The Reaction of 5-Ethylidenebicyclo[2.2.1]hept-2-ene with Chlorosulfonyl Isocyanate[1]

EMIL J. MORICONI AND CLEMENTINA C. JALANDONI[2]

Department of Chemistry, Fordham University, New York, New York 10458

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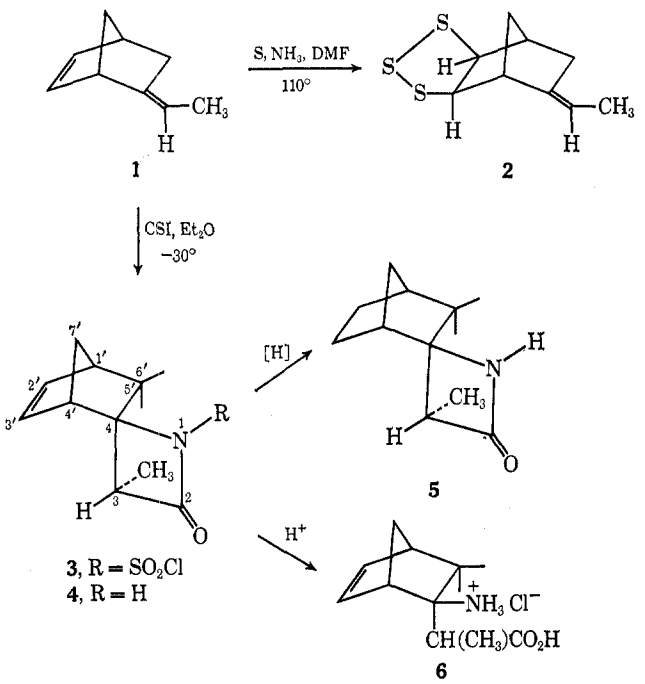
The high yield and selective and stereospecific "active" sulfuration of norbornene and 5-ethylidenebicyclo[2.2.1]hept-2-ene (**1**) to give *exo*-3,4,5-trithiatricyclo[5.2.1.$0^{2,6}$]decane and its 8-ethylidine derivative (**2**), respectively, has recently been reported.[3] Since this new reaction may well proceed *via* an ionic mechanism,[4] it is significant that in these and other norbornyl olefins and diolefins, sulfur adds exclusively to the norbornenyl ring double bond.

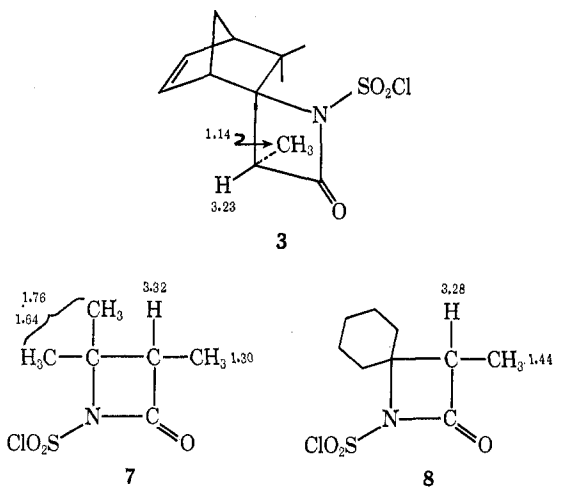
Since we too had noted such exclusivity in the cycloaddition reactions of chlorosulfonyl isocyanate (CSI) with bridged bi- and tricyclic olefins,[5] we wish to report an unusual divergence from this now expected pathway in the reaction of CSI with **1**.



Thus, treatment of **1** with electrophilic CSI led in 85% yield to the single β-lactam, 1-chlorosulfonyl-3-methyl-2-azetidinone-4-spiro-5′-bicyclo[2.2.1]hept-2′-ene (**3**), in which exclusive attack had occurred at the exocyclic double bond. In the nmr, the two vinyl protons in **3** appeared as coupled doublets at δ 6.40 and 6.08. The Markovnikov orientation of cycloadduct **3** was determined by the location in the nmr of methine and methyl protons. Sufficient N-chlorosulfonyl-β-lactams have been prepared to provide chemical shift data for such protons on C atoms adjacent to N and/or C=O functions of the azetidinone ring. A comparison of the relevant nmr data for two of these reference compounds, 1-chlorosulfonyl-3,4,4-trimethyl-2-azetidinone (**7**),[6] 1-chlorosulfonyl-3-methyl-1-azaspiro[3.5]nonan-2-one (**8**),[6] and **3** are summarized in Chart I. Finally, the stereochemistry of **3** is based

CHART I

NMR DATA FOR N-CHLOROSULFONYL-β-LACTAMS. CHEMICAL SHIFTS (δ) ARE INDICATED FOR METHYL AND METHINE PROTONS



on the precedented attack of CSI at the exo face of norbornyl olefins[5] and the observed stereospecificity of such cycloadditions to olefins.[7,8]

The strained electron-deficient carbonyl group in **3** appeared at 5.48 μ in the infrared as well as the expected SO_2 bands at 7.06 and 8.43 μ.[5] At room temperature, exposed to the atmosphere, β-lactam **3** decomposed to colored products within hours, while at −20° such decomposition occurred much more slowly. As with norbornadiene– and dicyclopentadiene–CSI adducts, **3** did not react further with CSI, while treatment of **1** with excess CSI led only to **3**.

Removal of the electronegative SO_2Cl function in **3** with thiophenol–pyridine in acetone afforded the unsubstituted β-lactam, 3-methyl-2-azetidinone-4-spiro-5′-bicyclo[2.2.1]hept-2′-ene (**4**), in which all nmr signals were now shifted upfield and the NH proton appeared at δ 7.60. Catalytic reduction of **4** led to the completely saturated tricyclic β-lactam **5** in which the bridgehead protons, no longer allylic, are shifted upfield to δ 2.32 and 2.15. In the infrared, the C=O bands in both **4** and **5** appeared as doublets at 5.66 μ. Hydrolysis of **4** with concentrated hydrochloric acid quantitatively converted it into the amino acid hydrochloride **6**.

The results reported herein add further to the confusing data already available on cycloadditions with norbornenyl systems. Thus, while the electrophile dichlorocarbene adds exclusively to the cyclopentene ring double bond in dicyclopentadiene,[9] CSI adds only

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(2) Graduate Research Assistant (1966–1968) on a grant[1] supported by the NIH; taken entirely from the Ph.D. thesis of C. C. Jalandoni, Fordham University, 1969.

(3) T. C. Shields and A. N. Kurtz, *J. Amer. Chem. Soc.*, **91**, 5415 (1969).

(4) W. A. Pryor, "Mechanisms of Sulfur Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 97–109.

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(7) E. J. Moriconi and J. F. Kelly, *Tetrahedron Lett.*, 1435 (1968).

(8) H. Bestian, H. Biener, K. Clauss and H. Heyn., *Ann.*, **718**, 94 (1968).

(9) L. Ghosez, P. Laroche, and L. Bastens, *Tetrahedron Lett.*, 3795 (1964).

to the norbornenyl ring double bond in the same system;[5] further, while "activated" sulfur adds exclusively to the norbornenyl ring double bond in **1**, CSI adds only to the exocyclic double bond. In this latter reaction, whatever the balance between steric factors (involving the approaching electrophile) and the intrinsic reactivity (of each double bond in **1**), the surprising result discourages even tentative mechanistic speculation without further and more comprehensive experimental data.

Experimental Section

Reaction of 5-Ethylidenebicyclo[2.2.1]hept-2-ene (1)[10] with CSI.—A solution of 5.0 g (0.04 mol) of **1** in 20 ml of absolute ether was cooled to −30° by means of a Dry Ice–ethanol bath. To this was added dropwise a solution of 5.9 g (0.04 mol) of CSI in 15 ml of absolute ether. The mixture was stirred at −30° for 30 min, then warmed to room temperature, and stirred again for an additional 30 min. Approximately half of the solvent was removed by passing a stream of nitrogen through the solution and gentle heating. Cooling at −20° for 6 hr afforded the colorless crude **1-chlorosulfonyl-3-methyl-2-azetidinone-4-spiro-5′-bicyclo[2.2.1]hept-2′-ene (3)**. Recrystallization from pentane yielded 9.4 g (86%) of **3** as fine needles: mp 69–70°; ir (CCl_4) 5.48 (C=O), 7.06 and 8.43 μ (SO_2); nmr ($CDCl_3$) δ 1.14 (d, 3, J = 7.5 Hz, CH_3) 1.80 (m, 2, C-7′ protons), 2.25 (m, 2, C-6′ protons), 3.02–3.33 (m, 3, C-3, -1′, -4′ protons), 6.08 (split doublet, 1, C-2′ proton), 6.40 (split doublet, 1, C-3′ proton).

Anal. Calcd for $C_{10}H_{12}NSO_3Cl$: C, 45.89; H, 4.62; N, 5.35. Found: C, 45.59; H, 4.86; N, 5.26.

Treatment of 1 equiv of **1** with 2 equiv of CSI gave only the monoadduct **3**.

Reduction of 3 with Benzenethiol–Pyridine.—A solution of 0.64 g (0.008 mol) of pyridine in 7 ml of acetone was added slowly to a solution of 1.77 g (0.007 mol) of **3** and 1.49 g (0.014 mol) of benzenethiol in 18 ml of acetone cooled to −30° in a Dry Ice–ethanol bath. After 4 hr, 18 ml of water was added dropwise. Phenyl disulfide precipitated and the mixture was filtered while still cold. The solution was extracted with three 50-ml portions of ether, dried (Na_2SO_4), filtered, and evaporated. The residual oil was extracted with 50 ml of boiling pentane and the extract was cooled to −20° for 24 hr to yield 0.40 g (36%) of **3-methyl-2-azetidinone-4-spiro-5′-bicyclo[2.2.1]hept-2′-ene (4)**: mp 97–98°; ir (CCl_4) 2.94 (free NH), 3.12 (bonded NH), 5.66 μ (C=O, doublet); nmr ($CDCl_3$) δ 1.06 (d, 3, J = 7.5 Hz, CH_3), 1.66 (split singlet, 4, C-6′, -7′ protons), 2.87 (broad complex, 3, C-3, -1′, -4′ protons), 6.03 (split doublet, 1, C-2′ proton), 6.22 (split doublet, 1, C-3′ proton), 7.60 (broad singlet, 1, NH).

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.84; H, 8.02; N, 8.44.

The analytical sample was prepared by sublimation at 88–89° (0.25 mm).

Catalytic Hydrogenation of 4.—A solution of 0.76 g (0.005 mol) of **4** in 40 ml of absolute ethanol was hydrogenated (5% Pd–C) at an initial hydrogen pressure of 38 psi in a Parr shaker for 1 hr. The catalyst was filtered and the ethanol was evaporated *in vacuo*. The solid residue was recrystallized twice from pentane to give 0.49 g (65%) of **3-methyl-2-azetidinone-4-spiro-2′-bicyclo-[2.2.1]heptane (5)**: mp 76–77°; ir (CCl_4) 2.95 (NH, free), 3.15 (bonded NH), 5.66 μ (C=O, doublet); nmr ($CDCl_3$) δ 1.18 (d, 3, J = 7.5 Hz, CH_3), 1.45 (broad complex, 8, C-3′, -5′, -6′, -7′ protons), 2.15 (broad singlet, 1, C-4′ proton), 2.32 (broad singlet, 1, C-1′ proton) 3.00 (q, 1, J = 7.5 Hz, C-3 proton) 7.38 (broad singlet, 1, NH).

Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.47. Found: C, 72.61; H, 9.14; N, 8.45.

Hydrolysis of 4 with Hydrochloric Acid.—A 0.30-g (0.002 mol) sample of **4** was dissolved in just enough concentrated HCl to cover the solid material and allowed to stand at room temperature for 2 hr. The thick, transparent paste was dried under vacuum with P_2O_5 giving a white solid. Recrystallization from methanol–ether gave 0.37 g (97%) yield of the amino acid hydrochloride (**6**): mp 245–247° dec; ir (KBr) 3.39 (NH), 5.87 μ (C=O); nmr (D_2O) δ 1.37 (d, 3, J = 7.5 Hz, CH_3) 1.82 (broad singlet, 4, C-6, -7 protons), 2.57 [q, 1, J = 7.5 Hz, $-CH(CH_3)COOH$], 3.12 (broad singlet, 2, C-1, -4 protons), 6.20 (m, 1, C-2 proton), 6.42 (m, 1, C-3 proton).

Anal. Calcd. for $C_{10}H_{16}NO_3Cl$: C, 55.17; H, 7.41; N, 6.43. Found: C, 54.87; H, 7.25; N, 6.72.

(10) Graciously supplied in research quantities by Union Carbide Corp., Chemicals and Plastics, South Charleston, W. Va. 25303.

Registry No.—**1**, 16219-75-3; **3**, 24265-81-4; **4**, 24265-82-5; **5**, 24265-83-6; **6**, 24265-84-7; chlorosulfonyl isocyanate, 1189-71-5.

5-Tetrazolyl Ylides

LELAND HUFF, DAVID M. FORKEY, DONALD W. MOORE, AND RONALD A. HENRY

Chemistry Division, Code 605, Naval Weapons Center, China Lake, California 93555

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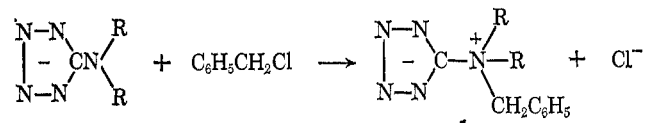
The monoalkylation of a 5-substituted tetrazole, as its anion, normally leads to a mixture of 1- and 2-alkyl-5-substituted tetrazoles; the ratio of isomers is influenced by the nature of the 5 substituent.[1] Even when this substituent is amino or substituted amino, ring alkylation, rather than alkylation on the *exo* nitrogen atom, has been reported to occur preferentially.[2] It has now been found that the monobenzylation of sodium 5-dimethylaminotetrazole in aqueous ethanol gives not only the expected, previously undescribed, 1- and 2-benzyl isomers, poorly soluble in water and readily soluble in benzene, but a third isomer (29% yield), poorly soluble in benzene and soluble in water. The solubility behavior and the high melting point (205° *vs.* 78 and 95°, respectively) suggested the novel ylide **1** (R = CH_3), which would result from benzylation on the *exo* nitrogen. Support



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for this assignment comes from the ^1H nmr spectrum; the signal for methyl protons is shifted to lower field while that for the benzyl methylene protons is shifted to higher field than those observed with either the 1 or 2 isomer (Table I). The chemical-shift values found for the ylides are in the range normally observed for similar quaternary ammonium salts. For example, benzyltrimethylammonium iodide (in Polysol) gives values of τ 6.77 and 5.18 for the methyl and benzyl methylene proton shifts.

The nmr spectrum of the diethyl ylide (**1**, R = C_2H_5) shows the same complex phenyl multiplet observed for the dimethyl compound and the chemical shift of the benzyl methylene protons is nearly the same. Convincing proof of tetrahedral substitution on the exo nitrogen is provided by the 2-Hz splitting of the ethyl

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