solvent under reduced pressure gave compound (6a) and the tarry residue. The tarry residue was submitted to column chromatography on silica gel. From a CHCl₃-acetone (10:1) fraction, compounds (6b, 7a) were obtained.

**6a:** mp 267-269 °C (EtOH-CHCl₃) (0.61 g, 43%). IR (KBr) cm⁻¹: 3460 (NH), 2220 (CN), 1650 (CO). UV (EtOH) λmax (log ε) nm: 232 (4.23), 267 (4.26), 350 (4.40). ¹H-NMR (DMSO-d₆): 5.28 (2H, s, CH₂Ar), 7.28 (1H, s, C₂-H), 7.29 (5H, s, Ar-H), 7.42-7.86 (5H, m, Ar-H), 7.98 (1H, s, C₅-H), 8.06 (1H, s, =NH). Anal. Calcd for C₂₁H₁₅N₅O: C, 71.38; H, 4.28; N, 19.82. Found: C, 71.04; H, 4.41; N, 19.59.

**6b:** mp 235-238 °C (EtOH-CHCl₃) (0.51 g, 35%). IR (KBr) cm⁻¹: 3450 (NH), 2220 (CN), 1660 (CO). UV (EtOH) λmax (log ε) nm: 207 (4.41), 350 (4.18). ¹H-NMR (CDCl₃): 1.44 (3H, t, J = 7 Hz, CH₂CH₃), 2.54 (3H, s, SCH₃), 4.48 (2H, q, J = 7 Hz, CH₂CH₃), 5.31 (2H, s, CH₂Ar), 6.84 (1H, s, =NH), 7.24-7.27 (5H, m, Ar-H), 7.34 (1H, s, C₂-H). Anal. Calcd for C₁₈H₁₇N₅O₂S: C, 58.84; H, 4.66; N, 19.06. Found: C, 58.64; H, 4.73; N, 18.96.

**7a:** mp 78-79 °C (EtOH-CHCl₃) (0.44 g, 30%). IR (KBr) cm⁻¹: 1735 (CO), 1685 (CO), 1575 (CO). UV (EtOH) λmax (log ε) nm: 248 (4.06), 360 (3.75). ¹H-NMR (DMSO-d₆): 1.32-1.35 (6H, m, 2xCH₂CH₃), 4.36-4.44 (4H, m, 2xCH₂CH₃), 4.99 (2H, s, CH₂Ar), 7.32-7.42 (5H, m, Ar-H), 7.56 (1H, s, C₂-H), 10.48 (1H, s, C₅-H). Anal. Calcd for C₁₉H₁₉N₃O₅: C, 61.78; H, 5.18; N, 11.38. Found: C, 61.48; H, 5.24; N, 11.14.

REFERENCES


