Cyclization of ethyl *endo*-5-norbornene-2-carboxylate with hetarene sulfenyl chlorides

*V. K. Osmanov,[a] G. N. Borisova,[a] V. V. Kachala,[b] and A. V. Borisov[a]**

[a]R. E. Alekseev Nizhny Novgorod State Technical University, 24 ul. Minina, 603950 Nizhny Novgorod, Russian Federation. Fax: +7 (831) 436 2311. E-mail: avb1955@rumbler.ru
[b]N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5328. E-mail: vvk@ioc.ac.ru

Cyclization of ethyl *endo*-5-norbornene-2-carboxylate with 1,3-benzothiazole-2-sulfenyl and 3-methoxycarbonylpyridine-2-sulfenyl chlorides follows two directions, namely, electophilic lactonization of unsaturated ester or polar cycloaddition of sulfenylating reagent to the multiple bond accompanied by ring closure by the nitrogen atom of the thiohetaryl fragment.

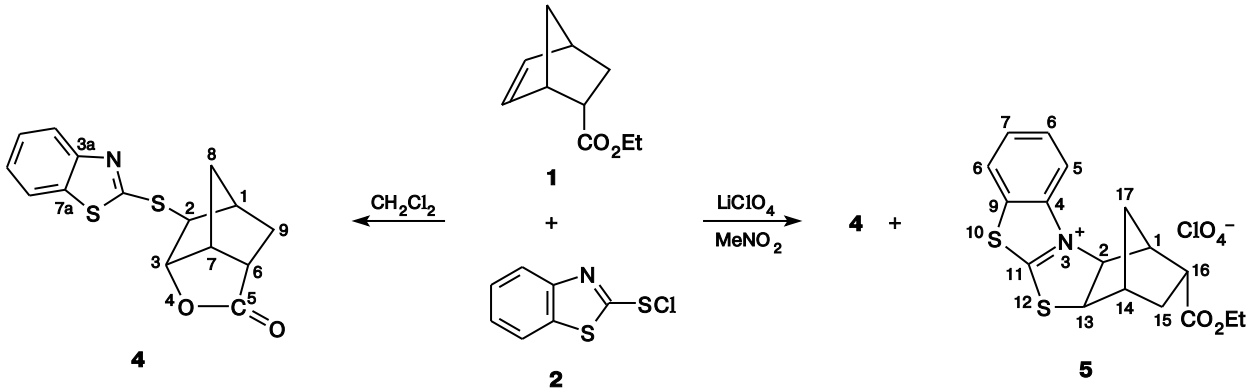
Key words: heterocyclization, sulfenyl chlorides, electrophilic addition, bicyclo[2.2.1]-heptanes.

Reactions of *endo*-5-norbornene-2-carboxylic acid or its esters with different electrophiles including sulfenyl chlorides usually give γ-lactones, which are the products of transannular cyclization occurring at the oxygen atom of the carboxy or alkoxycarbonyl groups of the starting substrate.[1—5]

In the present work it was found that in the reactions of ethyl *endo*-5-norbornene-2-carboxylate (**1**) with 1,3-benzothiazole-2-sulfenyl chloride (**2**) or 3-methoxycarbonylpyridine-2-sulfenyl chloride (**3**) the lactonization is completed by the heterocyclization involving the ring closure at the nitrogen atom of the hetaryl fragment of the sulfenylating reagent. The ratio of the competing directions of cyclization changed depending on the nature of the reaction medium and the reactant. Thus, the reaction of unsaturated ester **1** with sulfenyl chloride **2** in dichloromethane resulted exclusively in γ-lactone **4** in 81% yield. When the reaction was carried out in a lithium chloride—nitromethane system, polycyclic product **5** of the polar cycloaddition of the reactant at the double bond[6—8] formed in 10% yield along with the major product, γ-lactone **4** (77%) (Scheme 1).

The reaction of **1** with sulfenyl chloride **3** in dichloromethane furnished predominantly γ-lactone **6** (63%), however, *exo-cis*-cycloaddition of the reactant occurred also noticeably giving compound **7a** (25%). When the reaction was carried out in nitromethane, the cycloaddition of the reactant at the double bond dominants; the yields of compounds **6** and **7a** are 23 and 65%, respectively, whereas in the lithium perchlorate—nitromethane system,

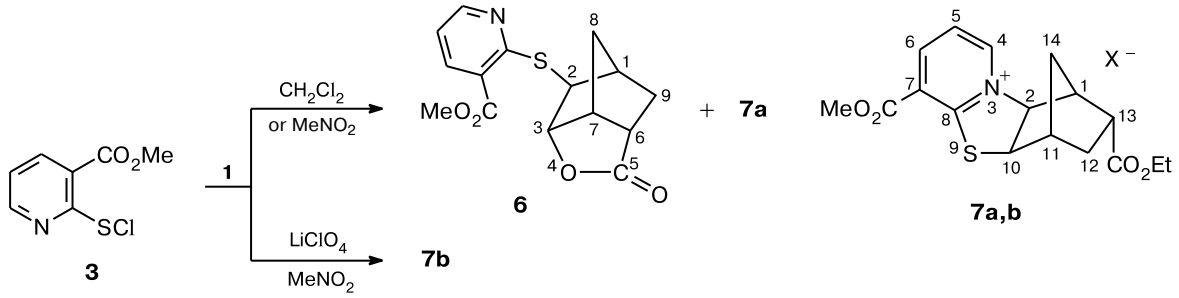
Scheme 1



Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 6, pp. 1260—1262, June, 2010.

1066-5285/10/5906-1289 © 2010 Springer Science+Business Media, Inc.

Scheme 2



X = Cl (**a**), ClO_4 (**b**)

the polar cycloaddition product, perchlorate **7b**, is exclusively formed in 87% yield (Scheme 2).

The structures of the compounds synthesized were established based on the data from ^1H and ^{13}C NMR spectroscopy and confirmed by elemental analysis. The signals in the NMR spectra were assigned using the data from COSY, HSQC, HMBS and NOESY experiments with compounds **4** and **7a** as the examples.

In the NOESY spectrum of compound **4**, the shift correlation for the following pairs of the protons H(7)/H(6), H(3)/H(2), H(3)/H_{anti}(8), H(2)/H(1), H(2)/H_{exo}(9), H(6)/H_{exo}(9), and H(6)/H_{endo}(9) were observed. These correlations allow unambiguous assignment of the structure of compound **4** as γ-lactone.

In the NOESY spectrum of compound **7a**, the correlations between the protons H(2)/H(4), H(2)/H(1), H(13)/H_{exo}(12), H(13)/H_{endo}(12), H(11)/H_{exo}(12), H(11)/H(10) were found. At the same time, no correlation peak of the proton pair H(2)/H(11) was observed in the NOESY spectrum. The HMBC spectrum of **7a** exhibited correlations between the protons and the carbon atoms through two and three bonds. In this case, the proton H(2) at δ 5.48 has two correlations with the sp^2-hybridized carbon atoms of the pyridine fragment. The HSQC spectrum is also in agreement with the mentioned assignment of the signals. Thus, the carbon atom at δ 76.12 corresponds to the proton H(2), which indicated direct bonding of this fragment to the N(3) nitrogen atom.

Experimental

The ^1H and ^{13}C NMR spectra were run on a Bruker Avance-600 instrument in DMSO-d_6.

Reaction of unsaturated ester 1 with reactants 2 and 3 in dichloromethane and nitromethane (general procedure). To a solution of unsaturated compound **1** (1.66 g, 10 mmol) in 20 mL of the solvent, a solution of sulfenyl chloride **2** or **3** (10 mmol) in 20 mL of the solvent was added at 20 °C. After 30 min, the solvent was removed *in vacuo*. The residue was extracted with boiling diethyl ether (50 mL), the solvent from the extract was evaporated, and the resulting residue recrystallized from hexane to give γ-lactones **4** and **6**. Compound **7a**, which is insoluble in diethyl ether, was recrystallized from methanol.

2-(1,3-Benzothiazol-2-ylsulfanyl)-4-oxatricyclo[4.2.1.$0^{3,7}$]-nonan-5-one (4). White crystals, m.p. 111—112 °C. Found (%): C, 59.47; H, 4.25. $C_{15}H_{13}NO_2S_2$. Calculated (%): C, 59.38; H, 4.32. ^1H NMR, δ: 1.60 (d, 1 H, H_{syn}(8), J = 11.7 Hz); 1.86 (d, 1 H, H_{endo}(9), J = 13.4 Hz); 1.94 (d, 1 H, H_{anti}(8), J = 11.7 Hz); 2.14 (td, 1 H, H_{exo}(9), J = 13.4 Hz, J = 3.5 Hz); 2.59 (br.s, 1 H, H(1)); 2.62 (d, 1 H, H(6), J = 3.5 Hz); 3.32 (br.s, 1 H, H(7)); 3.88 (d, 1 H, H(2), J = 2.5 Hz); 4.80 (d, 1 H, H(3), J = 4.8 Hz); 7.40 (t, 1 H, H(6′), J = 8.0 Hz); 7.48 (t, 1 H, H(5′), J = 8.0 Hz); 7.89 (d, 1 H, H(4′), J = 8.0 Hz); 8.06 (d, 1 H, H(7′), J = 8.0 Hz). ^{13}C NMR, δ: 33.80 (C(9)); 35.61 (C(8)); 37.43 (C(6)); 41.83 (C(1)); 45.95 (C(7)); 53.77 (C(2)); 85.72 (C(3)); 121.32 (C(4′)); 121.81 (C(7′)); 124.61 (C(6′)); 126.43 (C(5′)), 134.73 (C(7a′)); 152.74 (C(3a′)); 164.21 (C(2′)); 179.43 (C(5)).

Methyl 2-(5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]non-2-ylsulfanyl)-3-pyridinecarboxylate (6). White crystals, m.p. 136—137 °C. Found (%): C, 49.89; H, 4.83. $C_{15}H_{15}NO_4S$. Calculated (%): C, 59.00; H, 4.95. ^1H NMR, δ: 1.62 (d, 1 H, H_{syn}(8), J = 11.0 Hz); 1.78 (d, 1 H, H_{endo}(9), J = 12.2 Hz); 1.95 (d, 1 H, H_{anti}(8), J = 11.0 Hz); 2.14 (td, 1 H, H_{exo}(9), J = 12.2 Hz, J = 4.8 Hz); 2.45 (br.s, 1 H, H(1)); 2.62 (dd, 1 H, H(6), J = 11.0 Hz, J = 4.8 Hz); 3.24 (br.s, 1 H, H(7)); 3.78 (d, 1 H, H(2), J = 2.3 Hz); 3.88 (s, 3 H, OMe); 4.56 (d, 1 H, H(3), J = 4.8 Hz); 7.28 (dd, 1 H, H(5′), J = 8.5 Hz, J = 4.8 Hz); 8.24 (d, 1 H, H(4′), J = 8.5 Hz); 8.65 (d, 1 H, H(6′), J = 4.8 Hz).

13-Ethoxycarbonyl-7-methoxycarbonyl-9-thia-3-azoniatetracyclo[9.2.1.$0^{2,10}$.$0^{3,8}$]tetradeca-3(8),4,6-triene chloride (7a). Light brown crystals, m.p. 132—133 °C. Found (%): C, 55.11; H, 5.43. $C_{17}H_{20}ClNO_4S$. Calculated (%): C, 55.21; H, 5.45. ^1H NMR, δ: 1.24 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.1 Hz); 1.59 (d, 1 H, H_{syn}(14), J = 11.7 Hz); 1.61 (m, 1 H, H_{endo}(12)); 1.68 (d, 1 H, H_{anti}(14), J = 11.7 Hz); 1.97 (td, 1 H, H_{exo}(12), J =12.7 Hz, J =4.1 Hz); 2.64 (d, 1 H, H(11), J = 4.0 Hz); 3.09 (dt, 1 H, H(13), J = 11.6 Hz, J = 4.7 Hz); 3.17 (d, 1 H, H(1), J = 4.5 Hz); 3.93 (s, 3 H, OMe); 4.15 (q, 2 H, OCH_2, J = 14.2 Hz, J = 7.1 Hz); 4.17 (d, 1 H, H(10), J = 8.5 Hz); 5.48 (d, 1 H, H(2), J = 8.5 Hz); 7.83 (dd, 1 H, H(5), J = 7.8 Hz, J = 6.3 Hz); 8.81 (d, 1 H, H(6), J = 7.8 Hz); 8.89 (d, 1 H, H(4), J = 6.3 Hz). ^{13}C NMR, δ: 14.54 ($CH_2C\underline{H}_3$); 30.62 (C(12)); 33.45 (C(14)); 42.53 (C(13)); 45.15 (C(11)); 48.45 (C(1)); 50.92 (C(10)); 54.12 (CO$\underline{Me}$); 61.45 (OCH_2); 76.12 (C(2)); 123.27 (C(5)); 124.31 (C(7)); 145.62 (C(4)); 146.12 (C(6)); 163.02 ($\underline{C}O_2Et$); 173.43 ($\underline{C}O_2Me$).

Reaction of unsaturated ester 1 with reactants 2 and 3 in a lithium perchlorate—nitromethane system (general procedure). To a solution of $LiClO_4$ (1.06 g, 10 mmol) in nitromethane (30 mL), a solutions of sulfenyl chloride **2** or **3** (10 mmol) in nitromethane (20 mL) and of compound **1** (1.66 g, 10 mmol) in nitromethane (30 mL) were added at 20 °C. After 10 min, the precipitate of LiCl was filtered off and the solvent from filtrate was removed *in vacuo*. The reaction product of sulfenyl chloride **3**, compound **7b**, was recrystallized from methanol. The reaction products of sulfenyl chloride **2** were treated with boiling diethyl ether (50 mL). Removal of the solvent from the resulting extract afforded γ-lactone **4**. Heterocyclic product **5**, which is insoluble in diethyl ether, was recrystallized from methanol.

16-Ethoxycarbonyl-10,12-dithia-3-azoniapentacyclo-[12.2.1.0^{2,13}.0^{3,11}.0^{4,9}]heptadeca-3(11),4(9),5,7-tetraene perchlorate (5). Light brown crystals, m.p. 204—205 °C. Found (%): C, 47.14; H, 4.15. $C_{17}H_{18}ClNO_6S_2$. Calculated (%): C, 47.28; H, 4.20. ^{1}H NMR, δ: 1.33 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.1 Hz); 1.62 (m, 1 H, H_{endo}(15)); 1.65 (d, 1 H, H_{syn}(17), J = 11.2 Hz); 1.90 (d, 1 H, H_{anti}(17), J = 11.2 Hz); 2.07 (td, 1 H, H_{exo}(15), J =12.8 Hz, J = 4.8 Hz); 2.74 (d, 1 H, H(14), J = 4.8 Hz); 3.22 (dt, 1 H, H(16), J = 11.9 Hz, J = 5.0 Hz); 3.29 (d, 1 H, H(1), J = 4.8 Hz); 4.26 (m, 2 H, OCH_2); 4.79 (d, 1 H, H(13), J = 8.5 Hz); 5.36 (d, 1 H, H(2), J = 8.5 Hz); 7.68 (t, 1 H, H(7), J = 7.8 Hz); 7.73 (d, 1 H, H(8), J = 8.0 Hz); 7.84 (t, 1 H, H(6), J = 7.8 Hz); 8.31 (d, 1 H, H(5), J = 8.0 Hz).

13-Ethoxycarbonyl-7-methoxycarbonyl-9-thia-3-azoniatetracyclo[9.2.1.0^{2,10}.0^{3,8}]tetradeca-3(8),4,6-triene perchlorate (7b). Light brown crystals, m.p. 179—180 °C. Found (%): C, 47.11; H, 4.57. $C_{17}H_{20}ClNO_8S$. Calculated (%): C, 47.06; H, 4.65. The ^{1}H NMR spectrum is identical to that of compound **7a**.

References

1. J. A. Berson, D. A. Ben-Efraim, *J. Am. Chem. Soc.*, 1959, **81**, 4083.
2. A. Factor, T. G. Traylor, *J. Org. Chem.*, 1968, **33**, 2607.
3. D. N. Ford, W. Kitching, P. R. Wells, *Aust. J. Chem.*, 1969, **22**, 1157.
4. K. C. Nicolaou, S. P. Seitz, W. J. Sipio, J. F. Blount, *J. Am. Chem. Soc.*, 1979, **101**, 3884.
5. I. Fleming, J. P. Michael, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1549.
6. R. R. Schmidt, *Angew. Chem., Int. Ed.*, 1973, **12**, 212.
7. C. K. Bradsher, *Adv. Heterocycl. Chem.*, 1974, **16**, 289.
8. A. V. Borisov, V. K. Osmanov, G. N. Borisova, Zh. V. Matsulevich, G. K. Fukin, *Mendeleev Commun.*, 2009, **19**, 49.

Received December 24, 2009