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

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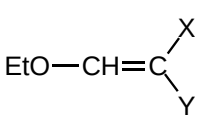
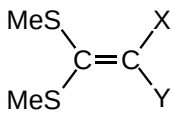
Abstract - The reaction of [1,2,4]triazolium salts (**4a, b**) with polarized alkenes (**1a, b, 2a**) in the presence of K_2CO_3 in $CHCl_3$-EtOH gave the corresponding triazolium *N*-allylides (**5a-c**). Thermolyses of the *N*-allylides (**5a-c**) afforded the 7-imino[1,2,4]triazolo[2,3-*a*]pyridiniumide 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]



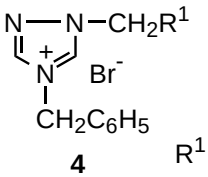
1

	X	Y
a	CN	CN
b	COOEt	COOEt
c	COOEt	NO_2



2

	X	Y
a	CN	CN
b	COOMe	CN
c	H	NO_2



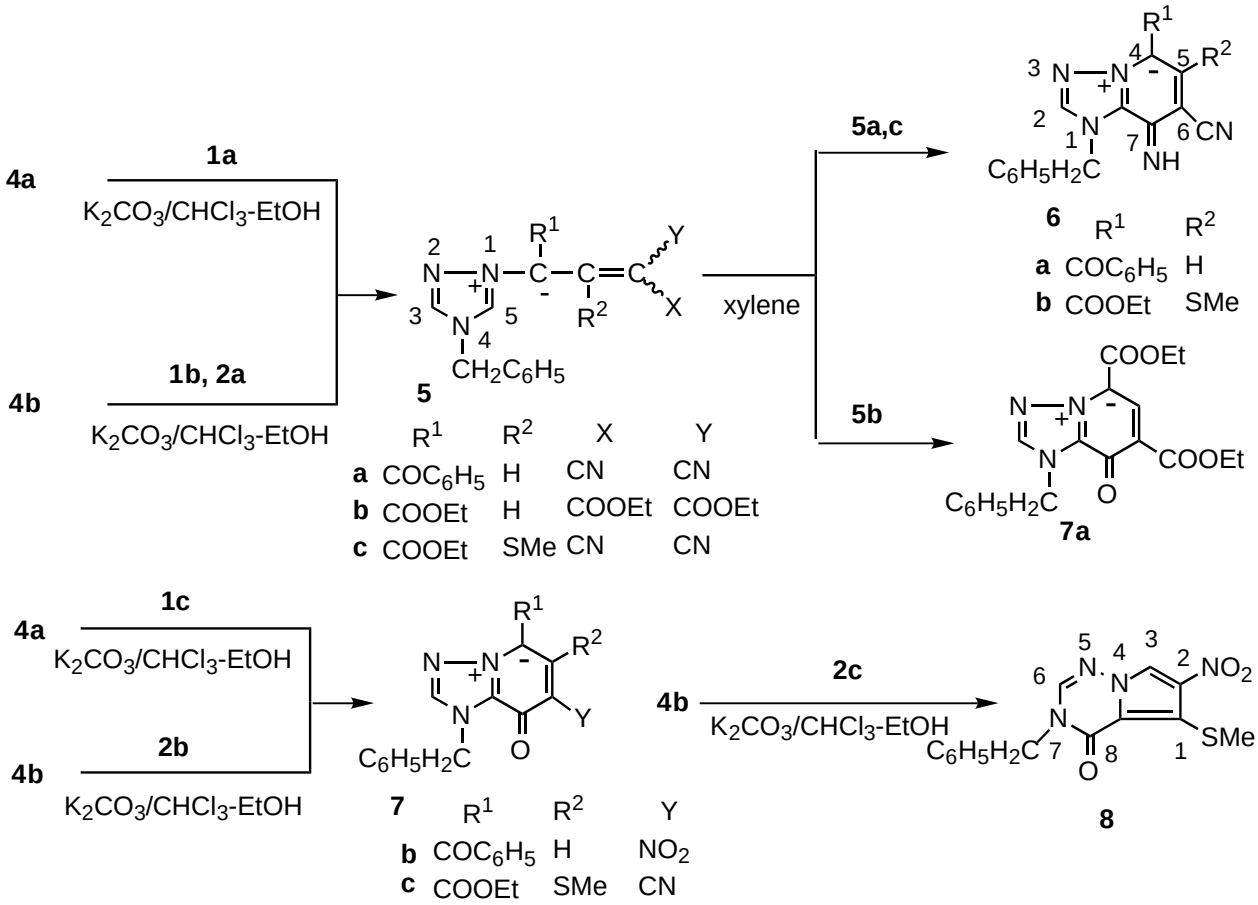
4

	R^1
a	COC_6H_5
b	COOEt

Scheme 1

We describe here a new study on the 1-phenacyl- or 1-carbethoxymethyl-4-benzyltriazolium salt systems (**4a,b**). The polarized alkenes (**1a-c, 2a-c**)[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**).[7] The reaction of the crude salts (**4a, b**) with alkenes (**1a, b, 2a**) in the presence of K_2CO_3 in $CHCl_3$-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.

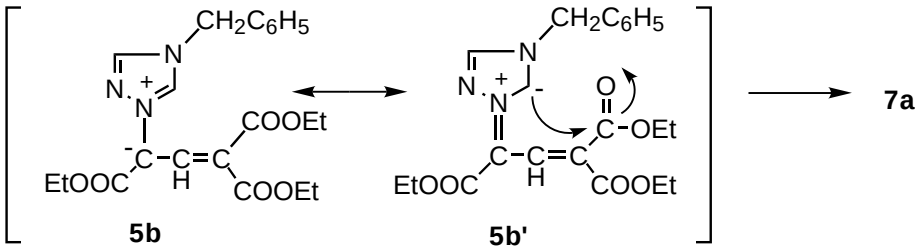


Scheme 2

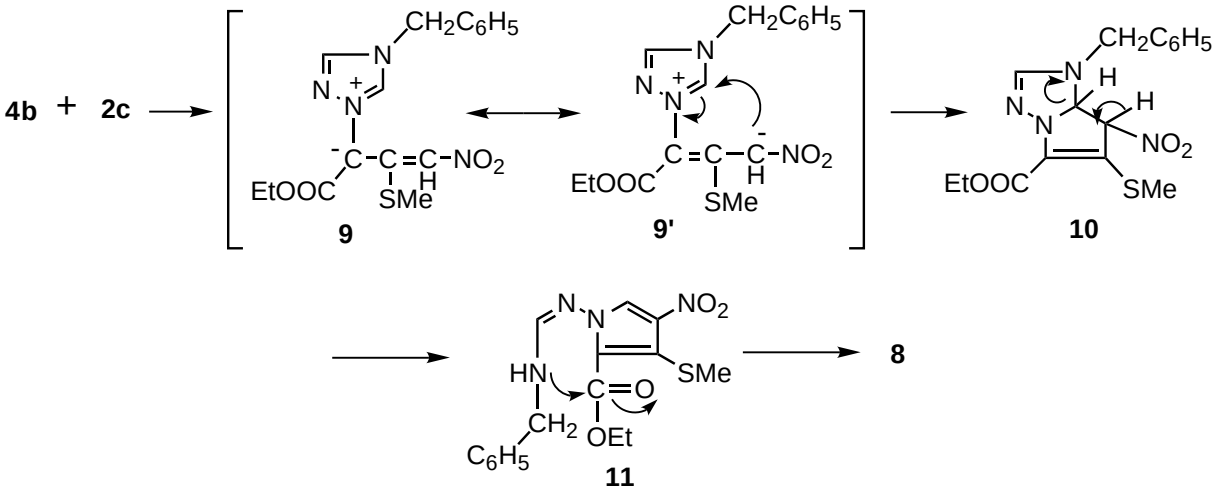
In addition, the reaction of the salts (**4a,b**) with alkenes (**1c, 2b**) in the presence of K_2CO_3 directly gave the back-donated 1,6-cyclization products (**7b, c**). On the other hand, treatment of **4b** with 2,2-bis(methylthio)-1-nitroethylene (**2c**) afforded pyrrolo[2,1-*f*][1,2,4]triazine derivative (**8**) (Scheme 2).

In our previous paper,[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[2b] and Meth-Cohn,[1e] the formation of **8** may be rationalized as outlined in Scheme 4. Thus, 1,5-dipolar cyclization of **9'** gives **11** resulting from the cleavage of **10** and the product (**8**) arises from **11**.



Scheme 3



Scheme 4

In conclusion the triazolium *N*-allylide (**5**) which had two electron-withdrawing groups at the 3-position of the allylide group participated in back-donated 1,6-cyclization to produce the mesomeric betaines (**6**,**7**). The high efficiency of the back-donated 1,6-cyclization, due to the resonance structure (**5b'**), in thermolysis of the *N*-allylide of the resulting mesomeric betaine, [1,2,4]triazolo[2,3-*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. ^{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 (δ). 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 K_2CO_3 (1.21 g, 8 mmol) in $CHCl_3$-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 $CHCl_3$ (4x30 mL) and the combined extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel. From a benzene-$CHCl_3$ (1:1) fraction, compounds (**5a**, **7b,c**) and the oily products (**5b,c**) were obtained. From a benzene-$CHCl_3$ (20:1) fraction, compound (**8**) was obtained.

5a: mp 219-221 ℃ (EtOH-$CHCl_3$) (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). ^{1}H-NMR (DMSO-d_6): 5.61 (2H, s, CH_2Ar), 7.18 (1H, s, CH=), 7.43-7.47 (10H, m, Ar-H), 9.42 (1H, s, C_3-H), 10.42 (1H, s, C_5-H). *Anal.* Calcd for $C_{21}H_{15}N_5O$: C, 71.38; H, 4.28; N, 19.82. Found: C, 71.01; H, 4.39; N, 19.69.

7b: mp 276-278 ℃ (EtOH-$CHCl_3$) (0.34 g, 23 %). IR (KBr) cm^{-1}: 1650 (CO), 1625 (CO). UV (EtOH) λmax (log ε) nm : 232 (3.53), 337 (3.60). ^{1}H-NMR (DMSO-d_6): 6.05 (2H, s, CH_2Ar), 7.38-7.54 (5H, m, Ar-H), 7.62-7.78 (5H, m, Ar-H), 8.15 (1H, s, C_2-H), 9.44 (1H, s, C_5-H). *Anal.* Calcd for $C_{20}H_{14}N_4O_4$: C, 64.17; H, 3.77; N, 14.97. Found: C, 64.13; H, 3.87; N, 14.65.

7c: mp 193-196 ℃ (EtOH-$CHCl_3$) (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). ^{1}H-NMR ($CDCl_3$): 1.41 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 2.58 (3H, s, SCH_3), 4.48 (2H, q, J =7 Hz, $C\underline{H}_2CH_3$), 6.05 (2H, s, CH_2Ar), 7.37-7.53 (5H, m, Ar-H), 8.28 (1H, s, C_5-H). *Anal.* Calcd for $C_{18}H_{16}N_4O_3S$: 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-CH_2Cl_2) (0.56 g, 44 %). IR (KBr) cm^{-1}: 1690 (CO). UV (EtOH) λmax (log ε) nm: 280 (4.36). ^{1}H-NMR ($CDCl_3$): 2.63 (3H, s, SCH_3), 5.05 (2H, s, CH_2Ar), 7.36 (5H, s, Ar-H), 7.61 (1H, s, C_3-H), 8.05 (1H, s, C_6-H). *Anal.* Calcd for $C_{14}H_{12}N_4O_3S$: 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 $CHCl_3$ (4x30 mL) and the combined extracts were washed with water and dried (Na_2SO_4). 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 $CHCl_3$-acetone (10:1) fraction, compounds (**6b, 7a**) were obtained.

6a: mp 267-269 °C (EtOH-$CHCl_3$) (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). ^{1}H-NMR (DMSO-d_6): 5.28 (2H, s, CH_2Ar), 7.28 (1H, s, C_2-H), 7.29 (5H, s, Ar-H) 7.42-7.86 (5H, m, Ar-H), 7.98 (1H, s, C_5-H), 8.06 (1H, s, =NH). *Anal*. Calcd for $C_{21}H_{15}N_5O$: 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-$CHCl_3$) (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). ^{1}H-NMR ($CDCl_3$): 1.44 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 2.54 (3H, s, SCH_3) 4.48 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 5.31 (2H, s, CH_2Ar), 6.84 (1H, s, =NH), 7.24-7.27 (5H, m, Ar-H), 7.34 (1H, s, C_2-H). *Anal.* Calcd for $C_{18}H_{17}N_5O_2S$: 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-$CHCl_3$) (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). ^{1}H-NMR (DMSO-d_6): 1.32-1.35 (6H, m, 2x$CH_2C\underline{H}_3$), 4.36-4.44 (4H, m, 2x$C\underline{H}_2CH_3$), 4.99 (2H, s, CH_2Ar), 7.32-7.42 (5H, m, Ar-H), 7.56 (1H, s, C_2-H), 10.48 (1H, s, C_5-H). *Anal*. Calcd for $C_{19}H_{19}N_3O_5$: C, 61.78; H, 5.18; N, 11.38. Found: C, 61.48; H, 5.24; N, 11.14.

REFERENCES

1. a) V. Boekelheide and N. A. Fedoruk, *J. Am. Chem. Soc.*, 1968, **90**, 3830. b) H. G. O. Becker, D. Nagel, and H. J. Timpe, *J. Prakt. Chem.*, 1973, **315**, 97. c) K. Matsumoto, *J. Syn. Org. Chem. Japan*, 1974, **32**, 731. d) Y. Tamura, Y. Sumida, S. Haruki, and M. Ikeda, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 575. e) O. Meth-Cohn, *Tetrahedron Lett.*, **1975**, 413. f) T. Uchida and K. Matsumoto, *Synthesis*, **1976**, 209. g) A. Kakehi, S. Ito, T. Funahashi, and Y. Ota, *J. Org. Chem.*, 1976, **41**, 1570. h) A.

Kakehi, S. Ito, K. Uchiyama, Y. Konno, and K. Kondo, *ibid.*, 1977, **42**, 443. i) H. J. Timpe, H. G. O. Becker, and R. Radeglia, *J. Prakt. Chem.*, 1977, **319**, 945.

2. a) F. J. Swinbourene, J. H. Hunt, and G. Klinkert, *Adv. Heterocycl. Chem.*, 1978, **23**, 103. b) R. M. Acheson and N. F. Elmore, *ibid.*, 1978, **23**, 263. c) E. C. Taylor and I. J. Turchi, *Chem. Rev.*, 1979, **79**, 181. d) Y. Tamura and M. Ikeda, *Adv. Heterocycl. Chem.*, 1981, **29**, 71.
3. a) Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, K. Takahashi, and S. Ide, *Heterocycles*, 1990, **31**, 977. b) Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, K. Takahashi, S. Ide, K. Furuno, and K. Torisu, *ibid.*, 1991, **32**, 2217. c) Y. Matsuda, M. Yamashita, K. Takahashi, S. Ide, K. Torisu, and K. Furuno, *ibid.*, 1992, **33**, 295. d) Y. Matsuda, M. Yamashita, K. Takahashi, S. Ide, T. Itou, C. Motokawa, and Y. Chiyomaru, *Chem. Pharm. Bull.*, 1994, **42**, 454. e) Y. Matsuda, Y. Chiyomaru, C. Motokawa, and T. Nishiyori, *Heterocycles*, 1995, **41**, 329. f) Y. Matsuda, Y. Chiyomaru, K. Furuno, and T. Nishiyori, *ibid.*, 1995, **41**, 2777. g) Y. Matsuda, K. Katou, T. Nishiyori, T. Uemura, and M. Urakami, *ibid.*, 1997, **45**, 2197.
4. a) Y. Tominaga and Y. Matsuda, *J. Heterocycl. Chem.*, 1985, **22**, 937. b) M. Kolb, *Synthesis*, **1990**, 171.
5. a) Y. Tominaga and Y. Matsuda, *J. Syn. Org. Chem. Japan*, 1985, **43**, 669. b) Y. Matsuda and H. Gotou, *Heterocycles*, 1987, **26**, 2757. c) Y. Matsuda, H. Gotou, M. Yamashita, K. Takahashi, S. Ide, K. Furuno, K. Torisu, T. Itou, and C. Motokawa, *ibid.*, 1992, **34**, 2277.
6. a) E. G. de Bollemount, *Bull. Soc. Chim. Fr.*, 1902, **25**, 20. b) O. Diels, H. Gärtner, and R. Kaack, *Ber.*, 1922, **55**, 3439. c) R. Gompper and W. Töpfl, *Chem. Ber.*, 1962, **95**, 2861. d) M. Prystas and J. Gut, *Coll. Czech. Chem. Commun.*, 1963, **28**, 2501. e) B. S. Thyagarajan and P. V. Gopalakrishnan, *Tetrahedron*, 1964, **20**, 1051.
7. A. Couture, A. Lablache-Combier, P. Grandclaudon, and G. Surpateanu, *Heterocycles*, 1990, **31**, 2111.