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Intermolecular and intramolecular cycloaddition reactions of 1-ethyl-1,2,4-triazinium salts with alkynes

Nataliya N. Mochulskaya, Anatoly A. Andreiko, Valery N. Charushin,* Boris V. Shulgin, Dmitry V. Raikov and Vladimir I. Solomonov

Department of Organic Chemistry, Urals State Technical University, 620002 Ekaterinburg, Russian Federation.
Fax: +7 3432 74 0458; e-mail: charushin@prm.uran.ru

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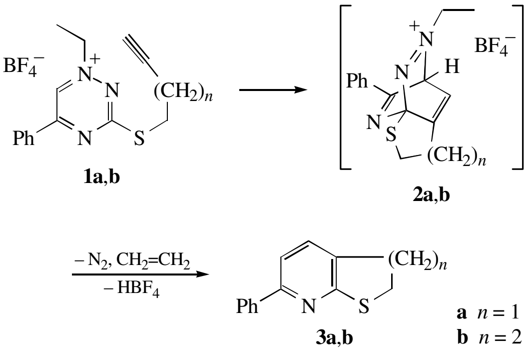
Azomethyne ylides generated from 3-alkylthio substituted 1-alkyl-5-aryl-1,2,4-triazinium salts 4a–c on treatment with triethylamine undergo 1,3-dipolar cycloaddition with dimethyl acetylenedicarboxylate to give pyrrolo[2,1-*f*][1,2,4]triazines, while 1-ethyl-5-phenyl-1,2,4-triazinium salts 1a,b bearing the C≡C bond in the side-chain 3-alkynylthio substituent react with acetylenes to undergo either intermolecular 1,3-dipolar cycloaddition or intramolecular inverse electron demand Diels–Alder reactions.

Inverse electron demand Diels–Alder reactions of π-deficient aza-aromatics is a powerful synthetic methodology.[1] *N*-Alkyl-1,2,4-triazinium salts are appropriate substrates to be used in these (4 + 2) cycloaddition reactions. Indeed, we found that 1-ethyl-5-phenyl-1,2,4-triazinium salts bearing acetylenic 3-butynylthio (compound **1a**) or 4-pentynylthio (compound **1b**) substituents at C-3 can undergo intramolecular (4 + 2) cycloaddition reaction under very mild conditions, thus being transformed into thieno[2,3-*b*]- **3a** or thiopyrano[2,3-*b*]pyridines **3b** (Scheme 1).[2]



Scheme 1

On the other hand, *N*-alkylpyridinium and other azinium salts, especially those bearing the CH_2W fragment at the quaternary nitrogen (W is an electron-withdrawing group) are precursors of N-heterocyclic ylides, which can undergo 1,3-dipolar (3 + 2) cycloaddition reactions with both alkenes and acetylenes. The feature of *N*-alkyl-1,2,4-triazinium salts is that electron-withdrawing groups W in the *N*-alkyl fragment are not necessary to generate ylides, as found by the dimerisation into 4*a*,4*b*,9,10-tetrahydro-1,3,6,8,8*a*,10*a*-hexaazaphenanthrenes.[3,4] In continuation of our studies on the behaviour of 1-alkyl-1,2,4-triazinium salts,[5–7] we report that deprotonation of 1-ethyl-3-alkylthio-5-aryl-1,2,4-triazinium salts **4a**–**c** with triethylamine (TEA) results in azomethine ylides **5a**–**c** (non-stabilised species), which react *in situ* with dimethyl acetylenedicarboxylate (DMAD) to form pyrrolo[2,1-*f*][1,2,4]triazines **6a**–**c** in good yields (Scheme 2).[†] Attempts to use other alkynes, such as phenylacetylene, di(4-nitrophenyl)acetylene and di(pyridin-2-yl)acetylene, as dipolarophiles in the reaction with **4c** were unsuccessful.

When irradiated with UV light or pulsed electron beams, pyrrolo[2,1-*f*][1,2,4]triazines **6a**–**c** were found to exhibit intense luminescence giving emission in the region 450–650 nm with maxima at 500 nm and the light output comparable with that of stilbene.[‡]

It was interesting to examine the chemical behaviour of 3-alkynylthio-1,2,4-triazinium salts **1a**,**b** on treatment with DMAD, *i.e.*, when both types of cycloaddition reactions [(4 + 2) and (3 + 2)] can compete with each other. We found that, in case of a 4-pentynylthio substituent (*n* = 2), the intermolecular 1,3-dipolar cycloaddition reaction of **1b** with DMAD leading to pyrrolotriazine **7** (47% yield) proceeds much faster than the intramolecular Diels–Alder reaction, while 3-butynylthio substituted 1-ethyl-1,2,4-triazinium salt **1a** (*n* = 1) undergoes predominantly the intramolecular ring transformation into thieno[2,3-*b*]pyridine **3a** in 44% yield (Scheme 3). Both reactions were carried out under identical conditions with triethylamine in absolute ethanol at room temperature. Although in both reactions we cannot exclude the formation of minor quantities of alternative products, moderate yields of **3a** and **7** can be

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[†] All new compounds gave expected ^1H NMR spectra, mass spectra and satisfactory elemental analyses.

3a: Dimethyl acetylenedicarboxylate (0.08 g, 0.56 mmol) was added to a suspension of 1-ethyl-3-(3-butynylthio)-5-phenyl-1,2,4-triazinium tetrafluoroborate **1a** (0.18 g, 0.50 mmol) in 4 ml of absolute ethanol, and then triethylamine (0.06 g, 0.55 mmol) was added dropwise with stirring. The reaction mixture was stirred at room temperature for 36 h. After filtration, the solvent was removed *in vacuo*. Flash dry-column chromatography on silica gel (hexane–acetone, 4:1) gave 6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (0.047 g, 44% yield) as white crystals, mp 82–83 °C (lit.,[2] mp 83 °C).

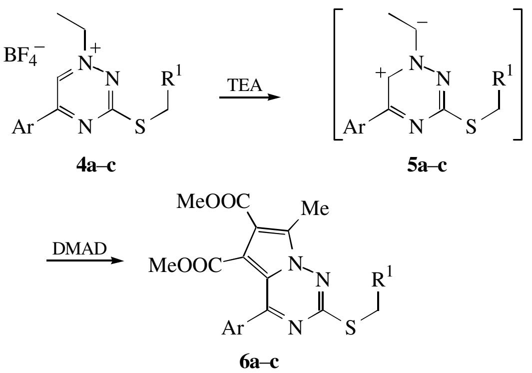
6a: Dimethyl acetylenedicarboxylate (0.21 g, 1.46 mmol) was added to a suspension of 5-(4-bromophenyl)-1-ethyl-3-propylthio-1,2,4-triazinium tetrafluoroborate (0.52 g, 1.22 mmol) in 4 ml of absolute ethanol, and then triethylamine (0.14 g, 1.34 mmol) was added dropwise with stirring. The reaction mixture was stirred at room temperature for 72 h to precipitate a yellow crystalline product, which was collected by filtration and recrystallised from ethanol to yield 0.23 g (40%) of 4-(4-bromophenyl)-5,6-dimethoxycarbonyl-7-methyl-2-propylthiopyrrolo[2,1-*f*]-1,2,4-triazine as a yellow product, mp 126–128 °C. ^1H NMR ($CDCl_3$) δ: 1.09 (t, 3H, SCH_2CH_2*Me*), 1.85 (m, 2H, SCH_2CH_2Me), 2.79 (s, 3H, Me), 3.20 (t, 2H, SCH_2CH_2Me), 3.47 (s, 3H, COOMe), 3.88 (s, 3H, COOMe), 7.54 (d, 2H, BrC_6H_4), 7.62 (d, 2H, BrC_6H_4). MS, *m*/*z* (%): 479 (58, $[M + 1]^+$), 478 (16, M^+), 477 (55), 464 (27), 462 (26), 446 (48), 444 (35), 438 (20), 437 (100), 436 (23), 435 (93).

Compounds **6b** and **6c** were obtained analogously to **6a**.

6b: yield 65%, yellow crystals, mp 108–110 °C. ^1H NMR ($CDCl_3$) δ: 1.48 (t, 3H, SCH_2*Me*), 2.80 (s, 3H, Me), 3.21 (q, 2H, SCH_2Me), 3.39 (s, 3H, COOMe), 3.87 (s, 3H, COOMe), 7.4–7.6 (m, 3H, Ph), 7.6–7.7 (m, 2H, Ph). MS, *m*/*z* (%): 386 (23, $[M + 1]^+$), 385 (100, M^+), 357 (21), 352 (41), 294 (32), 262 (20).

6c: yield 40%, yellow crystals, mp 165–167 °C. ^1H NMR ($[^2H_6]$DMSO) δ: 2.61 (s, 3H, SMe), 2.76 (s, 3H, Me), 3.35 (s, 3H, COOMe), 3.82 (s, 3H, COOMe), 7.4–7.6 (m, 5H, Ph). MS, *m*/*z* (%): 372 (34, $[M + 1]^+$), 371 (100, M^+), 340 (22), 339 (35), 280 (35), 252 (22), 239 (21).

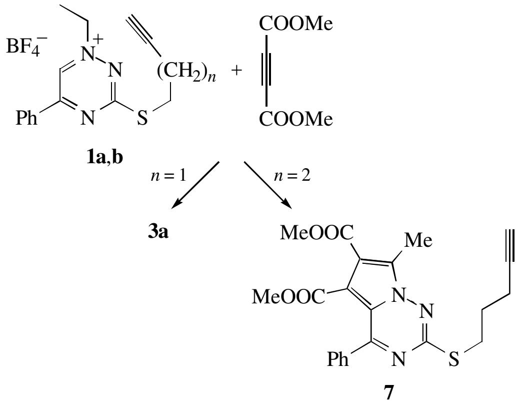
7: Dimethyl acetylenedicarboxylate (0.18 g, 1.26 mmol) was added to a suspension of 1-ethyl-3-(4-pentenylthio)-5-phenyl-1,2,4-triazinium tetrafluoroborate **1b** (0.39 g, 1.05 mmol) in 5 ml of absolute ethanol, and then triethylamine (0.12 g, 1.16 mmol) was added dropwise with stirring. The reaction mixture was allowed to stand at room temperarure for 24 h. The solvent was removed *in vacuo*. Flash dry-column chromatography on silica gel (hexane–ethyl acetate, 4:1) gave 5,6-dimethoxycarbonyl-7-methyl-2-(4-pentenylthio)-4-phenylpyrrolo[2,1-*f*][1,2,4]triazine (0.208 g, 47%): yellow solid, mp 80–82 °C. ^1H NMR ($CDCl_3$) δ: 1.99 (t, 1H, C≡CH, *J* 2.8 Hz), 2.07 (m, 2H, SCH_2CH_2, *J* 7.0 Hz), 2.42 (td, 2H, $CH_2C{\equiv}CH$, *J* 2.8 Hz, *J* 7.0 Hz), 2.80 (s, 3H, Me), 3.32 (t, 2H, SCH_2, *J* 7.0 Hz), 3.39 (s, 3H, COOMe), 3.87 (s, 3H, COOMe), 7.4–7.6 (m, 3H, Ph), 7.6–7.7 (m, 2H, Ph). MS, *m*/*z* (%): 423 (24, M^+), 396 (24), 395 (100), 384 (78), 371 (25), 364 (38), 357 (41), 267 (23).



a R^1 = Et, Ar = 4-BrC$_6$H$_4$
b R^1 = Me, Ar = Ph
c R^1 = H, Ar = Ph

Scheme 2

explained by side reactions of starting 1,2,4-triazinium salts **1a**,**b**, such as dequaternisation[5] and dimerisation,[3,4] as experimentally found by TLC. Thus, the conversion of 1-ethyl-3-alkynylthio-1,2,4-trazinium salts **1a**,**b** into thieno[2,3-*b*]-pyridine **3a** or pyrrolo[2,1-*f*][1,2,4]triazine **7** depends on the length of the side chain bearing the acetylenic fragment. The found phenomenon is consistent with well-known features of the intramolecular Diels–Alder reactions of alkynyl-substituted pyrazines, pyrimidines and 1,2,4-triazines.[2,8–11] In these ring transformations, the formation of bridged intermediates like **2** (Scheme 1) with an annelated five-membered ring is more favourable as compared to cycloadducts **2** condensed with a six-membered ring.[2,8–11] As a consequence, intramolecular Diels–Alder reactions leading to azines condensed with five-membered rings proceed much faster and require milder conditions.[2,8–11]



Scheme 3

The above results demonstrate a new interesting property of 1,2,4-triazinium salts to undergo two modes of cycloaddition reactions with alkynes. Evidence for the structures of **3a**, **6a–c** and **7** is provided by ^{1}H NMR spectroscopy and mass spectrometry.[†]

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[‡] For measuring the photoluminiscence spectra, compounds **6a–c** and **7** were irradiated with monochromatic UV light at a wavelength of 310 nm followed by measuring emission with the second monochromator equipped with a photoelectric multiplier (1050 V) and an automatic potentiometer. The radioluminiscence and scintillation characteristics of compounds **6a–c** and **7** were obtained using special nanosecond techniques. The test materials were excited by irradiation with pulsed electron beams at a high current density (pulse duration of 2 ns, electron energy of 100–200 keV, current density of 100–700 A cm^{-2}) using a Radan electron accelerator. The spectra in the range 300–800 nm were measured by a charge-connecting detector (CCD) equipped with a computer.