Addition Reactions of the Uniparticulate Electrophile Chlorosulfonyl Isocyanate to Highly Strained Bicyclic Hydrocarbons

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Abstract: The addition of chlorosulfonyl isocyanate to a variety of bicyclo[1.1.0]butanes and to bicyclo[2.1.0]-pentane has been studied. The cycloadditions proceed rapidly with overall retention of configuration at the two reacting centers of the strained hydrocarbons to afford chiefly the derived lactams. By observing the effect of various methyl substitution patterns on the bicyclobutane ring system and the behavior of tricyclo[4.1.0.0^{2,7}]heptane and bicyclo[2.1.0]pentane, it has proven possible to advance a mechanism which accords with all the observations. The course of the reactions is believed to involve initial S$_E$2-like attack at the less hindered bridgehead carbon atom, subsequent cyclobutyl-to-cyclopropylcarbinyl carbonium ion rearrangement *or* conformational ring inversion, and collapse of the zwitterion. The choice between skeletal rearrangement and cyclobutyl or cyclopentyl cation ring inversion appears to be dictated by stability considerations (extent of substitution, etc.).

Although alkenes and polyenes are characterized by their ready reaction with electrophilic reagents, it is noteworthy that the discoveries which have advanced our knowledge of this field have relied almost exclusively on biparticulate electrophiles, *i.e.*, species which can formally fragment into two distinct particles during reaction.[3] This is understandable, since reagents such as hydrogen chloride, bromine, and the like have long been available at little cost. Such reagents are recognized to lead most frequently to stereospecific trans addition and occasionally to stereoselective cis addition. Accordingly, the stereochemical course of such reactions has been attributed to the relative stabilities of the onium and open carbonium ions which in turn are determined largely by the nature of the biparticulate species and the structure of the unsaturated system.[4] When the onium ion is favored, trans products result, while stabilization of the open carbonium ion can lead to cis addition.

In contrast, when a *uniparticulate electrophile*, a reagent incapable of fragmentation, is allowed to react with an olefin, a cyclic product generally results.[5] Geometric constraints, when applicable, are recognized to play a major role in determining the structure of the addition product.[6] Additionally, such reagents constitute unusually effective probes for use in examining competitive rate situations[7] and in trapping transient carbonium ions which could otherwise pass undetected.[8,9] Their capability to accomplish the latter objective is the result of well-established kinetic preferences for intramolecular reactions.

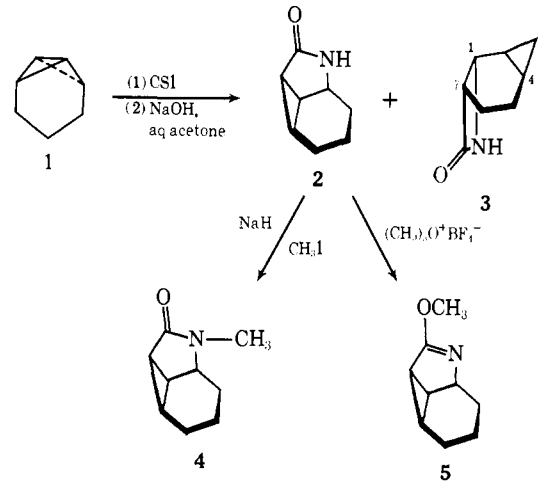
Since the initial synthesis of chlorosulfonyl isocyanate (CSI) reported by Graf in 1956,[10] it has become clear that this exceptionally reactive heterocumulene is a particularly useful uniparticulate electrophile.[11] Whereas unactivated olefins do not normally react with isocyanates, the structural elements in CSI, particularly the polar chlorosulfonyl group, enhance its reactivity such that (2 + 2) cycloaddition to simple alkenes occurs readily. Furthermore, as the complexity and degree of unsaturation in the olefinic substrate are appropriately increased, 1,4, 1,5, and 1,6 addition of CSI can also be realized.[7-9,12] In addition to the interesting mechanistic consequences of these transformations, the various lactam products have found application in a wide range of novel synthetic undertakings of which the azabullvalene,[8a,13] azasemibullvalene,[9] azocine,[14] and azocinyl dianion systems[15] are representative.

(1) Senior Education Awardee, American Cyanamid Co., 1969–1970.
(2) NATO Postdoctoral Fellow, 1970–1972.
(3) For an extensive survey, see P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," Elsevier Publishing Co., New York, N. Y., 1966.
(4) W. R. Dolbier, Jr., *J. Chem. Educ.*, **46**, 342 (1969).
(5) The stereospecific addition of chlorosulfonyl isocyanate to cis and trans alkenes is exemplary: (a) E. J. Moriconi and J. F. Kelly, *Tetrahedron Lett.*, 1435 (1968); (b) H. Bestian, H. Biener, K. Clauss, and H. Heyn, *Justus Liebigs Ann. Chem.*, **718**, 94 (1968); (c) L. A. Paquette, M. J. Wyvratt, and G. R. Allen, Jr., *J. Amer. Chem. Soc.*, **92**, 1763 (1970).
(6) Contrast, for example, the addition of bromine [S. Winstein and M. Shatavsky, *Chem. Ind. (London)*, 56 (1956)] and chlorosulfonyl isocyanate [E. J. Moriconi and W. C. Crawford, *J. Org. Chem.*, **33**, 370 (1968)] to norbornadiene.
(7) (a) L. A. Paquette, S. Kirschner, and J. R. Malpass, *J. Amer. Chem. Soc.*, **91**, 3970 (1969); (b) L. A. Paquette, S. Kirschner, and J. R. Malpass, *ibid.*, **92**, 4330 (1970).
(8) (a) L. A. Paquette and T. J. Barton, *ibid.*, **89**, 5480 (1967); (b) L. A. Paquette, J. R. Malpass, and T. J. Barton, *ibid.*, 91, 4714 (1969).
(9) (a) L. A. Paquette, *Tetrahedron Lett.*, 2133 (1968); (b) L. A. Paquette and G. R. Krow, *J. Amer. Chem. Soc.*, 91, 6107 (1969).
(10) R. Graf, *Chem. Ber.*, **89**, 1071 (1956).
(11) For recent reviews, see (a) R. Graf, *Angew. Chem.*, **80**, 179 (1968); *Angew. Chem., Int. Ed. Engl.*, 7, 172 (1968); (b) E. J. Moriconi, *Mech. React. Sulfur Compounds*, **3**, 131 (1968).
(12) Additional examples of nonvicinal bonding by the CSI reagent have recently appeared: (a) E. J. Moriconi and W. C. Meyer, *Tetrahedron Lett.*, 3823 (1968); (b) P. Goebel and K. Clauss, *Justus Liebigs Ann. Chem.*, **722**, 122 (1969); (c) E. J. Moriconi, C. F. Hummel, and J. F. Kelly, *Tetrahedron Lett.*, 5325 (1969); (d) R. Askani, *Angew. Chem.*, **82**, 176 (1970); *Angew. Chem., Int. Ed. Engl.*, 9, 167 (1970).
(13) (a) L. A. Paquette, T. J. Barton, and E. B. Whipple, *J. Amer. Chem. Soc.*, **89**, 5481 (1967); (b) L. A. Paquette, G. R. Krow, J. R. Malpass, and T. J. Barton, *ibid.*, **90**, 3600 (1968); (c) L. A. Paquette and G. R. Krow, *ibid.*, **90**, 7149 (1968); (d) L. A. Paquette and J. R. Malpass, *ibid.*, **90**, 7151 (1968); (e) L. A. Paquette, J. R. Malpass, G. R. Krow, and T. J. Barton, *ibid.*, **91**, 5296 (1969); (f) L. A. Paquette, G. R. Krow, and J. R. Malpass, *ibid.*, **91**, 6107 (1969); (g) L. A. Paquette, J. R. Malpass, and G. R. Krow, *ibid.*, **92**, 1980 (1970).
(14) (a) L. A. Paquette and T. Kakihana, *ibid.*, 90, 3897 (1968); (b) L. A. Paquette and J. C. Philips, *ibid.*, 90, 3898 (1968); (c) L. A. Paquette T. Kakihana, J. F. Hansen, and J. C. Philips, *ibid.*, **93**, 152 (1971).
(15) (a) L. A. Paquette, J. F. Hansen, T. Kakihana, and L. B. Anderson, *Tetrahedron Lett.*, 533 (1970); (b) L. A. Paquette, T. Kakihana, and J. F. Hansen, *ibid.*, 528 (1970); (c) L. B. Anderson, J. F. Hansen, T. Kakihana, and L. A. Paquette, *J. Amer. Chem. Soc.*, **93**, 161 (1971); (d) L. A. Paquette, J. F. Hansen, and T. Kakihana, *ibid.*, **93**, 168 (1971); (e) L. A. Paquette and T. Kakihana, *ibid.*, **93**, 174 (1971).

It was our intent in the present study to examine the consequences of adding CSI to σ bonds rich in p character, and highly strained bicyclic hydrocarbons were selected for this purpose. Past investigations with CSI have established that cyclopropanes merely undergo rearrangement to olefins prior to electrophilic addition[16] and that cyclopropenes afford products arising only from ring opening of transient cycloproply cations.[17] As will be seen, these types of considerations do not gain importance in uniparticulate electrophilic additions to bicyclo[1.1.0]butanes and bicyclo[2.1.0]-pentane.[18]

Results

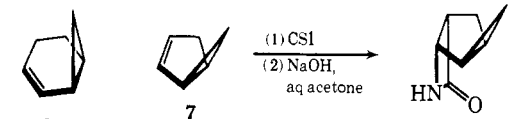
Our initial efforts were involved with tricyclo[4.-1.0.$0^{2,7}$]heptane (**1**). Exposure of **1** to an equimolar amount of CSI in methylene chloride solution at $-78°$ for 2.25 hr and then at room temperature for 6.25 hr led after alkaline hydrolysis to lactams **2** (37%) and **3** (9%). The presence in **2** of a lactam function



1 2 3 4 5

was apparent from the intense infrared (KBr) carbonyl stretching frequency at 1695 cm^{-1}. Its 60-MHz spectrum in $CDCl_3$ is characterized by a broad >NH absorption at δ 6.75, a multiplet of area 1 centered at 4.08, and a broad nine-proton envelope in the 1.08–2.34 region. Conversion of **2** to its N-methyl derivative **4** caused a shift in the infrared carbonyl band to 1660 cm^{-1} ($CHCl_3$), but only minor alterations in the nmr (see Experimental Section). In contrast, the presence of a double bond in derived imino ether **5** results in sufficient downfield shifting of the allylic protons to reveal multiplets of area 1 at 4.30 and 2.10 in addition to the methyl singlet at 3.80 and the broad multiplet (8 H) at 1.08–2.02. These data reveal that **2** is not a β-lactam; rather, the nmr spectra are consistent only with the presence in **2** of a cyclic five-ring lactam whose carbonyl group is bonded to a cyclopropane carbon which bears a single hydrogen. Particularly informative is the chemical shift of the low-field multiplets in **2** and **4** (δ 4.08 and 3.84) which are clearly recognizable as protons adjacent to amide nitrogen, since α-carbonyl protons (not incorporated into cyclopropane rings) invariably resonate at higher field (δ 3.10–3.60).[7-9,13-15,19]

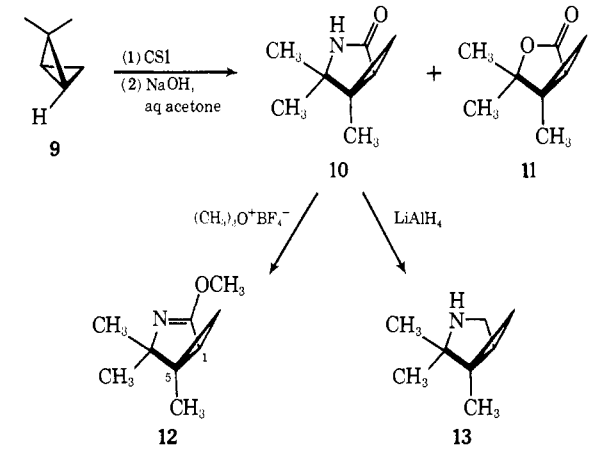
Minor product **3** exhibited a 1750-cm^{-1} carbonyl absorption ($CHCl_3$) typical of β-lactams. Inspection its nmr spectrum revealed multiplets at δ 1.13 and 0.52 (2 H each) suggestive of a fused cyclopropane ring and a one-proton doublet (J = 5.0 Hz) at 4.04 assignable to H_1. The appearance of H_1 as a simple doublet due to unique coupling with H_7 is consistent only with an anti relationship of the three- and four-membered rings.[20] The formation of **3** is explicable on the basis of acid-catalyzed rearrangement of **1** to norcarene (**6**) and subsequent cycloaddition of CSI to this vinylcyclopropane. The same rearrangement, catalyzed by aluminum chloride, has been previously noted.[21]



6 7 8

Evidence in support of this assumption was gained through the direct preparation of **8** from bicyclo-[3.1.0]hexene (**7**). The spectral properties of this β-lactam correspond closely to those of **3** (see Experimental Section).

When 1,2,2-trimethylbicyclo[1.1.0]butane (**9**) was treated with CSI in methylene chloride solution at $-78°$, a rapid reaction occurred. Hydrolysis and column chromatography of the product mixture led to the isolation of lactam **10** (43%) and lactone **11** (4%). Infrared carbonyl absorption at 1685 cm^{-1} ($CHCl_3$) gave the first indication that **10** was a five-membered lactam. The nmr spectrum of **10** had a multiplet centered at δ 1.68 that was assigned to H_1. The remaining two cyclopropyl protons appeared as a multiplet at 0.67–1.00 and the singlet methyl absorptions were seen at 1.31 (3 H) and 1.22 (6 H). To establish



9 10 11 12 13

the orientation of the lactam functionality relative to

(16) E. J. Moriconi, J. F. Kelly, and R. A. Salomone, *J. Org. Chem.*, 33, 3448 (1968).

(17) T. J. Barton, R. Rogido, and J. C. Clardy, *Tetrahedron Lett.*, 2081 (1970).

(18) While this work was in progress, there appeared an independent report concerning the addition of CSI to bicyclo[2.1.0]pentane: E. J. Moriconi and C. P. Dutta, *J. Org. Chem.*, 35, 2443 (1970). These authors have suggested, but not proven, that one alternative is a stepwise electrophilic attack by CSI on the bridgehead carbon atom of this hydrocarbon.

(19) The variation in chemical shift of α-carbonyl cyclopropyl protons with changes in the conformational relationship of H_α and >C=O has recently been evaluated in rigid tricyclic cyclopropyl ketones: S. A. Monti, *ibid.*, 35, 380 (1970).

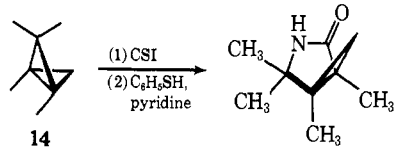
(20) P. K. Freeman, M. F. Grostic, and F. A. Raymond, *ibid.*, 30, 771 (1965); P. K. Freeman, F. A. Raymond, and M. F. Grostic, *ibid.*, 32, 24 (1967).

(21) W. R. Moore, H. R. Ward, and R. F. Merritt, *J. Amer. Chem. Soc.*, 83, 2019 (1961).

the cyclopropane ring, **10** was converted to imino ether **12** and also reduced to amine **13**. In **12**, H_1 appeared as a well-defined doublet of doublets (J = 8.0 and 3.0 Hz) at δ 1.86; as in the case of **5**, the chemical shift of this proton revealed its position to be adjacent to the methoxyl-bearing carbon. Confirmation of this point was realized in the nmr spectrum of **13** which showed the newly introduced methylene group to be a well-resolved AB pair. The B proton consisted of a doublet of doublets (J = 11.0 and 3.0 Hz) centered at δ 2.98 and was therefore positioned endo (*i.e.*, anti to the cyclopropane ring); the A proton (exo) was seen as a doublet (J = 11.0 Hz) at 2.62. The observed vicinal spin coupling interaction (3.0 Hz) of H_B with H_1 requires that the lactam carbonyl in **10** be adjacent to the cyclopropane ring.

Lactone **11** was a low-melting hygroscopic solid with an intense carbonyl band ($CHCl_3$) at 1765 cm^{-1}. Its structural assignment is based on the similarity of its nmr spectrum with that of lactam **10**.

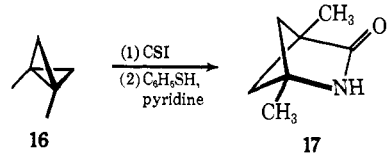
1,2,2,3-Tetramethylbicyclo[1.1.0]butane (**14**) was considered next. CSI in methylene chloride added rapidly to **14** to afford uniquely lactam **15** ($\nu_{max}^{CHCl_3}$ 1685 cm^{-1})



14 **15**

in 51% yield. The nmr spectrum of **15** which displays two cyclopropyl proton doublets in a typical AB pattern at δ 0.91 and 0.94 (J = 4 Hz) indicates that the C_1, C_3, and C_4 atoms of **14** are incorporated in the three-membered ring of this lactam product.

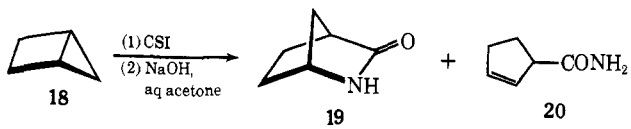
Under similar conditions, 1,3-dimethylbicyclo[1.1.0]-butane (**16**) gave rise to the interesting bicyclic lactam **17**. Assignment of structure to **17** follows unambiguously from the elemental analysis and spectral data. Whereas the infrared spectrum shows amide carbonyl absorption at 1745 cm^{-1} ($CHCl_3$, compare **2**, **10**, and



16 **17**

15), the nmr spectrum indicates the presence of four methylene protons as a multiplet at δ 1.45–2.47 and two nonequivalent tertiary methyl groups as sharp singlets at 1.31 and 1.20. No absorptions attributable to protons adjacent to a –CONH– functionality were seen.

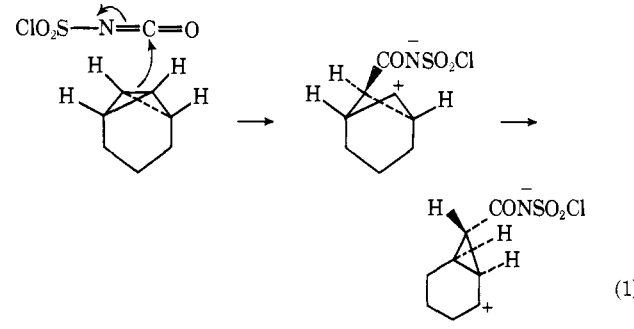
The addition of CSI to bicyclo[2.1.0]pentane (**18**) afforded a mixture of 2-azabicyclo[2.2.1]heptan-3-one (**19**) and cyclopentene-3-carboxamide (**20**). The structural assignments were substantiated by the infrared and nmr spectra of the products and their interconversion with known compounds.[18]



18 **19** **20**

Discussion

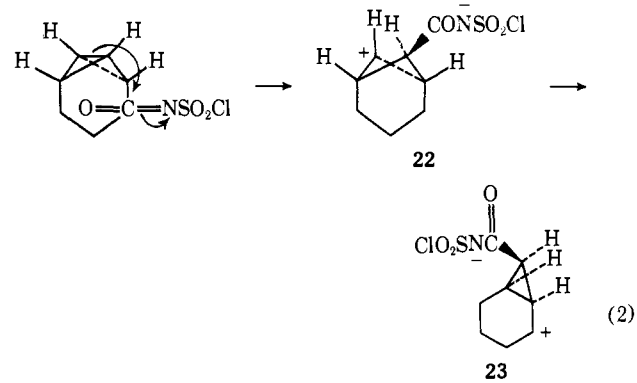
As noted earlier by Wiberg,[22] electrophilic attack on a bicyclobutane can *a priori* take place by (a) approach to the central bond symmetrically from above or below; (b) initial bonding to C_1 in SE2-like fashion from below the edge of the flap; and (c) approach to an edge (C_1–C_2) bond from either a line perpendicular to the $C_1C_3C_2$ plane or along a line bisecting the $C_1C_3C_2$ angle. In the particular case of tricyclo[4.1.0.0^{2,7}]heptane (**1**), attack at the central bond from inside the flap cannot occur for steric reasons; on the other hand, bonding in the opposite direction clearly positions the chlorosulfonyl isocyanate residue exo in the more stable 2-norcaranyl ion (**21**) where it cannot cyclize to give **2** (eq 1).[23] Accordingly, this mechanism is nonoperative.



(1)

21

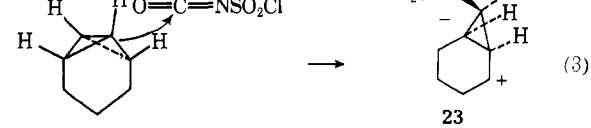
Attack at C_1 with rupture of the C_1–C_3 bond in SE2-like fashion would lead initially to **22** and subsequently to intermediate **23** with stereochemistry appropriate for cyclization (eq 2). Should electrophilic attack proceed by rupture of an edge bond, the identical norcaranyl ion **23** is formed directly (eq 3). In principle, therefore, the retention of configuration which occurs at both bicyclobutyl carbon atoms can be accommodated by the last two processes.



22

(2)

23



(3)

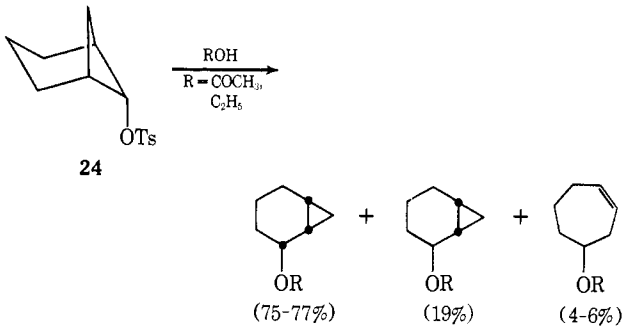
23

Although ultimate distinction between mechanisms 2 and 3 is of considerable significance, close scrutiny

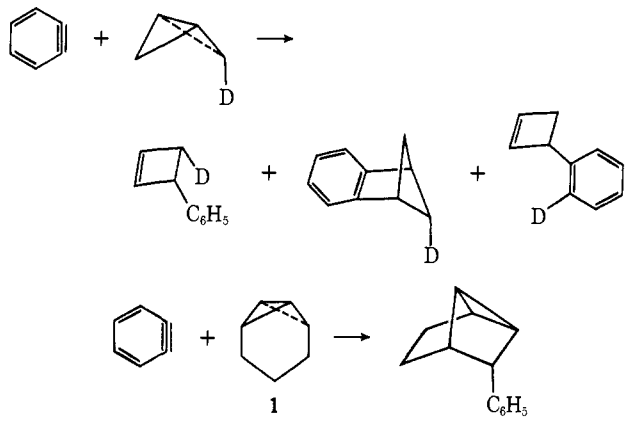
(22) K. B. Wiberg and G. Szeimies, *J. Amer. Chem. Soc.*, 92, 571 (1970).

(23) It should be noted that even should **21** be subject to cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement, the retention of stereochemistry known to be operative in such bond reorganizations would not alter the exo relationship of the –CONSO$_2$Cl function to the norcaranyl cation.

discloses that the question is an intricate one. The difficulty arises because the central bond initially fragmented in (2) is rapidly replaced by migration of an edge bond with structural and stereochemical consequences identical with those found in (3). Nevertheless, certain data suggest that mode 2 may be the preferred path for electrophilic addition to **1** and other bicyclobutanes. First, the facile conversion of 6-bicyclo[3.1.1]-heptyl cations such as **22** to norcaranyl cations (*e.g.*, **23**) has been previously established in the acetolysis and ethanolysis of **24**.[24] On the basis of the almost com-

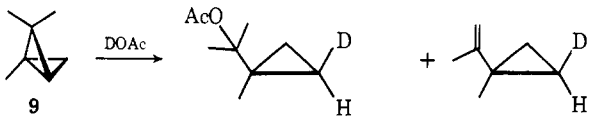


plete conversion to norcaranyl products (no internal return was noted) and the significant rate enhancement exhibited by **24**, there must exist a marked propensity for skeletal rearrangement as required by (2). Second, it is important to recall that although all the bicyclobutyl carbon–carbon bonds are endowed with π character, the 1,3 bond exhibits the greatest degree of unsaturation.[25] Third, in the addition of benzyne to bicyclobutane and **1**,[26] the attacking carbon–carbon multiple bond has been found to exhibit an overwhelming preference for backside attack at the 1,3 bond.

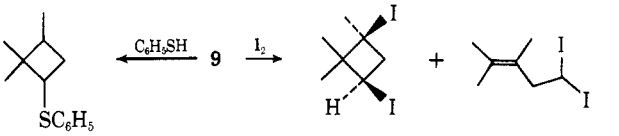


Because the intermediate in this instance is presumably a 6-bicyclo[3.1.1]heptyl radical, passage to norcaranyl products is not seen. Nevertheless, the preferred direction of approach and bond rupture processes are clearly evident.

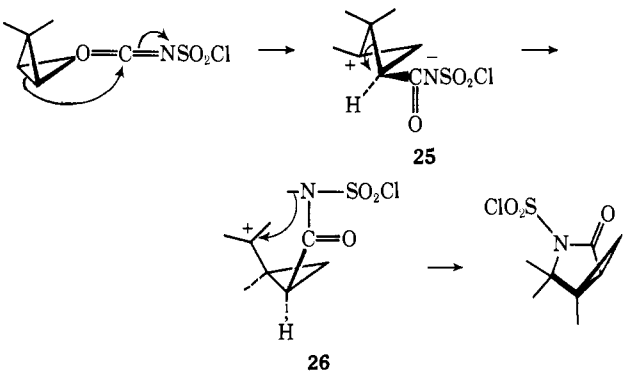
The case for 1,2,2-trimethylbicyclo[1.1.0]butane (**9**) is still more convincing.[27,28] Addition of CSI and acetic acid to **9** occurs not only with retention of configuration but also with essentially complete stereoselectivity. In both examples, the electrophile is seen



to attack exclusively the C_3 atom of the strained hydrocarbon. It can be seen that if reaction mode 3 were operative, the high stereoselectivity must necessarily be attributed to the differing steric environments at C_1 and C_3. In reaction mode 2, the stereoselectivity would be the result of differing cyclobutyl carbonium ion stabilities. In the first instance, introduction of a proximate methyl group would not be expected under ordinary circumstances to result in a change in reactivity leading to 100% selectivity. Additionally, the tetramethyl congener (**14**) is seen to react qualitatively as fast as **9** toward CSI, suggesting that the presence of the fourth methyl group has little rate-retarding influence. In the second case, it is significant to realize that thiophenol and iodine cleave the 1,3 bond of **9** in equally selective fashion. Thus, the experimental data,



when taken in conjunction with CNDO calculations of bicyclobutane–proton complexes of varying geometry, lead to the conclusion that the more highly strained 1,3 bond[29] in **9** is first ruptured by backside attack at C_3 to produce the more stable carbonium ion **25** which rapidly rearranges to **26** prior to collapse of the zwitterion. Intermediate **25** presumably is not trapped by collapse of the ion pair because the rate of



the cyclobutyl–cyclopropylcarbinyl rearrangement is faster than the conformational inversion required to achieve cyclization.

In the carbonium ion intermediates from initial CSI attack on **16** and **18** with central bond rupture, carbonium ion rearrangement is not electronically favorable and ring inversion, followed by cyclization, now competes favorably. At this time, it is not clear

(24) K. B. Wiberg and B. A. Hess, Jr., *J. Amer. Chem. Soc.*, **89**, 3015 (1967).

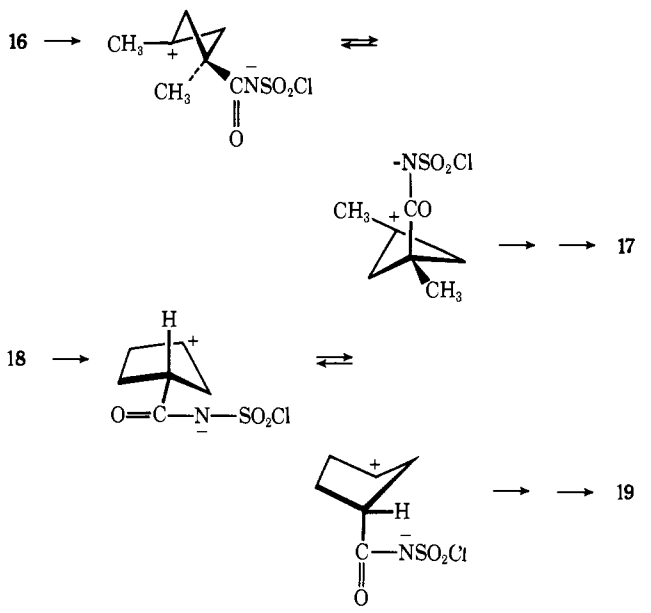
(25) M. Pomerantz, *ibid.*, **88**, 5349 (1966); M. Pomerantz, G. W. Gruber, and R. N. Wilke, *ibid.*, 90, 5040 (1968); J. M. Schulman and G. J. Fisanick, *ibid.*, **92**, 6653 (1970).

(26) P. G. Gassman and G. D. Richmond, *ibid.*, 90, 5637 (1968); **92**, 2090 (1970).

(27) L. Skattebøl, *Tetrahedron Lett.*, 2361 (1970). We thank Dr. Skattebøl for providing us with directions for the preparation of **9** well in advance of publication.

(28) W. R. Moore, K. G. Taylor, P. Müller, S. S. Hall, and Z. L. F. Gaibel, *ibid.*, 2365 (1970).

(29) (a) R. B. Turner, P. Goebel, W. von E. Doering, and J. F. Coburn, Jr., *Tetrahedron Lett.*, 997 (1965); (b) M. D. Harmony and K. Cox, *J. Amer. Chem. Soc.*, **88**, 5048 (1966); (d) I. Haller and R. Srinivasan, *J. Chem. Phys.*, **41**, 2745 (1964).



whether cyclopentene-3-carboxamide (**20**) is formed by way of a 1,5 proton transfer in the dipolar intermediate or by a direct ene reaction.[30]

Experimental Section

Reaction of Tricyclo[4.1.0.0^{2,7}]heptane with CSI. A solution of 4.416 g (47 mmol) of **1**[21] in 15 ml of dry methylene chloride was placed in a flask that had been previously exposed to ammonia vapors. This solution was cooled to −78° under nitrogen and 6.65 g (3.97 ml, 47 mmol) of chlorosulfonyl isocyanate was added over 15 min with stirring. After 2.25 hr at −78°, the solution was stirred at ambient temperature for 6.25 hr. The solvent was removed in a stream of dry nitrogen, and the residue was dissolved in acetone. Hydrolysis was performed by titration with 4 *N* NaOH (pH meter) and ice cooling. Extraction of the products with methylene chloride, followed by washing, drying, and evaporation of the combined organic layers, gave 4.5 g of amber oil that was chromatographed on silica gel. Elution with hexane–ether (1:1) afforded 568 mg (9%) of 9-azatricyclo[5.2.0.0^{2,4}]nonan-8-one (**3**) as white crystals: mp 91–93°, from acetone–hexane; $\nu_{max}^{CHCl_3}$ 3300 and 1750 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.74 (br, s, 1, >NH), 4.04 (d, J = 5.0 Hz, 1, H_1), 3.14 (m, 1, H_7), 1.42–2.75 (m, 5, methylenes and a cyclopropyl), 1.13 and 0.52 (m, 2 and 1, respectively, cyclopropyl).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.61; H, 8.02; N, 10.08.

Elution with ether furnished 2.36 g (37%) of 7-azatricyclo[4.3.0.0^{2,9}]nonan-8-one (**2**) as white crystals, mp 79–81°, from acetone–hexane: ν_{max}^{KBr} 3170 and 1695 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.75 (br s, 1, >NH), 4.08 (m, 1, >C*H*N<), and 1.08–2.34 (m, 9).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.82; H, 8.15; N, 9.95.

7-Methyl-7-azatricyclo[4.3.0.0^{2,9}]nonan-8-one (4). A solution of 1.70 g (12.4 mmol) of **2** in 15 ml of dry dimethylformamide was added to a slurry of 630 mg (15 mmol) of 57% sodium hydride–mineral oil dispersion (previously washed with ether) in 10 ml of dimethylformamide. The mixture was heated at 70–80° with stirring for 3 hr, at which time it was cooled in ice and 4.30 g (1.89 ml, 30 mmol) of methyl iodide was added below the surface *via* syringe. The mixture was stirred at room temperature for 15 min and an additional 30 mmol of methyl iodide was added similarly. The mixture was stirred at room temperature for 3 hr and then diluted with 100 ml of ether. The solid was collected and washed well with ether. Removal of the solvents from the combined filtrate and washings gave 1.94 g of yellow liquid, vpc analysis of which indicated it to be 88% **4**. A sample was purified by preparative scale vpc on a 5 ft × 0.25 in. column packed with 20% SE-30 on 60–80 mesh Chromosorb W at 182°. The collected material was recrystallized from ether–pentane to give white crystals: mp 53–54°; $\nu_{max}^{CHCl_3}$ 1660 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 3.72–4.00 (m, 1, >C*H*N<), 2.62 (s, 3, methyl), and 1.00–2.42 (m, 9).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.78; H, 8.57; N, 9.27.

7-Aza-8-methoxytricyclo[4.3.0.0^{2,9}]non-7-ene (5). A mixture of 275 mg (2.0 mmol) of **2** and 324 mg (2.18 mmol) of trimethyloxonium fluoroborate in 3 ml of dry methylene chloride was stirred under nitrogen at ambient temperature for 1 hr and then under gentle reflux for 1 hr. The solution was added dropwise to 2 ml of 50% potassium carbonate solution with ice cooling, and the mixture was filtered through glass wool. The inorganic salts were washed with methylene chloride and the combined organic solutions were dried over potassium hydroxide pellets. The solvent was removed and the residue was purified by preparative scale vpc on the above column at 105°. There was isolated 130 mg of **5**: ν_{max}^{neat} 1640 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.30 (m, 1, H_6), 3.80 (s, 3, methyl), 2.10 (m, 1, H_9), and 1.08–2.02 (m, 8).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.53; H, 8.77; N, 9.20.

Reaction of Bicyclo[3.1.0]hex-2-ene with CSI. A stirred solution of 944 mg (11.8 mmol) of **7**[20] in 3 ml of dry methylene chloride was treated with 1.67 g (0.97 ml, 11.8 mmol) of chlorosulfonyl isocyanate under nitrogen at −78°. After 3 hr at −78°, the mixture was kept at ambient temperature for 2 hr and worked up as above to give 839 mg of pale yellow liquid. This material crystallized from acetone–hexane to give 202 mg of white crystals, mp 103–105°. Chromatography of the remaining material on silica gel and elution with ether–hexane (1:1) afforded an additional 205 mg (28% total) of 8-azatricyclo[4.2.0.0^{2,4}]octan-7-one (**8**) as white crystals: mp 105–106°, from acetone–hexane: $\nu_{max}^{CHCl_3}$ 3300 and 1760 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.95 (br, s, 1, >NH), 4.05 (d, J = 4.0 Hz, 1, H_1), 3.34 (m, 1, H_6), 1.33–2.52 (m, 4, methylene and cyclopropyl), 0.50–1.17 (m, 1, cyclopropyl), and −0.13 (m, 1, cyclopropyl).

Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.14; H, 7.35; N, 11.17.

Continued elution of the column with ether gave only traces of additional crystalline material.

Reaction of 1,2,2-Trimethylbicyclo[1.1.0]butane with CSI. A solution of 9.015 g (0.094 mol) of **9**[27,28] in 30 ml of dry methylene chloride was treated as above with 13.3 g (7.85 ml, 0.094 mol) of CSI (2.5 hr, −78°). After hydrolysis and the customary processing, there was obtained 9.19 g of amber oil which was chromatographed on silica gel. Elution with petroleum ether–ether (3:1) afforded 527 mg (4%) of 4,4,5-trimethyl-3-oxabicyclo[3.1.0]hexan-2-one (**11**) as highly hygroscopic white crystals, mp 53–55° (sealed capillary), from pentane: $\nu_{max}^{CHCl_3}$ 1765 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.83–2.20 (m, 1, >C*H*CO–), 1.47, 1.38, 1.30 (s, 3 H each, methyls), and 1.00–1.25 (m, 2, cyclopropyl); calcd *m/e* 140.0837; obsd *m/e* 140.0839.

Elution of the column with petroleum ether–ether (1:1) and ether led to the isolation of 5.71 g (43%) of 4,4,5-trimethyl-3-azabicyclo[3.1.0]hexan-2-one (**10**), white crystals, mp 103–105°, from hexane: $\nu_{max}^{CHCl_3}$ 3310 and 1685 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.85 (br, s, 1, >NH), 1.68 (m, 1, H_1), 1.31 (s, 3, methyl), 1.22 (s, 6, methyls), and 0.67–1.00 (m, 2, cyclopropyl).

Anal. Calcd for $C_8H_{13}NO$: C, 69.03, H, 9.41; N, 10.06. Found: C, 68.97; H, 9.45; N, 9.86.

2-Methoxy-4,4,5-trimethyl-3-azabicyclo[3.1.0]hex-2-ene (12). A solution of 139 mg (1.0 mmol) of **10** in 2 ml of methylene chloride was added dropwise under nitrogen to a stirred suspension of 152 mg (1.03 mmol) of trimethyloxonium fluoroborate in 2 ml of the same solvent. The mixture was stirred at ambient temperature for 12 hr, the solvent was evaporated, and the residual solid was recrystallized from methylene chloride–ether. There was obtained 156 mg (65%) of the fluoroboric acid salt of **12** as white crystals: mp 123–124°; $\nu_{max}^{CH_2Cl_2}$ 3170 (broad), 1640, and 1055 cm^{-1} (broad).

Anal. Calcd for $C_9H_{16}BF_4NO$: C, 44.84; H, 6.69; N, 5.81 Found: C, 44.99; H, 6.67; N, 5.82.

A 104-mg sample of this substance was dissolved in methylene chloride and added with stirring to 1 ml of 50% potassium carbonate solution. The customary work-up gave 41 mg of colorless liquid possessing a sharp odor: $\delta_{TMS}^{CDCl_3}$ 3.73 (s, 3, methoxyl), 1.86 (d of d, J = 8.0 and 3.0 Hz, 1, H_1), 1.23 (s, 9, methyls), and 0.70 (m, 2, cyclopropyl).

1,2,2-Trimethyl-3-azabicyclo[3.1.0]hexane (13). A mixture of 400 mg (2.88 mmol) of **10** and 400 mg of lithium aluminum hydride in 15 ml of anhydrous ether was stirred at ambient temperature for 21 hr. The excess reducing agent was decomposed by dropwise addition of 4 *N* sodium hydroxide solution at 0°. The ether phase was decanted and the sludge was repeatedly extracted with additional ether. The combined organic layers were dried and evaporated, and the residue (372 mg) was partitioned between ether

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and 2 *N* sulfuric acid. Evaporation of the dried ether phase gave 16 mg (4% recovery) of **10**.

The acidic solution was rendered alkaline and extracted with ether. Evaporation of the dried ether solution afforded 339 mg (94%) of **13** (88% pure by vpc analysis). Preparative scale vpc purification on a 12 ft × 0.25 in. column packed with 20% Apiezon L/KOH (4:1) on 60–80 mesh Chromosorb W gave **13** as a colorless liquid: ν_{max}^{neat} 3210 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 2.98 (d of d, J = 11.0 and 3.0 Hz, 1, endo methylene), 2.62 (d, J = 11.0 Hz, 1, exo methylene), 1.80 (s, 1, >NH), 1.11 (s, 3, methyl), 1.07 (s, 6, methyls), 0.90–1.20 (m, 1, cyclopropyl), and 0.0–0.50 (m, 2, cyclopropyl).

Anal. Calcd for $C_8H_{15}N$: C, 76.74; H, 12.08. Found: C, C, 76.39; H, 12.00.

1,4,4,5-Tetramethyl-3-azabicyclo[3.1.0]hexan-2-one (15). A solution of 835 mg (7.5 mmol) of 1,2,2,3-tetramethylbicyclobutane (**14**)[28] in 30 ml of dry methylene chloride cooled to −78° was treated dropwise with a solution of 1.06 g (7.5 mmol) of CSI in methylene chloride (30 ml). After 4.5 hr, the solvent was evaporated under reduced pressure and the resulting pale yellow oil was triturated with ether to give 1.8 g of almost colorless crystals. This product was dissolved in acetone (5 ml) and the solution cooled to 0°. Thiophenol (1.8 g) in acetone (5 ml) was added, followed by the dropwise addition of pyridine (0.8 g) in acetone (10 ml). This mixture was stirred at 0° for 15 min and then water (50 ml) added. The pale yellow solid obtained from the organic phase was chromatographed on Florisil. Pentane–benzene (1:1) elution removed the diphenyl disulfide, whereas chloroform elution furnished 585 mg (51%) of **15** as colorless prisms, mp 137–137.5°, from methylene chloride–hexane: $\nu_{max}^{CHCl_3}$ 3390, 3190, and 1685 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 1.27 (s, 6, methyls), 1.23 and 1.19 (s, 3 H each, methyls), 0.91 and 0.49 (d, J = 4 Hz, 1H each, cyclopropyls).

Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.53; H, 9.84; N, 9.14.

1,4-Dimethyl-2-azabicyclo[2.1.1]hexan-3-one (17). 1,3-Dimethylbicyclo[1.1.0]butane[31] (1.57 g, 0.019 mol) was dissolved in 25 ml of dry methylene chloride (previously treated with basic alumina) and the solution was cooled to −78°. CSI (2.82 g, 0.02 mol) in the same solvent (30 ml) was added dropwise with stirring during 0.5 hr under nitrogen. The solution was stirred at −78° for 4 hr and at 0° for an additional 2 hr. The solvent was evaporated under reduced pressure at 25°, the pale brown oily residue was dissolved in acetone (15 ml), and this solution was treated with thiophenol (0.04 mol) and pyridine (0.025 mol) in the usual way. The resulting pale yellow oil was chromatographed on Florisil and elution with ether afforded 370 mg (15.5%) of **17** which was molecularly distilled and recrystallized from methylene chloride–pentane at 0° to give colorless prisms: mp 74.5–75°; $\nu_{max}^{CHCl_3}$ 1745 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.70 (br s, 1, >NH), 1.75–2.47 (m, 4, methylenes), 1.31 and 1.20 (s, 3 each, methyls).

Anal. Calcd for $C_7H_{11}NO$: C, 67.16; H, 8.86; N, 11.19. Found: C, 67.33; H, 8.89; N, 11.24.

Reaction of Bicyclo[2.1.0]pentane with CSI. A solution of 953 mg (14 mmol) of **18**[32] in 10 ml of dry methylene chloride cooled to −78° was treated dropwise with a solution of 1.99 g (1.17 ml, 14 mmol) of CSI in 2 ml of the same solvent. After 1 hr at −78°, the solution was stirred at room temperature for 5 hr, evaporated, and hydrolyzed with 4 *N* sodium hydroxide in aqueous acetone as before. Processing of the methylene chloride extracts and chromatography on silica gel afforded 480 mg (31%) of 2-azabicyclo[2.2.1]-heptan-3-one (**19**) as a colorless liquid which crystallized on cooling: mp 32–33° (lit.[18] mp 32–34°); ν_{max}^{neat} 3225 and 1745 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 7.00 (br s, 1, >NH), 4.09 (m, 1, >C*H*–N<), 3.51 (m, 1, >C*H*CO–), and 1.10–2.20 (m, 6, methylene).

Continuous extraction of the aqueous phase with methylene chloride for 3 days yielded 80 mg (7%) of cyclopentene-3-carboxamide, mp 136°, from methylene chloride (lit.[18] mp 135–137°): $\delta_{TMS}^{CDCl_3}$ *ca.* 5.8 (br m, 2, –NH_2), 5.62–5.90 (m, 2, vinyl), 3.38 (1, >C*H*CO–), and 1.73–2.61 (m, 4, methylene).

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α-Halo Sulfones. XVII. Directive Effects in the Chlorination of Thiapropellanes[1]

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Abstract: To probe the role of steric effects operative in the α-chlorination of sulfides, six thiapropellanes were exposed to the action of *N*-chlorosuccinimide and subsequently oxidized. Where applicable, the isomeric α-chloro sulfones were separated and their ratio in the product mixtures was determined. The configurations of the chlorine substituents, assigned initially on the basis of nmr correlations, were confirmed by X-ray structure analysis of two representative examples. The observed product distributions appear not to be due exclusively to steric factors, although such considerations are of considerable importance. Rather, the data suggest that electronic effects gain significance in those examples which have sites of unsaturation in close proximity to the developing sulfonium ion.

The synthetic scheme developed in this laboratory for the preparation of unsaturated propellanes endowed with at least one cyclobutene ring[5–7] depends upon the base-induced rearrangement of appropriate

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