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Regioselective Synthesis of Substituted Triazolium Salts *via* 1,3-Dipolar Cycloaddition Reactions

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Summary. The regioselectivity of 1,3-dipolar cycloaddition reactions of 1-aza-2-azoniaallene salts with α,β-unsaturated nitriles such as acrylonitrile or cyclohexylidene acetonitrile afforded only 1,2,4-triazolium salts *via* addition to the nitrile group, while the other expected pyrazolium salts were not observed. Moreover, 1-aza-2-azonia-allene salts reacted with other competitive systems such as α-iminonitrile derivatives yielding only triazolium salts *via* addition to the nitrile and not to the imino group. Treatment of cumulene with 3-pyridylnitrile afforded the pyridinium salt. However, 2,3-dimethyl-5-(2,6-dimethoxyphenyl)-[1,2,4]triazole could be prepared from cumulene and 2,6-dimethoxybenzonitrile. Some reactions of nitriles with 1-aza-2-azonia-allene salts prepared from 1,2,3-indantrione and 9-acetylphenanthrene are discussed.

Keywords. Cycloadditions; Olefins; Nitriles; Triazolium salt; Regioselectivity.

Introduction

Recently [1–6] it has been reported that 1-aza-2-azoniaallene salts underwent cycloaddition reactions to nitriles, acetylenes, olefins, isocyanates, and carbodiimides furnishing five-membered hetero-cycles. In many cases they rearranged spontaneously to other salts. While the cycloadditions with olefins and acetylenes seem to be concerted, the reactions of 1-aza-2-azoniaallene with nitriles, and probably also with isocyanates and carbodiimides, were likely to follow a two-step mechanism with nitrilium and acylium intermediates. It seemed of interest to study the applicability of the cycloaddition protocol for heterocumulenes **3** with nucleophilic compounds containing both active double bond and nitrile (α,β-unsaturated nitrile). The objective of such a study was to elucidate the site selectivity of this procedure with respect to a synthetic method to obtain substituted triazolium or pyrazolium salts. In addition, it was interesting to study the effect of steric hindrance.

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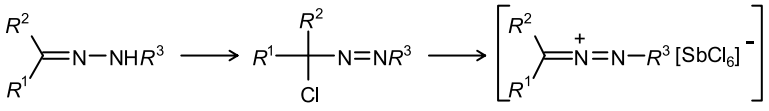
Results and Discussion

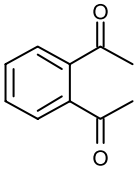
Hydrazones **1** of alkyl ketones were oxidized with *tert*-butyl hypochlorite to give the geminal chloroazo compounds **2**. They were treated with the *Lewis* acid $SbCl_5$ to afford the 1-aza-2-azoniaallene salts **3** as reactive intermediates [6]. The present study was undertaken to investigate the regioselectivity in 1,3-dipolar cycloaddition reactions of the cumulene **3** with α,β-unsaturated nitriles. It was found that reaction of **3a** with acrylonitrile or cyclohexylidene acetonitrile afforded the 1,2,4-triazolium salts **5a** and **5b** only, which rearranged spontaneously to the salts **6a** and **6b**, while the other expected products **7a** and **7b** could not be observed. This means that acrylonitrile did not react as an olefin, but exclusively as a nitrile to produce the triazolium salts **6a** and **6b** (Scheme 2). This was confirmed by elemental analysis and spectroscopic data. IR spectra showed no band for a cyano group and in the ^1H NMR spectrum olefinic protons appeared at $\delta = 6.21$ and 6.67 ppm. Note the complete regioselectivity of the cycloaddition of the α,β-unsaturated nitrile (Scheme 2).

It seemed of interest to study the applicability of the cycloaddition protocol for **3b** with another competitive system like α-iminonitrile compounds **8a** and **8b** which contain both C=N and C≡N in a conjugated system. It was found that the nitrile group of **8a** and **8b** reacted extremely fast with the cation **3b** to produce the triazolium salts **10a** and **10b** and no reactions were observed with the nucleophilic imino group. The reaction intermediate **3b** prefers the cycloaddition to the nitrile by a two step mechanism (Scheme 3).

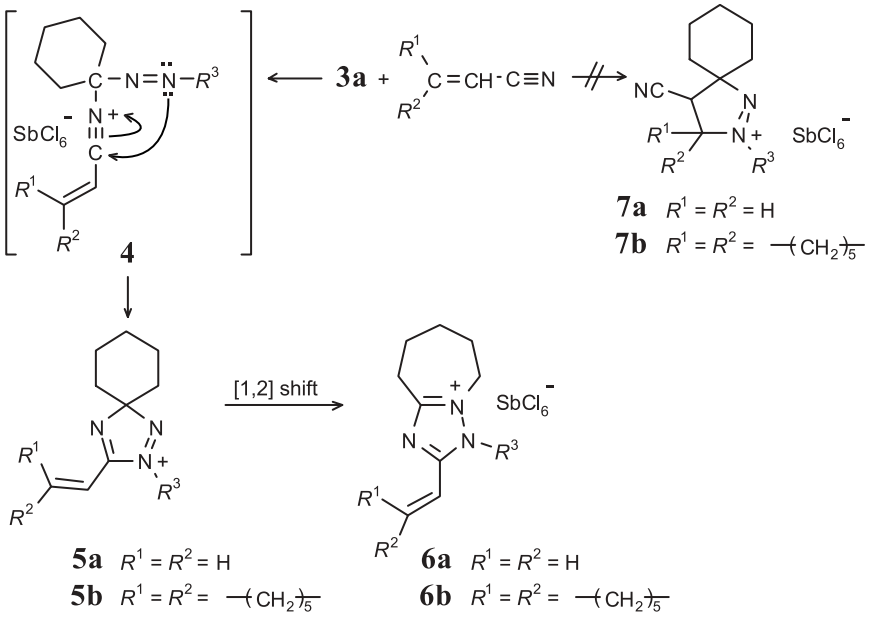
On the other hand, the reaction of the cumulene **3c** with 3-cyanopyridine in presence of $SbCl_5$ afforded **13**. The expected triazolium salt **14** did not form in



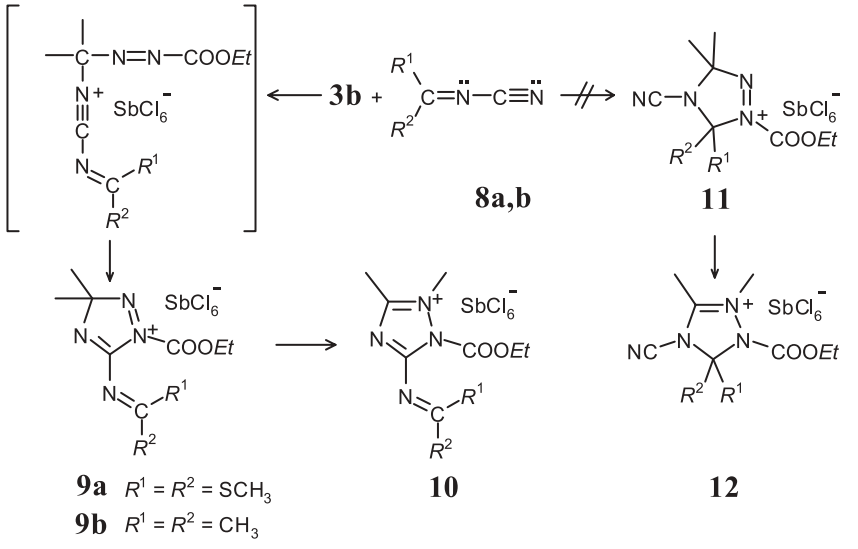
1 **2** **3**

	R^1	R^2	R^3
1a-3a	—(CH$_2$)$_5$—	—(CH$_2$)$_5$—	2,4,6-trichlorophenyl
1b-3b	CH_3	CH_3	$COOC_2H_5$
1c-3c	CH_3	CH_3	2,4,6-trichlorophenyl
1d-3d	CH_3	3-phenanthrenyl	2,4,6-trichlorophenyl
1e-3e			2,4,6-trichlorophenyl

Scheme 1

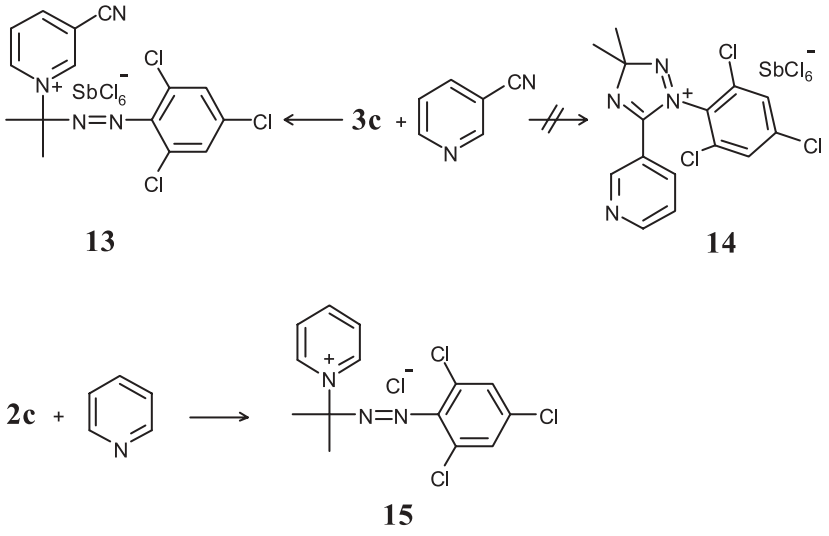


Scheme 2



Scheme 3

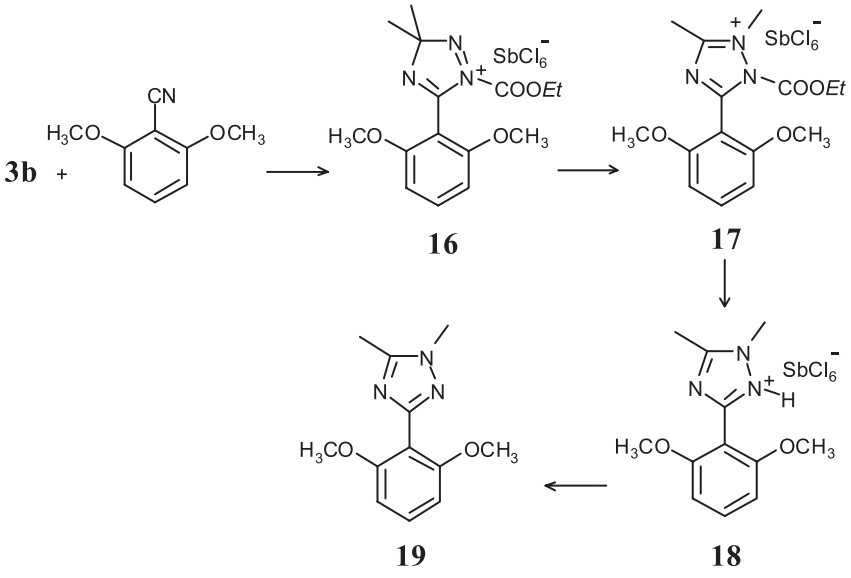
contrast to the reaction of cumulene **3c** with aromatic nitriles [7]. The structure of salt **13** was confirmed by elemental analysis and spectroscopic data. IR spectra showed the band for the cyano group at 2218 cm^{-1}. To confirm the site selectivity of the C=N in the pyridine ring and the nitrile attached to the pyridine ring, we treated the chloroalkylazo compound **2c** with pyridine in presence of CH_2Cl_2 at −10°C. This afforded at once *N*-[1-methyl-1-[(2,4,6-trichlorophenyl)azo]ethyl]-pyridinium chloride (**15**) in high yield. All of these products **13** and **15** are stable and not changed under reflux condition in acetonitrile.



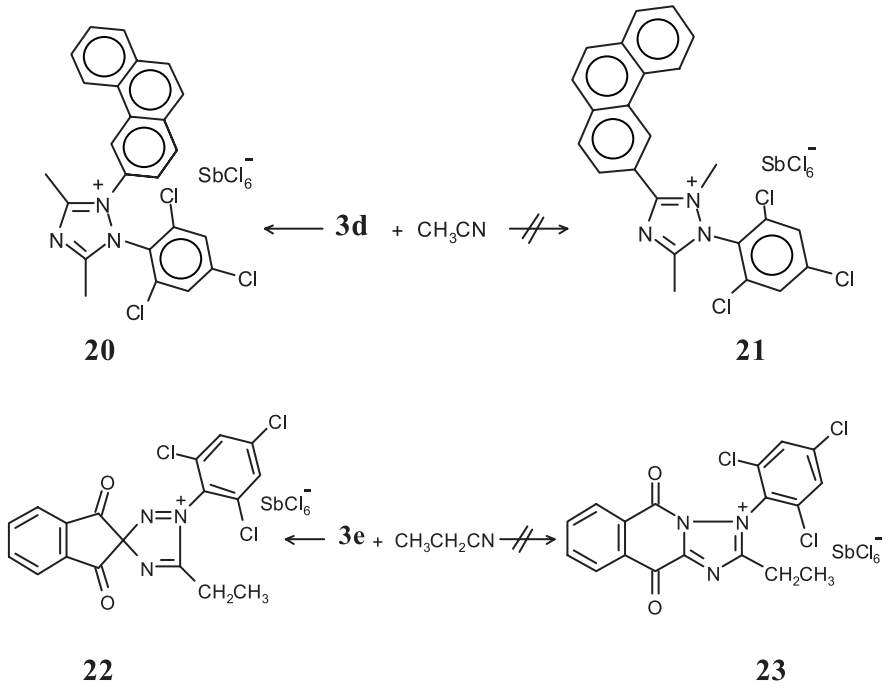
Scheme 4

When **3b** was treated with 2,6-dimethoxybenzonitrile in the presence of $SbCl_5$ at $-60^{\circ}C$, it afforded the expected triazolium salt **18** in high yield. This means, that there is no significant steric effect observed from the substituents surrounding the nitrile during the cycloaddition reactions. Treatment of **18** with aqueous sodium carbonate yielded 5-(2,6-dimethoxyphenyl)-2,3-dimethyl-[1,2,4]-triazole (**19**) as shown in Scheme 5.

Finally, treatment of **3d** with acetonitrile yielded **20** *via* the corresponding intermediate, which underwent a 1,2-shift of the aryl substituent R^2. The other



Scheme 5



Scheme 6

expected compound **21** obtained from methyl migration did not form. Furthermore, treatment of cumulene **3e** with propionnitrile afforded only the triazolium salt **22** without migration of the acyl group from carbon to nitrogen. Again, the expected triazolium salt **23** did not form (Scheme 6). The triazolium derivatives **22** and **23** could be easily distinguished by their ^{13}C NMR: the spiro carbon appears at $\delta = 91.81$ for **22**. The structures of all novel compounds were confirmed by their elemental and spectroscopic data.

Experimental

Melting points were measured on a Kofler hot stage microscope (Reichert, Vienna) and are uncorrected. ^{1}HNMR and ^{13}C NMR spectra were recorded on a Bruker DPX 200 spectrometer at 200 MHz (^{1}H) and 50 MHz (^{13}C); chemical shifts (δ) are given relative to internal *TMS* at 295 K. IR spectra were obtained on a Broad FT-IR-45 instrument. All experiments were carried out with exclusion of moisture. For all new compounds satisfactory elemental analyses were obtained.

*Preparation of Hydrazones **1***

A mixture of 100 mmol of ketone (cyclohexanone, acetone, acetylanthracene, or 1,2,3-indantrione) and 100 mmol of hydrazine in 70 cm^3 of methanol + 1 cm^3 of acetic acid was heated under reflux for 1 h. Evaporation of the solvent and crystallization of the residue afforded the pure hydrazone. Cyclohexanone (2,4,6-trichlorophenyl)hydrazone (**1a**) and acetone (2,4,6-trichlorophenyl)hydrazone (**1c**) were reported in Ref. [7]. Ethyl 3-isopropylidenecarbazate (**1b**) was obtained according to

Ref. [2]. 3-Acetylphenanthrene(2,4,6-trichlororphenyl)-hydrazone (**1d**) was obtained as reported in Ref. [3].

1,2,3-Indandione-2-(2,4,6-trichlorophenyl)hydrazone (**1e**, $C_{15}H_7Cl_3N_2O_2$)

Prepared from 1.60 g of 1,2,3-indantrione (10 mmol), 2.10 g of 2,4,6-trichlorophenylhydrazine (10 mmol); the red crystals were recrystallized from methanol to yield 3.07 g (87%); mp 222°C; IR (KBr): $\bar{\nu} = 3380, 3059, 1698, 1612, 1554\,cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 7.40$ (s, $2H_{trichlorophenyl}$), 7.82 (m, $4H_{ar}$), 13.09 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 123.25, 123.5, 128.91, 128.09, 129.32, 132.19, 133.19, 133.97, 135.35, 135.79, 138.91, 140.92, 185.38, 188.29$ ppm.

*Preparation of α-Chloroalkylazo Compounds **2***

The following compounds were synthesized according to literature: 1-[(1-chloro-1-methylethyl)azo]-2,4,6-trichlorobenzene (**2a**) and 1-[(1-chloro-cyclohexyl)azo]-2,4,6-trichlorobenzene (**2c**) [7], ethyl (1-chloro-1-methyl-ethyl)azocarboxylate (**2b**) [2], 1-[(1-chloro-1-methylphenanthrenyl)azo]-2,4,6-trichlorobenzene (**2d**) [3].

2-Chloro-2-(2,4,6-trichlorophenyl)azo-1,3-indandione (**2e**, $C_{15}H_6Cl_4N_2O_2$)

Prepared from 3.50 g of **1e** (10 mmol) [8]; yield: 3.28 g (85%) as red crystals; mp 260–268°C; ^1H NMR ($CDCl_3$): $\delta = 7.42$–8.00 (m, $6H_{ar}$) ppm.

Reaction of the α-Chloroalkylazo Compounds with Nitriles and Formation of [1,2,4]-Triazolium hexachloroantimonates

A solution of 2.99 g of $SbCl_5$ (10 mmol) in 10 cm^3 of CH_2Cl_2 was added dropwise to a cold (−60°C) solution of 10 mmol of the α-chloroalkylazo compound and 12 mmol of nitrile in 25 cm^3 of CH_2Cl_2. The mixture was stirred at −60°C for 2 h, then at 0°C for 1 h, and finally at room temperature for 15 min. The solvent was evaporated under reduced pressure and the remaining salt was purified by crystallization.

5,6,7,8-Tetrahydro-1-(2,4,6-trichlorophenyl)-2-vinyl-1H-[1,2,4]-triazolo[1,5-a]azepinium hexachloroantimonate (**6a**, $C_{15}H_{15}Cl_9N_3Sb$)

Prepared from 3.22 g of **2b** (10 mmol), 0.65 g of acrylonitrile (12 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue crystallized at −20°C from acetonitrile/ether to yield 5.09 g (75%) of white fine crystals; mp 180–181°C; IR (KBr): $\bar{\nu} = 3079, 2941, 1653, 1630, 1565, 1525, 1477, 1457\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 1.79$ (m, 6H), 3.32 (m, 2H), 4.29 (m, 2H), 6.21 (d, $J = 11.5$ Hz, $1H_{vinyl}$), 6.67 (q, $J = 16.8$ Hz, $2H_{vinyl}$) 8.31 (s, $2H_{trichlorophenyl}$) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.57, 25.56, 27.49, 28.29, 48.75$ (cyclohexylidene), 118.49, 122.43, 130.62, 134.31, 135.66, 140.72 (aryl and vinyl carbon), 155.87, 165.22 (2C = N for triazole ring) ppm.

2-(Cyclohexylidenemethyl)-5,6,7,8-tetrahydro-1-(2,4,6-trichlorophenyl)-1H-[1,2,4]-triazolo[1,5-a]azepinium hexachloroantimonate (**6b**, $C_{20}H_{23}Cl_9N_3Sb$)

Prepared from 3.22 g of **2a** (10 mmol), 1.44 g of cyclohexylideneacetonitrile (12 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was crystallized at −20°C from acetonitrile/ether to yield 3.95 g (53%) of fine crystals; mp 210°C; IR (KBr): $\bar{\nu} = 3083, 2940, 1652, 1631, 1570, 1525, 1479, 1457\,cm^{-1}$; ^1H

NMR (*DMSO*-d_6): $\delta = 1.27$–2.63 (m, 16H), 3.33 (m, 2H), 4.30 (m, 2H), 5.71 (m, $1H_{olefin}$), 8.30 (s, $2H_{trichlorophenyl}$) ppm.

5-(N-Dimethyldithioiminocarbonate)-1-ethoxycarbonyl-2,3-dimethyl-1H-[1,2,4]-triazolium hexachloroantimonate (**10a**, $C_9H_{17}Cl_6N_4O_2S_2Sb$)

Prepared from 1.78 g of **2b** (10 mmol), 1.46 g of $(H_3CS)_2C{=}NCN$ (10 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was crystallized from acetonitrile to yield 3.67 g (60%) of yellow fine crystals; mp 175°C; IR (KBr): $\bar{\nu} = 3082$, 2937, 1710, 1643, 1530, 1457 cm^{-1}. ^1H NMR (CD_3CN): $\delta = 1.42$ (t, $J = 7.2$ Hz, CH_3), 2.57 (s, CH_3), 2.71 (s, $2SCH_3$), 4.02 (s, CH_3), 4.55 (q, $J =$ 7.2Hz, CH_2) ppm.

1-Ethyoxycarbonyl-2,3-dimethyl-5-(2-propyleneimino)-1H-[1,2,4]-triazolium hexachloroantimonate (**10b**, $C_9H_{17}N_4O_2Sb$)

Prepared from 1.78 g of **2b** (10 mmol), 0.82 g of $(H_3C)_2C{=}NCN$ (10 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was crystallized from acetonitrile to yield 2.52 g (46%) of yellow fine crystals; mp 161°C (dec); IR (KBr): $\bar{\nu} = 3079$, 2940, 1716, 1645, 1533, 1456 cm^{-1}; ^1H-NMR (CD_3CN): $\delta = 1.40$ (t, $J = 7.2$ Hz, CH_3), 2.30 (s, CH_3), 2.44 (s, CH_3), 2.57 (s, CH_3), 4.00 (s, CH_3), 4.53 (q, $J = 7.2$ Hz, CH_2) ppm.

3-Cyano-1-[1-methyl-1-[(2,4,6-trichlorophenyl)azo]ethyl]pyridinium hexachloroantimonate (**13**, $C_{15}H_{12}Cl_9N_4Sb$)

Prepared from 2.86 g of **2c** (10 mmol), 1.04 g of 3-pyridylcarbonitrile (10 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the yellow solid residue was a mixture of **17** and 3-cyanopyridinium pentachloroantimonate salt. After boiling with $CHCl_3$, pure **13** separated after cooling the filtrate. Yield of fine yellow crystals was 2.41 g (35%); mp 190°C: IR (KBr): $\bar{\nu} = 3079$, 2218, 1625, 1558, 1472, 1378 cm^{-1}. ^1H NMR (*THF*-d_8): $\delta = 2.71$ (s, CH_3), 2.81 (s, CH_3), 7.47(s, $1H_{py}$), 7.75 (s, $2H_{ar}$), 8.61 (m, $2H_{py}$), 9.23 (d, $J = 8.2$ Hz, $1H_{py}$) ppm.

1-[1-Methyl-1-[(2,4,6-trichlorophenyl)azo]ethyl]pyridinium chloride (**15**, $C_{14}H_{13}Cl_4N_3$)

Prepared from 2.86 g of **2c** (10 mmol), and 0.79 g of pyridine (10 mmol); the yellow solid formed was separated by filtration and recrystallized from CH_2Cl_2 to yield 3.10 g (85%) of yellow crystals; mp 138°C; IR (KBr): $\bar{\nu} = 3082$, 1612 cm^{-1}; ^1H NMR (CD_3CN): $\delta = 2.18$ (s, CH_3), 2.32 (s, CH_3), 7.66 (s, $2H_{ar}$), 8.23 (t, $J = 7.0$ Hz, $2H_{py}$), 8.65 (t, $J = 7.0$ Hz, $1H_{py}$), 9.29 (d, $J = 6.6$ Hz, $2H_{py}$) ppm.

3-(2,6-Dimethoxyphenyl)-1,5-dimethyl-1H-[1,2,4]-triazolium hexachloroantimonate (**18**, $C_{12}H_{16}Cl_6N_3O_2Sb$)

Prepared from 1.78 g of **2b** (10 mmol), 1.47 g of dimethoxybenzonitrile (10 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was a mixture of **17** and **18**, which yielded after crystallization at −15°C from $CHCl_3$, 3.00 g (53%) of yellow crystals **18**; mp 220–222°C; IR (KBr): $\bar{\nu} = 3261$, 3072, 2928, 1627, 1608, 1554, 1484, 1378 cm^{-1}; ^1H NMR (CD_3CN): $\delta = 2.71$ (s, CH_3), 3.89 (s, $2OCH_3$), 3.97 (s, NCH_3), 6.82 (d, $J = 8.5$ Hz, $2H_{ar}$), 7.58 (t, $J = 8.5$ Hz, H_{ar}), 12.50 (br, NH) ppm; ^1H NMR ($CDCl_3$): $\delta = 3.11$ (s, CH_3, 4.00 (s, $2OCH_3$), 4.14 (s, NCH_3), 6.71 (d, $J = 8.5$ Hz, $2H_{ar}$), 7.52 (t, $J = 8.5$ Hz, H_{ar}) ppm; ^{13}C NMR (CD_3CN): $\delta = 11.02$ (CH_3), 38.19 (NCH_3), 57.42 ($2OCH_3$), 105.85, 127.50, 135.59, 147.20 (C_{ar}), 152.2, 160.35 (2C = N for triazole ring) ppm.

3-(2,6-Dimethoxyphenyl)-1,5-dimethyl-1H-[1,2,4]-triazole (**19**, $C_{12}H_{15}N_3O_2$)

A solution of 4.0 g of Na_2CO_3 in 15 cm^3 of H_2O was added dropwise at room temperature to a solution of 10 mmol of triazolium salt **15** in 15 cm^3 of $CHCl_3$. The mixture was stirred for 30 min and then extracted with 2×20 cm^3 of $CHCl_3$. The combined organic extracts were dried over anhydrous Na_2SO_4 and the solvent was evaporated. The residue was purified by column chromatography with $CHCl_3$:CH_3OH (20:1) as the eluent. The product was crystallized from aqueous ethanol to give 1.50 g (64%) of yellowish white crystals; mp 110°C; IR (KBr): $\bar{\nu} = 3075$, 1628, 1598, 1554, 1491, 1378 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): $\delta = 2.42$ (s, CH_3), 3.68 (s, $2OCH_3$), 3.78 (s, NCH_3), 6.51 (d, $J = 8.5$ Hz, $2H_{ar}$), 7.20 (t, $J = 8.5$ Hz, H_{ar}) ppm.

3,5-Dimethyl-2-(3-phenanthrenyl)-1-(2,4,6-trichlorophenyl)-1H-[1,2,4]-triazolium hexachloroantimonate (**20**, $C_{24}H_{17}Cl_9N_3Sb$)

Prepared from 4.36 g of **2d** (10 mmol), 1.23 g of acetonitrile (30 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was crystallized from acetonitrile to yield 5.20 g (66%) of yellowish crystals; mp 192°C; IR (KBr): $\bar{\nu} = 3077$, 1620, 1565, 1553, 1478, 1373 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.02$ (s, CH_3), 2.64 (s, CH_3), 7.13 (d, $J = 9.0$ Hz, $1H_{ar}$), 7.60 (m, $6H_{ar}$), 8.07 (s, $2H_{trichlorophenyl}$), 8.64 (d, $J = 9.0$ Hz, $1H_{ar}$), 8.87 (d, $J = 8.0$ Hz, $1H_{ar}$) ppm.

5′-Ethyl-1,3-dioxo-1′-(2,4,6-trichorophenyl)spiro[indan-2,3′-3′H-[1,2,4]-triazolium hexachloroantimonate] (**22**, $C_{18}H_{11}Cl_9O_2Sb$)

Prepared from 3.88 g of **2e** (10 mmol), 0.73 g of CH_3CH_2CN (12 mmol), and 2.99 g of $SbCl_5$ (10 mmol); the residue was crystallized at −20°C from acetonitrile/ether to yield red crystals (5.35 g, 72%); mp 241°C; IR (KBr): $\bar{\nu} = 3186$, 3077, 1722, 1678, 1630, 1587, 1536, 1471, 1437 cm^{-1}; ^{1}H NMR (CD_3CN): $\delta = 1.16$ (t, $J = 7.4$ Hz, CH_3), 2.62 (q, $J = 7.4$ Hz, CH_2), 7.77–8.02 (m, $6H_{ar}$) ppm; ^{13}C NMR (CD_3CN): $\delta = 8.43$ (CH_3), 23.34 (CH_2), 91.81 (spiro-C), 109.11, 124.50, 126.57, 130.36, 133.50, 134.24, 139.70, 148.00 (aryl and C = N), 182.36, 189.68 (2C = O) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 8.18$ (CH_3), 30.10 (CH_2), 87.66 (spiro-C), 122.57, 122.93, 123.09, 124.48, 129.19, 130.15, 131.03, 135.24, 135.83, 136.04, 145.50 (aryl and C = N), 169.25, 173.50 (2C = O) ppm.

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