SYNTHESIS OF BI- AND TRICYCLIC MESOIONIC [1,2,4,6]THIATRIAZINE-1,1,3-TRIOXIDES

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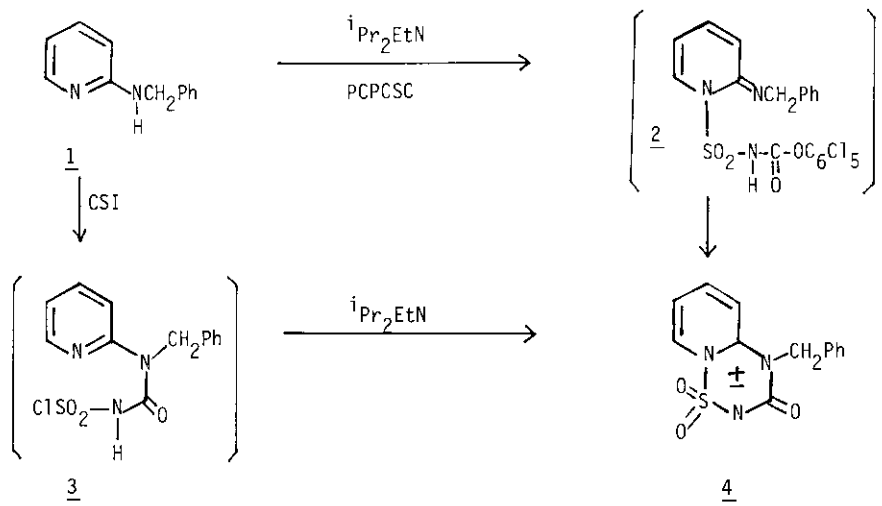
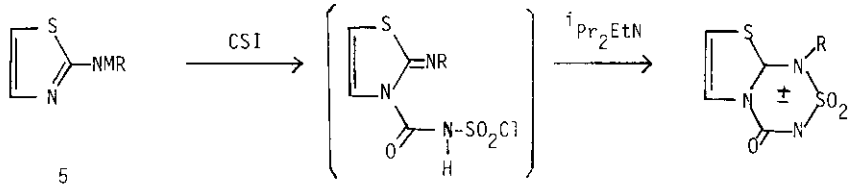
Abstract - The reaction of N-substituted aminoheterocycles with chlorosulfonyl isocyanate (CSI) or pentachlorophenyl N-chlorosulfonylcarbamate (PCPCSC) affords bi- and tricyclic mesoionic [1,2,4,6]thiatriazine-1,1,3-trioxides in the presence of ethyldiisopropylamine.

Numerous examples of six-membered mesoionic compounds are found in the literature and reviewed.[1] Malonyl dichlorides,[2] their ester derivatives,[3] carbon suboxide,[4] ethoxy- or phenoxycarbonyl isocyanate and their thio derivatives[5] are very useful reagents for the syntheses of mesoionic compounds. Since CSI has two functional groups of NCO and SO_2Cl, it can be used as cyclizing reagent for mesoionic compounds, but has recieved scant attention.[6] We wish to report the syntheses of mesoionic compounds from the reaction of CSI or PCPCSC with N-substituted aminoheterocycles.



2-Benzylaminopyridine reacted with PCPCSC in chloroform at room temperature producing mesoionic 1-benzylpyrido[1,2-b][1,2,4,6]thiatriazine-2,4,4-trioxide (4). Karady and co-workers[6a] already reported compound 4 which was synthesized from the reaction of 2-benzylaminopyridine and CSI in the presence of a tertiary amine base. Structure 4 was assigned by the comparison with authentic sample.[7]

2-Alkylaminothiazoles reacted with CSI producing the intermediate 6 which cyclized on the addition of a tertiary base to afford mesoionic 1-alkylthiazolo[2,3-c][1,2,4,6]thiatriazine-2,2,4-trioxides (7). The structure of 7 was assigned by the study of ^{1}H NMR and IR of intermediate 6a and ^{1}H NMR of intermediate 3. Presence of exocyclic imine bond was verified on the base of ^{1}H NMR chemical shift and imino stretching band in IR of 6a.



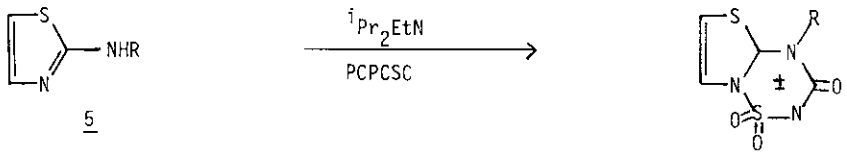
5 6 7

R: a=CH_2Ph
b=Et

^{1}H NMR data ($CDCl_3$, 60 MHz)

3	6a		
NCH_2	NCH_2	NCH	SCH
5.30 s	4.64 s, 4.74 s	7.87 d, J=5 Hz	6.68 d, J=5 Hz

PCPCSC resulted in mesoionic compound 8, which is the regioisomer of 7, with 2-alkylamino-thiazoles in the presence of a tertiary amine base. The structure of 8 are assigned by comparison with the ^{1}H NMR chemical shifts of 7.



5

R: a=CH_2Ph

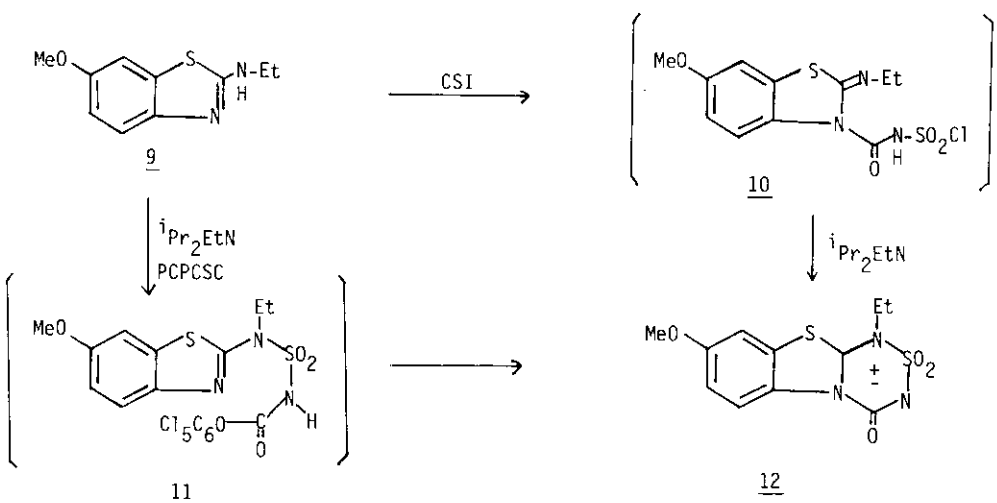
b=Et

8

^1H NMR data ($CDCl_3$ + CF_3COOH, 80 MHz)

	NCH	SCH	NCH_2	CH_3
7a	8.04 d, J=5 Hz	6.95 d, J=5 Hz	5.26 s	
7b	8.02 d, J=5 Hz	7.03 d, J=5 Hz	4.19 q, J=7 Hz	1.61 t, J=7 Hz
8a	7.88 d, J=5 Hz	7.20 d, J=5 Hz	5.35 s	
8b	7.90 d, J=5 Hz	7.32 d, J=5 Hz	4.18 q, J=7 Hz	1,48 t, J=7 Hz

Mesoionic compound 12 was obtained from the reaction of 2-ethylamino-6-methoxybenzothiazole with CSI or PCPCSC in the presence of a tertiary base. Product structure from A path (9-10-12) was assigned by ^1H NMR chemical shift of intermediate 10. ^1H NMR chemical shift of methylene groups in exocyclic and endocyclic imine intermediate 10 are 3.50 ppm and 4.25 ppm, respectively,[8] but this intermediate 10 has N-CH_2 resonance at 3.50 ppm. Product structure of B path (9-11-12) was determined by comparison with the data of the product from A path.



9

10

11

12

Pentachlorophenoxy group is the good leaving group.[9] PCPCSC cyclized with at room temperature, but ethyl- or phenyl N-chlorosulfonylcarbamate did not afford mesoionic compound at reflux condition in ethyl acetate or xylene.

EXPERIMENTAL

Melting points are uncorrected. IR and ^{1}H-NMR spectra were recorded on Perkin-Elmer Model 283 B grating infrared spectrometer and Varian T-60A or Varian FT-80A Spectrometer, respectively. Mass spectra were taken at an ionizing voltage of 70 eV on a Hewlett-Packard 5985 GC/MS instrument.

General Procedure (method A)

An equimolar amount of N-substituted aminoheterocycle was added to the solution of CSI in chloroform at room temperature. After 2 h an equivalent of ethyldiisopropylamine was injected and stirred at room temperature for 6 h. White solid was collected by filtration.

General Procedure (method B)

An equimolar amount of PCPCSC was added to the solution of equimolar ethyldiisopropylamine and N-substituted aminoheterocycle in chloroform and stirred for 6 h at room temperature. White solid was collected by filtration.

Mesoionic 1-Benzylpyrido[1,2-b][1,2,4,6]thiatriazine-2,4,4-trioxide(4): Method B. yield = 46%. Mp 166-170°C (decomp.) IR(KBr): 1690, 1630, 1510, 1358, 1330, 1230, 1220, 1180, 1000, 780, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$ + CF_3COOH): 5.45 (s, 2H), 7.00-8.90 (m, 9H). Ms (m/z): 289 (M^+), 183 (M^+-SO_2NCO)

Mesoionic 1-Benzylthiazolo[2,3-c][1,2,4,6]thiatriazine-2,2,4-trioxide (7a): Method A. Yield = 68%. Mp 200-203°C (decomp.) IR(KBr): 1740, 1575, 1555, 1340, 1205, 1180, 995, 900, 700 cm^{-1}. ^{1}H NMR($CDCl_3$ + CF_3COOH): 5.26(s, 2H), 6.95(d, J=5 Hz, 1H), 7.46(s, 5H), 8.04(d, J=5Hz, 1H) Ms(m/z): 295(M^+), 189(M^+-SO_2NCO)

Mesoionic 1-Ethylthiazolo[2,3-c][1,2,4,6]thiatriazine-2,2,4-trioxide (7b) : Method A. Yield = 90%, Mp 213-216°C (decomp.) IR(KBr): 1720, 1580, 1560, 1390, 1330, 1315, 1310, 1205, 1180, 1090, 1005, 895 cm^{-1}. ^{1}H NMR($CDCl_3$ + CF_3COOH): 1.61(t, J=7Hz, 3H), 4.19(q, J=7Hz, 2H), 7.03(d, J=5Hz, 1H), 8.02(d, J=5Hz, 1H). Ms(m/z): 233(M^+), 205(M^+-CO), 127(M^+-SO_2NCO).

Mesoionic 1-Benzylthiazolo[3,2-b][1,2,4,6]thiatriazine-2,4,4-trixoide (8a): Method B. Yield = 52%. Mp 194-198°C (decomp.) IR(KBr): 1700, 1545, 1370, 1215, 995 cm^{-1}. ^{1}H NMR($CDCl_3$ + CF_3COOH):

5.35(s, 2H), 7.20(d, J=5Hz, 1H), 7.41(s, 5H), 7.88(d, J=5Hz, 1H). Ms(m/z): 295(M^+), 189(M^+-SO_2NCO).

Mesoionic 1-Ethylthiazolo[3,2-b][1,2,4,6]thiatriazine-2,4,4-trioxide (8b): Method B. Yield = 65%, Mp 225-227°C (decomp.) IR(KBr): 1710, 1570, 1380, 1355, 1290, 1205, 1015, 755 cm^{-1}. ^1H NMR ($CDCl_3$ + CF_3COOH): 1.48(t, J=7Hz, 3H), 4.18(q, J=7Hz, 2H), 7.32(d, J=5Hz, 1H), 7.90(d, J=5Hz, 1H). Ms(m/z): 233(M^+), 127(M^+-SO_2NCO).

Mesoionic 4-Ethyl-7-methoxybenzothiazolo[2,3-c][1,2,4,6]thiatriazine-1,3,3-trixoide(12): Method A. Yield = 60%. Mp 241-245°C (decomp.) IR(KBr): 1710, 1570, 1500, 1200, 1010 cm^{-1}. ^1H HMR ($CDCl_3$ + CF_3COOH): 1.50(t, J=7Hz, 3H), 4.00(s, 3H), 4.26(q, J=7Hz, 2H), 7.25-8.30(m, 3H). Anal. Calcd for $C_{11}H_{11}N_3O_4S_2$: C, 42.17; H, 3.54; N, 13.42. Found: C, 41.8; H, 3.30; N, 13.8. Method B. Yield = 58%. Anal. Calcd for $C_{11}H_{11}N_3O_4S_2$: C, 42.17; H, 3.54; N, 13.42. Found: C, 41.9; H, 3.25; N, 13.9.

REFERENCES AND NOTES

1. W. Friedrichsen, T. Kappe, and A. Böttcher, Heterocycles, 1982, 19, 1083.
2. W. Friedrichsen, E. Kujath, G. Liebezeit, R. Schmidt, and I. Schwarz, Liebigs Ann. Chem., 1978, 1655; T. Kappe, W. Golser, M. Hariri, and W. Stadlbauer, Chem. Ber., 1979, 112, 1585.
3. R.A. Coburn and R.A. Glennon, J. Heterocycl. Chem., 1973, 10, 487; R.A. Coburn and R.A. Glennon, J. Pharm Sci., 1973, 67, 1785; R.A. Coburn and R.A. Glennon, J. Med. Chem., 1974, 17, 1025; R.A. Glennon, M.E. Rogers, R.G. Bass, and S.B. Ryan, J. Pham. Sci., 1978, 67, 1762; R.A. Glennon, M.E. Rogers, and M.K. Said, J. Heterocycl. Chem., 1980, 17, 337; R.A. Glennon, R.G. Bass, and E. Schubert, J. Heterocycl. Chem., 1979, 67, 1726.
4. K.T. Potts and M. Sorm, J. Org. Chem., 1971, 36, 8; K.T. Potts and R.K.C. Hsia, J. Org. Chem., 1973, 38, 3485; T. Kappe and R.K. Zadeh, Synthesis, 1975, 247.
5. R.A. Coburn and B. Bhooshan, J. Org. Chem., 1973, 38, 3868; R.A. Coburn and B. Bhooshan, J. Heterocycl. Chem. 1975, 12, 187; W. Stadlbaur and T. Kappe, Chem. Ber., 1976, 109, 3661.
6. 6a, S. Karady, J.S. Amato, D. Dortmund, A.A. Patchett, R.A. Reamer, R.J. Tull, and L.M. Weinstock, Heterocycles, 1979, 12, 815; 6b, **idem**., 1979, 12, 1199.
7. *1660 cm^{-1} may be the mistyping of 1690 cm^{-1} in IR of 4.*
8. J.S. Kang and D.Y. Oh, unpublished result.
9. P. Dvortsak, G. Resofszki, M. Huhn, and L. Zalantai, Tetrahedron, 1976, 32, 2117.

Received, 21st April, 1986