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Synthesis of condensed sulfur- and nitrogen-containing heterocycles *via* polar cycloaddition of hetarene sulfenyl chlorides to a C–C multiple bond

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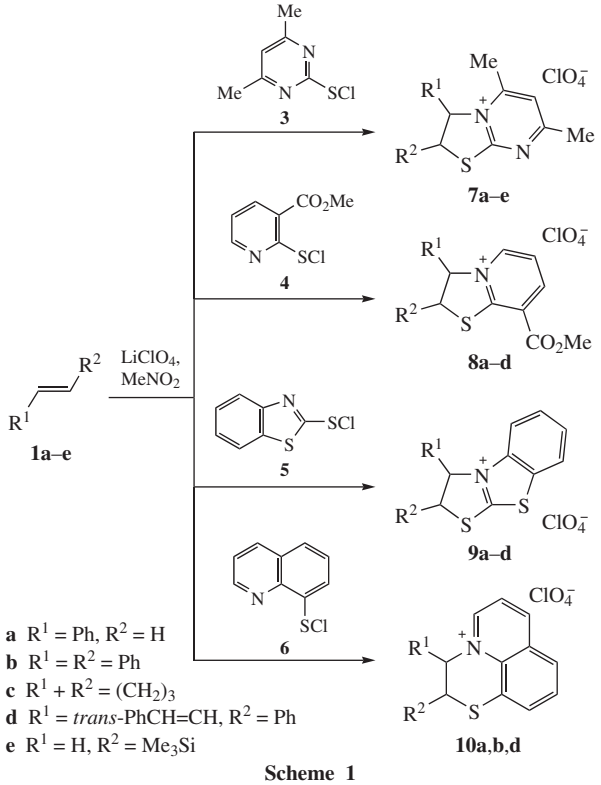
The reactions of HetSCl, where Het = 4,6-dimethyl-2-pyrimidyl, 3-methoxycarbonyl-2-pyridyl, 1,3-benzothiazol-2-yl and 8-quinolyl, with a carbon–carbon multiple bond in the $LiClO_4$–$MeNO_2$ system lead to the formation of products of polar cycloaddition of sulfur-containing electrophile with ring closure by the nitrogen atom of the HetS fragment.

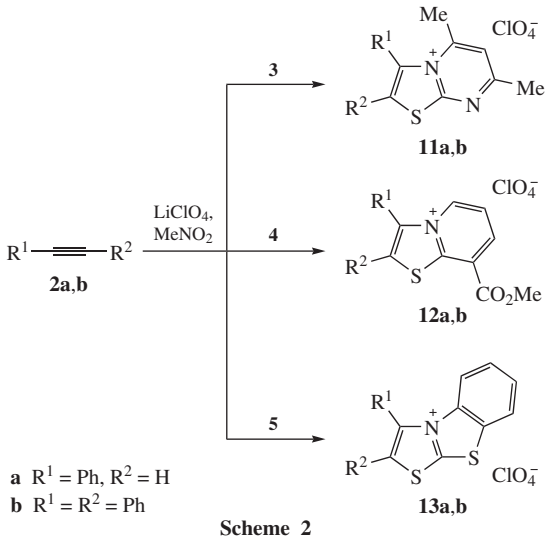
In polar cycloaddition reactions of sulfenylating reagents to carbon–carbon multiple bond, the atom of sulfur usually acts as internal nucleophile and three-, four - and five-membered cyclic sulfonium salts are formed.[1–5] The participation of other centers of sulfenylating reagents in the ring closure in Ad_E-reac-tions of alkenes, dienes and alkynes is extremely rare.[6,7]

We report here the new synthesis of condensed sulfur–nitrogen-containing heterocycles based on polar cycloaddition to carbon–carbon multiple bond of hetarene sulfenyl chlorides containing in hetarene fragment potentially nucleophilic atom of nitrogen. As model substrates, we used unsaturated compouds **1a–e** and **2a**,**b**. As reagents 4,6-dimethyl-2-pyrimidinesulfenyl chloride **3**, 3-methoxycarbonyl-2-pyridinesulfenyl chloride **4**, 1,3-benzothiazole-2-sulfenyl chloride **5** and 8-quinolinesulfenyl chloride **6** were applied. Note that reactions of sulfenyl chlorides **3**, **4**, **6** with unsaturated compounds were not studied, and the reaction of sulfenyl chloride **5** with styrene, for example, gives only usual β-chlorosulfide.[8] For stimulation of cycloaddition the $LiClO_4$–$MeNO_2$ system was applied.[7,9–17]

The interaction of **1a–e** and **2a**,**b** with **3–6** proceeded readily upon mixing these reagents in nitromethane in the presence of lithium perchlorate at 20 °C and resulted in the formation of derivatives of 2,3-dihydro[1,3]thiazolo[3,2-*a*]pyrimidin-4-ium **7a–e**, 2,3-dihydro[1,3]thiazolo[3,2-*a*]pyridin-4-ium **8a–d**, 2*H*,3*H*-benzo[*d*][1,3]thiazolo[2,3-*b*][1,3]thiazol-4-ium **9a–d**, 2,3-dihydro[1,4]thiazino[2,3,4-*ij*]quinolin-4-ium **10a**,**b**,**d**, [1,3]thiazolo[3,2-*a*]pyrimidin-4-ium **11a**,**b**, [1,3]thiazolo[3,2-*a*]-pyridin-4-ium **12a**,**b** and benzo[*d*][1,3]thiazolo[2,3-*b*][1,3]-thiazol-4-ium **13a**,**b** (Schemes 1 and 2, Table 1).[†,‡]



Scheme 1



Scheme 2

† *General procedure.* A solution of $LiClO_4$ (1.06 g, 10 mmol) in $MeNO_2$ (30 ml) was quickly added to a solution of sulfenyl chloride **3–6** (10 mmol) in $MeNO_2$ (10 ml) at 20 °C. After 1 min a solution of unsaturated compound **1a–e** or **2a**,**b** (10 mmol) in $MeNO_2$ (20 ml) was added. The mixture was stirred for 5–10 min. The precipitate of LiCl was separated by filtration, and the filtrate was evaporated to leave a solid residue, which was recrystallized from methanol.

Table 1 Polar cycloaddition of HetSCl to C–C multiple bond.

Unsaturated compound	Sulfenyl chloride	Product	Yield (%)	Mp/°C
1a	**3**	**7a**	75	116–117
1b	**3**	**7b**	52	218–220
1c	**3**	**7c**	72	100–101
1d	**3**	**7d**	67	128–129
1e	**3**	**7e**	65	121–122
2a	**3**	**11a**	82	125–126
2b	**3**	**11b**	73	245–247
1a	**4**	**8a**	87	111–112
1b	**4**	**8b**	83	180–182
1c	**4**	**8c**	78	125–127
1d	**4**	**8d**	65	245–247
2a	**4**	**12a**	83	105–106
2b	**4**	**12b**	89	114–115
1a	**5**	**9a**	92	111–112
1b	**5**	**9b**	61	222–224
1c	**5**	**9c**	75	105–107
1d	**5**	**9d**	65	222–224
2a	**5**	**13a**	83	195–197
2b	**5**	**13b**	87	237–239
1a	**6**	**10a**	92	218–220
1b	**6**	**10b**	63	240–242
1d	**6**	**10d**	61	110–111

The structure of the products has been confirmed by elemental analysis, IR, NMR (^{1}H and ^{13}C) spectroscopy and mass spectrometry, as well as the X-ray analysis performed on compounds **8c** and **9d** (Figures 1 and 2).§,¶

The X-ray crystallographic study of **8c** and **9d** revealed that each of compounds represents the separate ionic pair consisting of an organic cation and the perchlorate anion. The torsion angle H(6)C(6)C(10)H(10) in **8c** is –1.9° and it characterizes the *cis*-connection at the formation of N(1)C(1)S(1)C(10)C(6) cycle. In compound **9d** torsion H(14)C(14)C(15)H(15A) angle is 157.0° and it testifies about the *cis*-connection at the formation of N(1)C(1)S(2)C(14)C(15) cycle.

There are two possible routes of preparing heterocyclization products **7**–**13**. The first is the electrophilic addition-cyclization reaction of sulfur-containing electrophiles to unsaturated compounds (π-route).[7] The second is the intramolecular cyclization of initially formed 1,2-adducts (σ-route).[7] Control experiments

‡ The synthesis of compounds **9d** and **10a** was previously reported.[9,11]

§ All new compounds gave satisfactory analytical and spectroscopic data.

¶ *Crystallographic data for* **8c**: $C_{12}H_{14}ClNO_6S$, $M_r = 335.75$, orthorhombic, space group $P2_12_12_1$, $a = 8.8193(4)$, $b = 9.6074(4)$ and $c = 16.3251(8)$ Å, $V = 1383.23(11)$ Å^3, $Z = 4$, $T = 100(2)$ K, $F_{000} = 696$, $d_{calc} = 1.612$ g cm^{-3}, $\mu = 0.454$ mm^{-1}, $\theta = 2.46$–$24.99°$, reflections collected 7573, independent reflections 2437 [$R_{int} = 0.0143$], GOF = 1.015, $R = 0.0204$ [$I > 2\sigma(I)$], $wR_2 = 0.0544$ (all data), largest diffraction peak and hole 0.213/–0.171 e Å^{-3}, absolute structure parameter –0.03(4).

Crystallographic data for **9d**: $C_{23}H_{18}ClNO_4S_2$, $M_r = 471.95$, monoclinic, space group $P2_1/n$, $a = 9.5967(11)$, $b = 17.5458(18)$ and $c = 12.5202(13)$ Å, $\beta = 96.696(2)°$, $V = 2093.8(4)$ Å^3, $Z = 4$, $T = 100(2)$ K, $F_{000} = 976$, $d_{calc} = 1.497$ g cm^{-3}, $\mu = 0.414$ mm^{-1}, $\theta = 2.01$–$25.00°$, reflections collected 11296, independent reflections 3690 [$R_{int} = 0.0276$], GOF = 1.041, $R = 0.0351$ [$I > 2\sigma(I)$], $wR_2 = 0.0892$ (all data), largest diffraction peak and hole 0.438/–0.250 eÅ^{-3}.

Low-temperature diffraction data were collected on a Bruker-AXS Smart Apex I diffractometer with graphite-monochromated MoKα radiation ($\lambda = 0.71073$ Å). All structures were solved by direct methods and refined against F^2 on all data by full-matrix least squares with SHELXTL.[21] Absorption correction was applied using SADABS.[22] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms in **8c**, **9d** were found from difference Fourier syntheses of electron density and refined isotropically. Numeration of atoms in Figures 1 and 2 does not correspond to IUPAC nomenclature.

CCDC 690473 and 690474 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

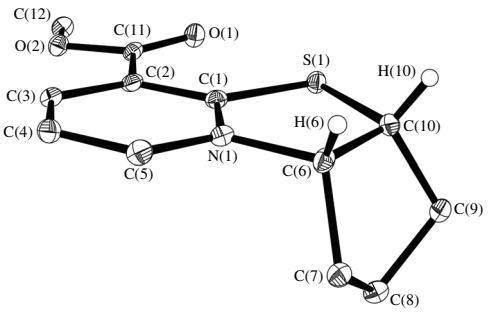


Figure 1 Molecular structure of **8c**. Anions ClO_4^- are omitted for clarity. Selected bond lengths (Å): S(1)–C(1) 1.7186(16), S(1)–C(10) 1.8284(16), O(1)–C(11) 1.199(2), N(1)–C(5) 1.349(2), N(1)–C(1) 1.348(2), N(1)–C(6) 1.493(2), O(2)–C(11) 1.335(2), O(2)–C(12) 1.455(2).

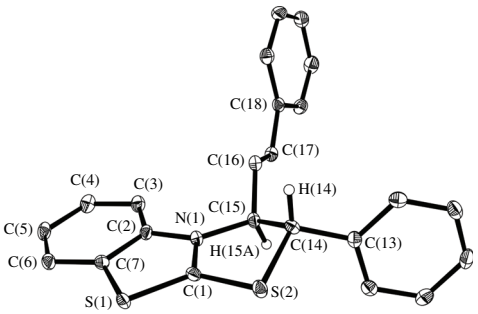
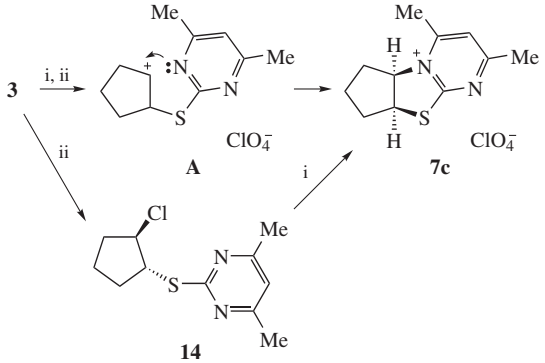


Figure 2 Molecular structure of **9d**. Anions ClO_4^- are omitted for clarity. Selected bond lengths (Å): S(1)–C(1) 1.699(2), S(1)–C(7) 1.748(2), N(1)–C(1) 1.330(3), N(1)–C(2) 1.406(3), N(1)–C(15) 1.498(2), C(1)–S(2) 1.706(2), S(2)–C(14) 1.851(2).

have shown that in the $LiClO_4$–$MeNO_2$ system the preformed products of 1,2-addition of hetarene sulfenyl chlorides to unsaturated compounds really undergo intramolecular cyclization. However, the rate of these transformations is reduced in comparison with the rate of the formation of heterocyclization products in Ad_E-reactions directly. Thus, interaction of **3** with **1c** in the $LiClO_4$–$MeNO_2$ system proceeded for 7 min and resulted in the formation of salt **7c** (Schemes 1 and 3, Table 1). Compound **7c** (70%) is formed as a result of transformation of 1,2-chlorosulfide **14** in $MeNO_2$ in the presence of 1 equiv. of $LiClO_4$ but full conversion of **14** is reached for 96 h (Scheme 3).

The formation of compounds **7**–**13** *via* a π-route can be explained by $[3^+ + 2]$[1,18,19] and $[4^+ + 2]$[1,20] polar cycloaddition between hetarene sulfenyl chlorides and unsaturated compounds in the $LiClO_4$–$MeNO_2$ system. Lithium perchlorate as a Lewis acid activates sulfenyl chlorides and in result of the electrophilic addition of generated cationoid reagents to a carbon–carbon multiple bond, cationic intermediates of type **A** are possibly formed in the product-determining stage (Scheme 3). Intramolecular nucleophilic attack of carbocationic center by the hetarene nitrogen gives products of heterocyclization. This



Scheme 3 *Reagents and conditions*: i, $LiClO_4$, $MeNO_2$; ii, **1c**, $MeNO_2$.

mechanism of the reaction is supported by experimental observations. Thus, reactions of hetarene sulfenyl chlorides with cyclic and bicyclic alkenes lead exclusively to the formation of the *cis*-fused products.[12,16,17] The formation of skeletal-rearrangement products of heterocyclization in the sulfenylation of 3,3-dimethyl-1-butene[15] and 3,4,5,6-tetrafluorotricyclo[6.2.2.0^{2,7}]-dodeca-2(7),3,5,9,11-pentaene[14] suggests also the carbocationic reaction mechanism.

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