39-882 (8-56)   **6-56**   **PRE-CAULIN**   **3-39**
 # 12.A1 E1.21 **# R1.12 E1.21**   **# R1.12 11.A1**

4-33   **51-1093 (37-655)37-655 (7-53)**   **7-53**
 # 11.A1 11.A1   **# A1.11 A1.11**   **# 21.E1 E1.21**   **R2.11**

Figure 8. Selected reactions from ptilocaulin syntheses.

additions followed by cleavage of one of the two bonds so created, but the average weight ratio for the group C cleavage routes in general is larger than in A and B and so tends to justify our basis of not generating such routes.

The final group (D) of ten syntheses is a miscellaneous collection of routes not produced by SYNGEN for clear reasons, the main one being that they are not nominally convergent, i.e., the last one or two constructions do not join two pieces (A and B) of three or more carbons. This group has the worst average weight ratio. The simplest overall conclusion is that the best of the published syntheses (in terms of the criterion of economy) are directly generated by the program, and that, specifically, the 13 group A syntheses which are all generated, average better in calculated weight ratios than those not produced by SYNGEN. The program of course also offers some interesting synthetic ideas not mirrored in the published group, several of which are collected as group E in Figure 7.

C. Ptilocaulin. The Snider synthesis[32] of ptilocautin also exemplifies a sequential construction route to a precursor labeled

"pre-caulin" in Figure 8. Using this as target SYNGEN produced nine first-level bondsets with 26 primary annelations (32 equivalents), among them the Snider synthesis, which is 39–682 → 8–56 → pre-caulin. Other bondsets are represented in the first-level annelations 3–30, 4–33, and 7–53, which also yield pre-caulin via the reactions labeled, the last (7–53) being a reductive alkylation of an intermediate which was in turn created by the only double affixation found for the target. This sequence, an aldol-Michael combination, is shown as 51–1093 → 37–655 → 7–53 → pre-caulin.

VI. Summary

The SYNGEN program was written to fit the requirements and protocol outlined at the outset, and it proves itself by producing known and reasonable syntheses. It operates within specific constraints without user intervention and assesses all possible paths within these constraints. Basically, the constraints are the following: (1) skeletal dissection into ordered bondset families which exhibit convergent assembly of synthons; (2) generation of consecutive constructions from real starting materials for each bondset. In order to avoid the necessity of a library of reactions, the reactions here are generated from broad mechanistic guidelines. To encompass all possibilities, the functionality is abstracted to a digital format ($z\pi$ at each carbon) and all reactions generated by adding $\Delta z\pi$-list operators all possible ways to product $z\pi$-lists. When extensive output appears it may be sorted and selected by the user in numerous ways to facilitate examination, using the SYNOUT program.

The intent of the program is to provide an optimal set of all the shortest, convergent syntheses. These can then serve as standards against which syntheses invented by practicing chemists may be compared.

(30) Wenkert, E.; Mueller, A.; Reardon, E. J.; Sathe, S. S.; Scharf, D. J.; Tosi, G. *J. Am. Chem. Soc.* **1970,** *92,* 7428.

(31) Weinreb, S. M.; Cvetovich, R. J. *Tetrahedron Lett.* **1983,** 861; *J. Am. Chem. Soc.* **1984,** *106,* 1443.

(32) Snider, B.; B.; Faith, W. C. *Tetrahedron Lett.* **1983,** 861; *J. Am. Chem. Soc.* **1984,** *106,* 1443.

Vinyl Cations. 42. Synthesis and Solvolysis of Substituted 1-Cyclobutenyl Nonaflates[1]

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Abstract: The 2-, 3- and 4-substituted as well as bicyclic nonaflates **19–27** were prepared by treating the corresponding cyclobutanones with nonafluorobutanesulfonic acid anhydride in the presence of 2,6-di-*tert*-butyl-4-methylpyridine as the buffer. Some of the substituted cyclobutanones were prepared by slight modification of the reported procedures. The kinetic and product studies of the 1-cyclobutenyl nonaflates were carried out in TFE–water mixtures. The solvolysis of all the 1-cyclobutenyl nonaflates is shown to proceed by an S_N1 mechanism involving nonclassical 1-cyclobutenyl cations **58**, which can rearrange to the cyclopropylidenemethyl (**59**) and homopropargyl ions **61** and **62**. The solvolysis products are derived by nucleophilic substitution of the solvent with one or more of the cations **58–62**. The kinetics of the nonaflates **19–27** indicate that the rate of solvolysis is strongly dependent on the substituent pattern of the cyclobutenyl system. The substituent effects are interpreted with the formation of the nonclassical structure **58** for the derived cation, with positive charges at C-2 and C-3.

1-Cyclobutenyl nonaflate (**1**)[2] solvolyzes in the highly ionizing and slightly nucleophilic solvent 2,2,2-trifluoroethanol (TFE) with a surprisingly high rate constant[3,4] via an S_N1 mechanism with

the formation of four-membered ring products **2** and **3** only.[2,5] According to ab initio and MINDO/3 calculations, the reactive intermediate formed during the solvolysis reaction, the 1-cyclobutenyl cation **4**, has a bridged nonclassical structure in which

(1) Vinyl cations part 41: Collins, C. J.; Hanack, M.; Stutz, H.; Auchter, G.; Schoberth, W. *J. Org. Chem.* **1983,** *48,* 5263.

(2) (a) Subramanian, L. R.; Hanack, M. *Angew. Chem.* **1972,** *84,* 714; *Angew. Chem., Int. Ed. Engl.* **1972,** *11,* 714. (b) Subramanian, L. R.; Hanack, M. *J. Org. Chem.* **1977,** *42,* 174.

(3) Subramanian, L. R.; Hanack, M. *Chem. Ber.* **1972,** *105,* 1465.

(4) Stang, P. J.; Rappoport, Z.; Hanack, M.; Subramanian, L. R. "Vinyl Cations"; Academic Press: New York, 1979.

(5) Hanack, M.; Carnahan, E. J.; Krowczynski, A.; Schobert, W.; Subramanian, L. R.; Subramanian, K. *J. Am. Chem. Soc.* **1979,** *101,* 100.
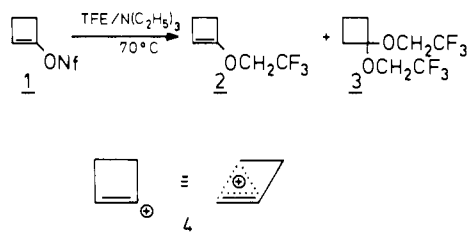
C-3 is equidistant from C-1 and C-2 (due to interaction of the C-2–C-3 σ bond with the vacant p orbital at C-1).[6]

1-Cyclobutenyl cations **10** also occur during the solvolysis of cyclopropylidenemethyl bromides **12** and 3-butynyl (homopropargyl) derivatives **5**[7] (Scheme I). In spite of the different starting materials, the solvolyses of **5**, **9** and **12** give comparable product compositions; predominantly the products **13–18** are formed. We explain this with an equilibrium between the vinyl cations **10** and **11** (Scheme I).[4,5,8–11]

Often in the solvolysis of **9** and **12**, the open-chain products **7** and **8** are also found. This could be explained by assuming that a third ion, the homopropargyl cation **6**, is also involved in the equilibrium of the reactive intermediates. However, such a primary carbenium ion should be very unstable.[11]

We report here on the syntheses and solvolyzes of 3-isopropyl- (**19**), 4-methyl- (**20**), 2,3-dimethyl- (**21**), and 2,4-dimethyl-1-cyclobutenyl nonaflates (**22**) as well as on the bicyclic 1-cyclobutenyl nonaflates **23–27**.
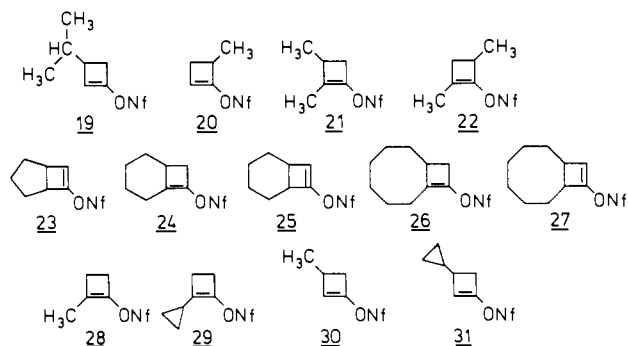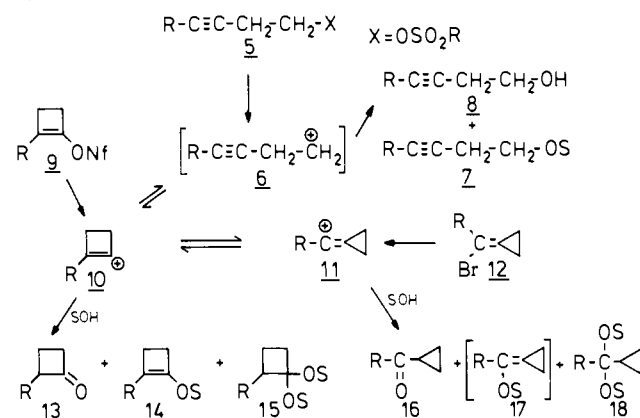

Syntheses

All 1-cyclobutenyl nonaflates used here were prepared[12] from the corresponding cyclobutanones **32** by treatment with nonafluorobutanesulfonic anhydride in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (**33**) as the buffer.[12b] Isomeric nonaflates **35** and **36** are formed if the
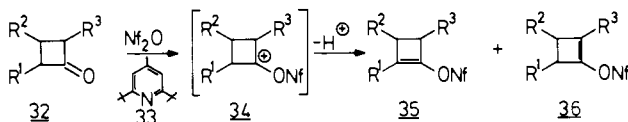
substituents in the starting ketone **32** are different. In all cases, the thermodynamically more stable nonaflates are formed predominantly.

The starting cyclobutanones were prepared according to literature procedures. 2-Cyclopropylcyclobutanone (**39**), 3-isopropylcyclobutanone (**40**), and 2,4-dimethylcyclobutanone (**41**) were, however, prepared in a more convenient manner as given in Scheme II by a variation of the
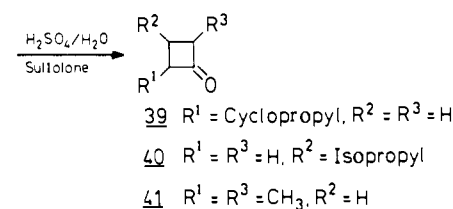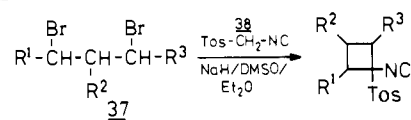
(6) Apeloig, Y.; Collins, J. B.; Cremer, D.; Bally, T.; Haselbach, E.; Pople, J. A.; Chandrasekhar, J.; Schleyer, P.v.R. *J. Org. Chem.* **1980**, *45*, 3496.
(7) (a) Hanack, M.; Bocher, S.; Herterich, I.; Hummel, K.; Vött, V. *Liebigs Ann. Chem.* **1970**, *733*, 5. (b) Hanack, M.; Bässler, T.; Eymann, W.; Heyd, W. E.; Kopp, R. *J. Am. Chem. Soc.* **1974**, *96*, 6686.
(8) Auchter, G.; Hanack, M. *Chem. Ber.* **1982**, *115*, 3402.
(9) Collins, C. J.; Hanack, M.; Stutz, H.; Auchter, G.; Schobert, W. *J. Org. Chem.* **1983**, *48*, 5260.
(10) Hanack, M.; Collins, C. J.; Stutz, H.; Benjamin, B. M. *J. Am. Chem. Soc.* **1981**, *103*, 2356.
(11) (a) Franke, W.; Schwarz, H.; Stahl, P. *J. Org. Chem.* **1980**, *45*, 3493. (b) Franke, W.; Schwarz, H. *J. Org. Chem.* **1981**, *46*, 2806.
(12) (a) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1975**, 255. (b) Hanack, M.; Hassdenteufel, J. R. *Chem. Ber.* **1982**, *115*.

Scheme I

Scheme II

39 R¹ = Cyclopropyl, R² = R³ = H

40 R¹ = R³ = H, R² = Isopropyl

41 R¹ = R³ = CH₃, R² = H

Table I. Absolute and Relative Rates of Solvolysis of Substituted 1-Cyclobutenyl Nonaflates in 80% TFE

nonaflate	temp, °C	$10^4 k$, s^{-1}	k_{rel} (70 °C)	H^*
1	70	0.152 ± 0.02^a	1	23.6
28	50	12.28 ± 0.14^a	600	20.2
30	50	0.301 ± 0.02	17	22.8
	70	2.52 ± 0.04		
20	70	1.4 ± 0.4	10	
29	50	8.74 ± 0.02	450	
31	50	0.281 ± 0.1	14	21.8
	70	2.09 ± 0.04		
19	50	0.252 ± 0.04	14	22.8
	70	2.10 ± 0.04		
21	30	28.5 ± 0.4	1 × 10⁴	
22	30	17.6 ± 0.5	5.5 × 10³	
23	30	2.3 ± 0.4	900	20.6
	50	20.26 ± 0.4		
24	15	70	4 × 10⁴	
25	30	3.05 ± 0.4	1.1 × 10³	
26	30	45	1.3 × 10⁴	
27	30	0.95 ± 0.4	400	

^{a} Measured in ethanol–water.

method developed by van Leusen.[13,14]

Solvolysis Results

1. Kinetic Studies. The reaction rates of all synthesized nonaflates in 80% trifluoroethanol were determined by automatic potentiometric titration.[15] The first-order rate constants are given in Table I. To estimate the relative rate ratios, some rates were extrapolated graphically or numerically to a solvolysis temperature of 70 °C. The relative solvolysis rates of differently substituted 1-cyclobutenyl nonaflates are very dependent on the substituents. The more stable the presumed cationic intermediates, the higher

(13) van Leusen, D.; van Leusen, A. M. *Synthesis* **1980**, 325.
(14) Machinek, R.; Lüttke, W. *Synthesis* **1975**, 255.
(15) Schneider, H.-J.; Schneider-Bernlöhr, H.; Hanack, M. *Liebigs Ann. Chem.* **1969**, *722*, 234.

were the observed reaction rates.

Methyl and cyclopropyl substituents at C-2 in **28** and **29** increase the solvolysis rate by a factor of 600 and 450, respectively, as compared to the unsubstituted 1-cyclobutenyl nonaflate (**1**). The same substituents at C-3 in **30** and **31** increase the rate by a factor of only 17 and 14, respectively.

The stabilizing effects of the electron-donating substituents methyl and cyclopropyl in the 2- or 3-positions of the 1-cyclobutenyl nonaflates show that the cyclobutenyl cations **42** carry a partial positive charge at C-2 and C-3, as expected for nonclassical structures. A rate-accelerating steric effect is partially responsible for the increase in the rate constant of the C-2-substituted 1-cyclobutenyl nonaflate as compared to the C-3 derivatives.

For comparison, the solvolysis rate of the 4-methyl-substituted 1-cyclobutenyl nonaflate **20** was also measured. **20** solvolyzes 10 times faster than the unsubstituted derivative **1**. This value is typical for the steric effect of a leaving group closer to the methyl substituent.[16] It signifies the importance of the substituent effect in the 3-position of the 1-cyclobutenyl cation, where a rate-accelerating steric effect is not possible.

The cyclopropyl-substituted 1-cyclobutenyl nonaflates **29** and **31** solvolyze somewhat more slowly than the methyl-substituted analogues **28** and **30** (Table I), although the cyclopropyl substituent in general stabilizes the positive charge distinctly better than the methyl group. This difference however is effective only when the cyclopropyl group can stabilize the cationic intermediate through its mesomeric effect.[17] Presumably the partial positive charge on C-2 and C-3 of the nonclassical cation **42** does not

R2 R3
R1 ONf   ———>
35   **42**
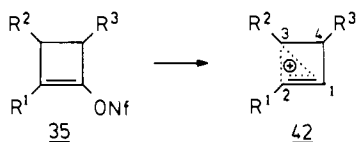
possess the favorable orbital geometry needed for an overlap with the orbitals of the three-membered ring. In other words, only inductive stabilization is possible.

When both methyl and cyclopropyl substituents exert solely their inductive effects, then the stabilizing effect of a methyl group toward a positive charge is slightly higher than that of the cyclopropyl substituent.[17] This explains the somewhat higher rate of solvolysis of methyl-substituted cyclobutenyl nonaflates as compared to cyclopropyl-substituted analogues.

The accelerating effects of the isopropyl and cyclopropyl substituents, at C-3 in **19** and **31**, with respect to **1**, respectively, are identical (both are 14).

The dimethyl-substituted 1-cyclobutenyl nonaflates **21** and **22** solvolyze by factors of 10.000 and 5.500 faster, respectively, than **1**. These values are exactly the multiplied values obtained, from the accelerating effects of 600, 17, or 10 for the 2-, 3-, and 4-methyl groups.

The 1-cyclobutenyl cations formed from the bicyclic 1-cyclobutenyl nonaflates **24** and **26** are alkyl-substituted at C-2 and C-3 similar to the cation produced from **21**. However, the relative solvolysis rates of **24** and **26** are higher than that of **21**. This can best be explained by the high ring strain of the bicyclic 1-cyclobutenyl nonaflates. The increasing ring strain increases the p character of the four-membered-ring σ bonds, which possibly produces a better interaction of the C-2–C-3 σ bond of the nonclassical 1-cyclobutenyl cation with the vacant p orbital at C-1. Moreover, the 1-cyclobutenyl nonaflates already possess a higher ground-state energy, which makes the separation of a leaving group easier. The ring strain distinctly increases from **26** to **24**, and the relative reactivity of these bicyclic nonaflates is consistent with this difference. The relative solvolysis rate of the 1-cyclobutenyl nonaflates **23**, **25**, and **27** vs. **1** are 900, 1100, and 400, respectively,

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(16) Pfeifer, W. D.; Bahn, C. A.; Schleyer, P.v.R.; Bocher, S.; Harding, C. E.; Hummel, K.; Hanack, M.; Stang, P. C. *J. Am. Chem. Soc.* **1971**, *93*, 1513.

(17) Brown, H. C.; Cleveland, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 2051.

Table II. Solvolysis Products of 2-Substituted 1-Cyclobutenyl Nonaflates **28** and **29** in Absolute Trifluoroethanol Buffered with Triethylamine

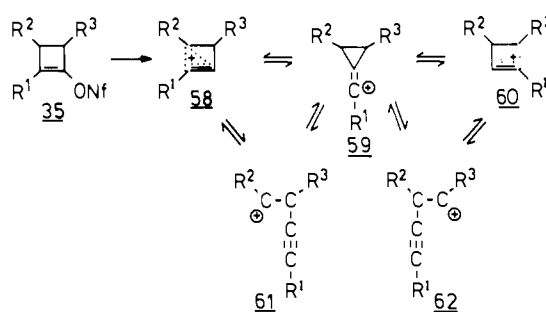| nonaflate	products, %			
	43	44	45 = (16)	46
28^{a,b}	95			3 (a, R = CH$_3$)
29^c	11	77^d	7^d	5 (b, R = cyclopropyl)

^{a} Solvolysis temperature: 50 °C. ^{b} 2% unidentified products. ^{c} Solvolysis temperature: 25 °C. ^{d} The ratio of dicyclopropylbis(2,2,2-trifluoroethoxy)methane (**44**) to dicyclopropyl ketone (**45**) changes with GC condition, whereby the total sum of the products remains constant. Probably **45** is formed from **44** during GC analysis.

Table III. Solvolysis Products of Unsubstituted Cyclobutenyl Nonaflate (**1**) and the 3-Substituted Cyclobutenyl Nonaflates **19**, **30**, and **31** in Trifluoroethanol Buffered with Triethylamine at 70 °C

non-aflate	products,^{d} %				
	47	48	49	50	unidentified
1	90^a				
19	31		66^b		c
30	34	1	63	1	1.5
31			87	1	12

^{a} 1,1-Bis(2,2,2-trifluoroethoxy)cyclobutane^2 is also formed to an extent of 10%. ^{b} Besides **49b**, other rearranged homopropargyl products were also formed (see Scheme V). ^{c} 3% of rearranged cyclobutenyl trifluoroether **66** was also formed. ^{d} **a**, R = H; **b**, R = i-C$_3$H$_7$; **c**, R = CH$_3$; **d**, R = cyclopropyl.

Scheme III

R2 R3
R1 ONf
35   ——>   R1 **58** ⇌   **59** ⇌   **60**
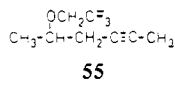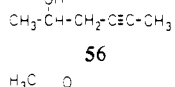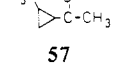
61   **62**
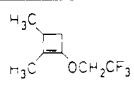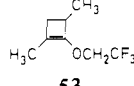
higher than the multiplicative effects that would have resulted for the correspondingly dialkyl-substituted cyclobutenyl nonaflates. This also must be due to ring strain.

2. Solvolysis Products. For an estimation of the solvolysis products, all synthesized 1-cyclobutenyl nonaflates were solvolyzed in a 100-fold excess of trifluoroethanol in the presence of triethylamine as the buffer. The solvolyses were monitored till completion of the reaction, and the product composition was determined by GC. Further heating of the solvolysis mixture after completion of the reaction showed no change in the product composition, indicating that the solvolysis products are stable under the reaction conditions. The products were identified and separated by GC.

The solvolysis products are listed in Tables II–IV; they were produced formally by the reaction of the equilibrating isomeric cations **58**–**62** (Scheme III) with the solvent. The product composition is found to be strongly dependent on the substitution.

No rearranged products were observed in the solvolysis of unsubstituted 1-cyclobutenyl nonaflate (**1**) in absolute trifluoroethanol. However, the product composition of the other 1-cyclobutenyl nonaflates **35** shows that, in the case of stabilizing substituents at the C-2 position, the rearrangement of the cyclobutenyl cation **58** to the cyclopropylidenemethyl cation **59**

Substituted 1-Cyclobutenyl Nonaflates

J. Am. Chem. Soc., Vol. 107, No. 18, 1985 5241

Table IV. Solvolysis Products of Dimethyl-Substituted Cyclobutenyl Nonaflates **21** and **22** in Absolute TFE and 80% TFE Buffered with Triethylamine at 25 °C

products	21 in abs TFE	21 in 80% TFE	22 in abs TFE	22 in 80% TFE
51	35	13	32.5	14
52		9/11		4/12
53	10	4	13	8
54 (cis/trans)		7/2		6/2
55	54	22	54.5	24
56		32		28
57		1		1
Σ**72**[a]	89	87	87	82
Σ**74**[b]	10	13	13	16

[a] Sum of subsequent products from cation **72**. [b] Sum of subsequent products from cation **74**.

occurs, while the C-3-substituted analogues favor the above rearrangement via the nonclassical structure **58** to the homopropargyl compounds **61**.

The effect of the cyclopropyl group is thereby significantly larger than that of the methyl or isopropyl group. The known stabilizing effect of the positive charge in the α position of the three-membered ring is responsible for the stability of cyclopropylidenemethyl cations **59a** (R[1] = cyclopropyl, R[2] = R[3] = H) and **59b** (R[2] = cyclopropyl, R[1] = R[3] = H). Therefore, **44b** and **49d** are the main solvolysis products of the 1-cyclobutenyl nonaflates **29** and **31** (see Tables II and III).

2- and 3-methyl-substituted 1-cyclobutenyl cations are less prone to rearrangement. In the case of the solvolysis of **30**, the products from homopropargyl cations **61** (R[2] = CH$_3$, R[1] = R[3] = H) and the isomeric cyclopropylidenemethyl cations **59** are formed in a ratio of 2:1, while for **28** no products from cyclopropylidenemethyl cations **59** (R[1] = CH$_3$, R[2] = R[3] = H) were found. However, in the solvolysis of **30** in 80% TFE, the cyclopropylmethyl ketone **45a** is formed in 2% yield.

The rearrangement tendency of 3-substituted cyclobutenyl cations (from the nonaflates **19**, **30**, and **31**) is greater than the tendency of the 2-substituted derivatives (i.e., from the nonaflates **28** and **29**). This points to a relatively high stability of a "saturated" carbenium ion, which exists in the equilibrium among the related intermediates. The 1-methyl-3-butynyl cation **61** (R[2] = CH$_3$, R[1] = R[3] = H) is obviously more stable than the isomeric 1-cyclobutenyl cation **58**. As the solvolysis products of **28** show, 2-alkyl-substituted 1-cyclobutenyl cations are probably more stable than the corresponding cyclopropylidenemethyl cation.

The homopropargyl compounds **46** (Table II) are formally the products derived from the primary carbenium ions **61** (R[2] = H). If the existence of this unstable intermediate in the equilibrium is excluded, then the formation of **46a** and **46b** can be explained by a nucleophilic attack of the solvent at C-3 of the first-formed

Scheme IV

Nu = Nucleophile
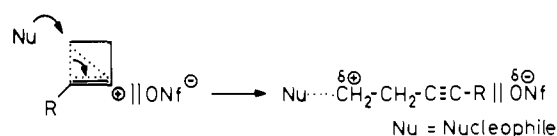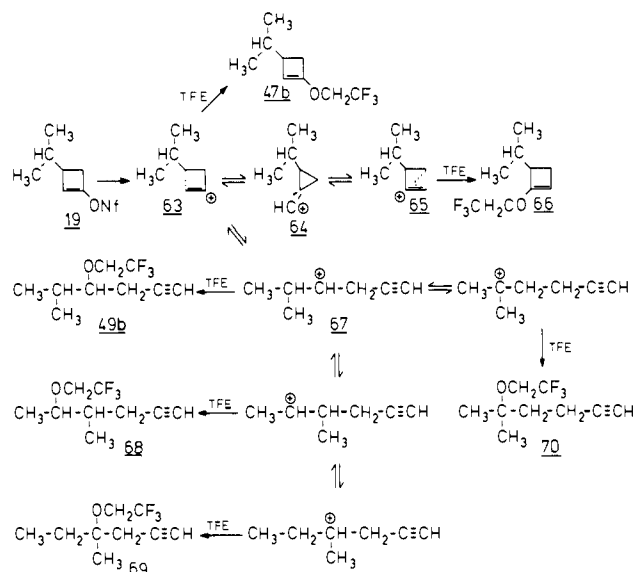
Scheme V

1-cyclobutenyl cation with subsequent ring opening according to Scheme IV. In the reaction shown in Scheme IV, disubstituted alkynes were formed, which are more stable than alkynes with a terminal triple bond, produced from 3-substituted cyclobutenyl nonaflate. The C-2, C-3 σ bond accordingly is better suited as a "leaving group" in 2-substituted 1-cyclobutenyl nonaflates, and therefore homopropargyl products are also formed in less nucleophilic solvents like TFE, in contrast to the unsubstituted 1-cyclobutenyl nonaflate (**1**). It could be shown, however, that homopropargyl products are also formed in the solvolysis of the unsubstituted 1-cyclobutenyl nonaflate (**1**) in strong nucleophilic solvents like ethanol/water.[2b,5]

The product composition from the solvolysis of 3-isopropyl-1-cyclobutenyl nonaflate (**19**) is of special interest. In this case, trifluoroethyl ethers **68–70** (Scheme V) are also formed besides **49b** (Table III). These are products from carbenium ions (Scheme V) formed from the initial homopropargyl cation **67** via a Wagner–Meerwein rearrangement and a subsequent 1,2-hydride shift. The total yield of the open-chain trifluoroethyl ethers **49b** and **68–70** from the solvolysis of **19** is about 66%, which is about the same as that of **49c** obtained from the solvolysis of **30**.

The observed rearrangement of **67** shows that this ion is actually present in the solvolysis mixture; i.e., in the case of 3-substituted 1-cyclobutenyl nonaflates, the homopropargyl products are not formed, at least to any great extent, from the above described nucleophilic attack at C-3 of 1-cyclobutenyl cations. A rearrangement of a C-3 isomer to a C-2 isomer, revealed by the isolation of 2-isopropylcyclobutenyl trifluoromethyl ether (**66**) from the solvolysis of 3-isopropylcyclobutenyl nonaflate (**19**), is observed for the first time. The rearrangement occurs via the cyclopropylidenemethyl cation **64** as an intermediate. However, the product ratio of C-3 isomer **47b** to C-2 isomer **66** shows that the cation **65** is less stable than the cation **63**, because the stabilizing substituent is at the C-4 position and does not contribute directly to the stabilization of the positive charge.

The dimethyl-substituted nonaflates **21** and **22** solvolyze in absolute TFE and TFE/water to give the same solvolysis products **51–57** in similar product ratios (Table IV). The proportion of homopropargyl products **55** and **56** is about the same as that from the solvolysis of 3-methyl-1-cyclobutenyl nonaflate (**30**), and the proportion of three-membered ring ketone **57** corresponds to that obtained from the solvolysis of 2-methyl-1-cyclobutenyl nonaflate

Scheme VI
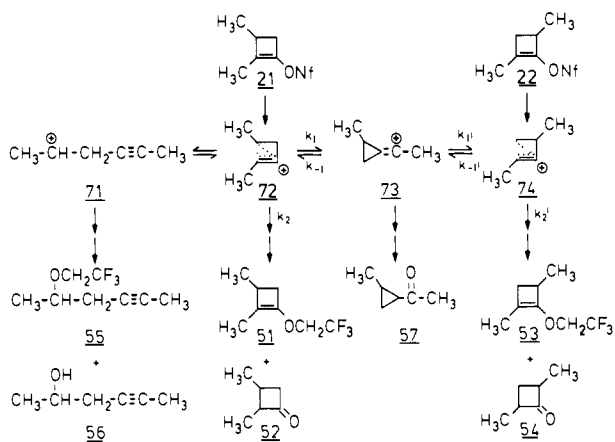
(28). As to be expected, the methyl group, which is not close to the vacant p orbital in the corresponding intermediates has no effect on the distribution of the products. 2,3- As well as 2,4-disubstituted enol ethers **51** and **53** and the corresponding cyclobutanones **52** and **54** are formed from the solvolysis of both the nonaflates **21** and **22**. This can only be explained as given in Scheme VI involving the equilibrium of both the 1-cyclobutenyl cations **72** and **74** via the cyclopropane intermediate **73** (Scheme VI).

The proportion of 2,3-disubstituted four-membered products **51** and **52** from both the nonaflates **21** and **22** was found to be 2–3 times higher than the 2,4-disubstituted products **53** and **54**. Also, the compounds **55** and **56** were formed from the cation **72**, which can rearrange to the homopropargyl cation **71**. A corresponding rearrangement of **74** does not take place, because this would lead to an unstable primary carbenium ion.
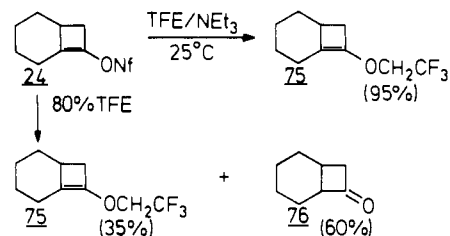
To summarize the situation for nonaflates **21** and **22** (Table IV), products from the 1-cyclobutenyl cation **72** substituted in the 2- and 3-positions were found in preponderance; i.e., the equilibrium of **72** ⇌ **74** lies clearly on the side of **72**. These results are in accord with nonclassical structures for the 1-cyclobutenyl cations: a methyl substituent in the 4-position has little influence on the stabilization of the cations, while the methyl group in the 3-position is situated directly at a carbon atom with partial positive charge whereby the inductive effect predominates.[18-20]

As seen from Table IV, the solvolysis of **21** and **22** does not give the same product mixture. For each, there is a small tendency toward the formation of products from those 1-cyclobutenyl cations, as can be seen arise directly from the corresponding 1-cyclobutenyl nonaflates. This allows a qualitative statement to be made on the relative magnitude of the rate constants k_1 and k_2 in Scheme VI. The reactive intermediates rearrange faster than they undergo substitution reaction to form solvolysis products.

The solvolysis reactions of the rest of the 1-cyclobutenyl nonaflates studied can be explained as follows.

During the solvolysis of 2-substituted 1-cyclobutenyl nonaflates, both the possible cyclobutenyl cations as well as the corresponding cyclopropylidenemethyl cations are always formed. For 1-cyclobutenyl nonaflates which do not carry a substituent at C-2, the cyclopropylidenemethyl intermediates are much less stable; i.e., the equilibration of 1-cyclobutenyl cations cannot compete with the substitution reaction of these cations. The formation of product **66** (Scheme V) from the solvolysis of **19** shows that the C-2-unsubstituted 1-cyclobutenyl cation **63** can also rearrange to the isomeric 1-cyclobutenyl cation **65**.[10]

In the solvolysis of bicyclo[4.2.0]oct-1(8)en-8-yl nonaflate (**24**) in absolute TFE and 80% TFE, only the unrearranged products, trifluoroethyl ether **75** and the ketone **76**, respectively, were formed. Bicyclo[6.2.0]dec-1(10)-en-10-yl nonaflate (**26**) could be solvolyzed only as a mixture with its isomer **27**. Because **26**

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possesses a much higher reactivity compared to **27** (cf. Table I), one could follow the formation of the solvolysis products by GC and assign the products to the corresponding 1-cyclobutenyl nonaflates. This assignment was confirmed by the isolation of **27** by preparative GC and its independent solvolysis (see below). The
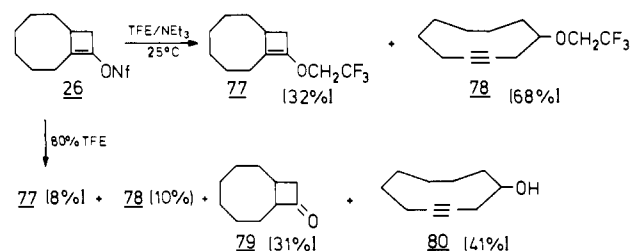

products **77–80** were identified by GC/MS as well as by the comparison of GC retention times with authentic samples in the cases of **78** and **80**.

The composition of the solvolysis products from **24** and **26** shows a clear dependence on the size of the annulated ring in the 2,3-position of cyclobutenyl cations. The bicyclo[4.2.0]octenyl nonaflate **24** gives exclusively products from 1-cyclobutenyl cation **81a**, while in the case of bicyclo[6.2.0]decenyl nonaflate (**26**),
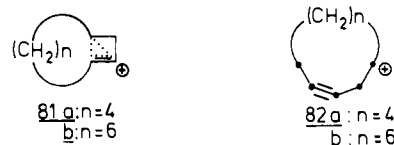
mostly products from the 10-ring homopropargyl cation **82b** are formed. No three-membered ring products were found in either case. The ratio of 4-ring products to homopropargyl products in the solvolysis of **26** is about the same as the one obtained in the solvolysis of 2,3-disubstituted cyclobutenyl nonaflates **21** and **22**. The rearrangement of **81** to **82**, which is not hindered in the bicyclo[6.2.0] system, does not take place however in the case of the bicyclo[4.2.0] system. Evidently the transition state which will lead to the formation of 3-cyclooctynyl cation **82a** is energetically so high that a rearrangement to this cation is no longer possible. The solvolysis of bicyclo[3.2.0]hept-6-en-6-yl nonaflate (**23**) in absolute TFE or 80% TFE also gives nonrearranged products **83**, **85**, and the homopropargyl derivatives **84** and **86**.
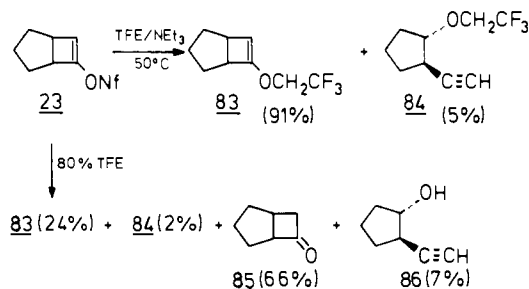
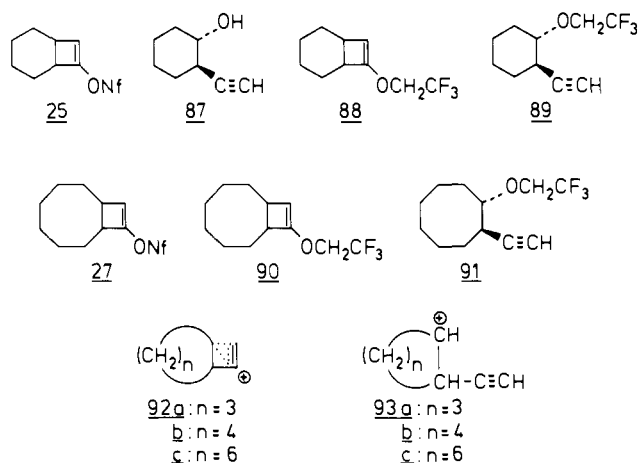The solvolysis of bicyclo[4.2.0]oct-7-en-7-yl nonaflate (**25**) in absolute TFE at room temperature gave two products, the MS of which corresponds to TFE ethers. A solvolysis in 80% TFE gave the same products, in addition to bicyclo[4.2.0]octan-7-one (**76**) and *trans*-2-ethynylcyclohexanol (**87**). Accordingly, the trifluoroethyl ethers which are formed in 50:50 ratio are assigned structures **88** and **89**.

The solvolysis of bicyclo[6.2.0]dec-9-en-9-yl nonaflate (27) in TFE at room temperature also gave two products, which are identified by MS as 90 and 91 (60:40).

The solvolysis products 83–91 were formed from the cations 92 and 93. The rearrangement tendencies of 92 and 93 are less predominant for bicyclic systems than for the corresponding dimethyl-substituted 1-cyclobutenyl cation 72. Rearrangement is highest in the bicyclo[4.2.0] system; i.e., 92b is relatively less stable compared to 93b. Due to hindrance of the chair conformation of the 6-ring, the conformational strain of the whole system gets much higher on going from 93b to 92b.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were obtained on a Philips Pye Unicam SP 1000 spectrophotometer. ^{1}H NMR spectra were recorded on Varian EM 360, Bruker WH 90, Bruker HFX90, and Bruker WM 400 spectrometers. ^{13}C NMR spectra were recorded on Bruker WP 80. Mass spectra were obtained on a Varian MAT 711 (70 eV) spectrometer. Mass spectra coupled with GC (glass capillary column, (see below) were obtained by using a Carlo Erba Fractovap 2000 chromatograph and Varian MAT 1125 spectrometer. Analytical GC were carried out on a Carlo Erba FTV 2150 gas chromatograph with FID detector and HP 3390A integrator: carrier gas, N_2; columns, Duranglas-WCOT capillary columns coated with (1) Silicon UCC W 982, (2) GE SE 30, (3) GE SE 52, and (4) Carbowax 20 M, respectively. Preparative GC were carried out by using a Hewlett-Packard 5722 gas chromatograph with thermal conductivity detector using helium as the carrier gas: columns, steel columns with 4-mm diameter packed with (1) UCC W 982, (2) OV 17, and (3) Carbowax 20 M, on Chromosorb PAW 80/100, respectively. Kinetics were carried out by using a Metrohm Combi-Titrator 3D. The composition of solvent mixture is given in volume percentage.

Synthesis of Cyclobutanones. Cyclobutanone, 2-methylcyclobutanone, 2-cyclopropylcyclobutanone,[5] 3-isopropylcyclobutanone,[21] 3-methyl-cyclobutanone, and 2,4-dimethylcyclobutanone[22] were synthesized according to and analogous to the method of van Leusen[13] (see below). The synthesis of 3-cyclopropylcyclobutanone has been described by us[8] previously. 2,3-Dimethylcyclobutanone,[23] bicyclo[3.2.0]heptan-6-one,[24] bicyclo[4.2.0]octan-7-one,[24] and bicyclo[6.2.0]decan-9-one[20] were prepared by slight modification of literature procedures by treating the corresponding olefin with dichloroketene followed by dehalogenation.

2-Cyclopropylcyclobutanone.[5] a. 1-Cyclopropyl-1,3-propanediol. To a magnetically stirred solution of 20 g (0.53 mol) of $LiAlH_4$ in absolute ether (1 L) was added dropwise 31.2 g (0.2 mol) of ethyl 3-cyclo-propyl-3-oxopropionate[25] in absolute ether (100 mL). After the solution was stirred overnight, water (20 mL), 15% NaOH (20 mL), and water (60 mL) were added in that order. The white precipitate formed was filtered, digested in absolute ether, and filtered again. The filtrate was concentrated, and the residue was distilled by using a short Vigreux

column: bp 85 °C (53 Pa); yield, 14.4 g (62%); ^{1}H NMR (CCl_4/Me_2SO-d_6) δ 0.1–0.6 (m, 4 H, cyclopropyl-CH_2), 0.6–1.05 (m, 1 H, cyclopropyl-CH), 1.45–1.9 (m, 2 H, CH_2CH_2Br), 2.8–3.3 (m, 1 H, $CHBr$), 3.45–3.8 (m, 2 H, CH_2Br), 4.1, 4.2 (2d, 1 H each, OH).

b. 1-Cyclopropyl-1,3-dibromopropane. To a suspension of 63 g (255 mmol) of triphenylphosphine in dry acetonitrile (250 mL) was added dropwise with stirring and under ice-cooling 39.7 g (248 mmol) of bromine. The inside temperature should not exceed 5 °C. After removal of the ice bath, 14.4 g (124 mmol) of 1-cyclopropyl-1,3-propanediol in acetonitrile (50 mL) was added in 20 min. The mixture was stirred for 10 min more, and most of the acetonitrile was removed on a rotary evaporator. The residue was taken up in pentane, filtered, and washed thrice carefully with pentane. The combined filtrate was concentrated and the residue distilled by using a short Vigreux column: bp 48 °C (100 Pa); yield, 26 g (86%); ^{1}H NMR ($CDCl_3$) δ 0.3–0.88 (2m, 4 H, cyclo-propyl-CH_2), 1.08–1.42 (m, 1 H, cyclopropyl-CH), 2.33–2.54 (m, 2 H, CH_2CH_2Br); 3.29–3.60 (m, 1H, $CHBr$), 3.56 (t, 2 H, CH_2CH_2Br); ^{13}C NMR ($CDCl_3$, 20.1 MHz) δ 6.8 (t), 9.0 (t), 19.9 (d), 31.2 (t, C-3), 41.9 (t, C-2), 60.3 (d, C-1); IR 3090, 3015, 2980, 2920 cm^{-1}.

c. 2-Cyclopropyl-1-isocyano-1-tosylcyclobutane. Sodium hydride (55–60% in paraffin, ca. 0.24 mol) was weighed into a 1-L three-necked flask, and the paraffin was washed out with petroleum ether under nitrogen and suspended in a mixture of absolute Me_2SO (200 mL) and absolute ether (70 mL). A solution of 17.2 g (88 mmol) of (p-toluene-sulfonyl)methyl isocyanide (38) and 24.1 g (105 mmol) of 1-cyclo-propyl-1,3-dibromopropane in a mixture of Me_2SO (50 mL) and ether (25 mL) was added dropwise in 1 h. The mixture was stirred for 45 min more, and 60 mL of water was added carefully. This way, the major amount of the product was precipitated. This was filtered and washed several times with ether. The aqueous layer was extracted with ether (4 × 100 mL), and the ether extracts were combined with the ether washings of the precipitate, washed with brine, and dried over Na_2SO_4. The residue obtained after removal of ether was combined with the major amount of the product obtained, stirred for 5 min with a mixture of ether (50 mL) and pentane (50 mL), and then cooled to –20 °C. The crude product obtained was filtered, dried in a desiccator, and used further without purification; yield, 20 g (83%); ^{1}H NMR ($CDCl_3$) δ –0.2–0.65 (m, 4 H, cyclopropane-CH_2), 0.7–1.1 (m, 1 H, cyclopropane-CH), 1.8–2.9 (m, 6 H, 4-ring-CH_2), 2.46 (s, 3 H, CH_3), 7.60 (AA'BB', 4 H, aromatic).

d. 2-Cyclopropylcyclobutanone. 2-Cyclopropyl-1-isocyano-1-tosyl-cyclobutane (55 mmol, 15 g) was suspended in sulfolane (60 mL). A mixture of 3 mL of water and 3 mL of concentrated H_2SO_4 was then added to it, stirred for 10 min, neutralized with concentrated $NaHCO_3$ solution, and extracted several times with pentane. The combined pentane extract was dried over $MgSO_4$ and concentrated, and the residue was condensed in a cold trap at 13 Pa: yield, 1.8 g (30%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.21, 0.41, 0.48 (3m, 2 H, 1 H, and 1 H each, respectively, cyclopropyl-CH_2), 0.88 (m, 1 H, cyclopropyl-CH). 1.64 (m, 1 H), 2.06 (m, 1 H), 2.77–2.97 (m, 2 H), 3.04 (m, 1 H).

3-Isopropylcyclobutanone.[21] a. 1-Isocyano-3-isopropyl-1-tosylcyclo-butane. Sodium hydride (55–60% in paraffin, ca. 0.29 mol, 12.7 g) was washed with petroleum ether to free the paraffin under nitrogen and then suspended in a mixture of absolute Me_2SO (250 mL) and absolute ether (90 mL). A solution of 20.8 g (106 mmol) of (p-toluenesulfonyl)methyl isocyanide (38) and 31 g (137 mmol) of 2-isopropyl-1,3-dibromo-propane[26] in a mixture of Me_2SO (60 mL) and ether (30 mL) was added in 45 min, whereby the mixture began to boil. The mixture was stirred for 1 h more, treated carefully with water (75 mL), and extracted with ether (2 × 125 mL, 1 × 75 mL, 1 × 50 mL). The combined ether extracts were washed with brine (3 × 50 mL) and dried over Na_2SO_4. The residue obtained by concentration of the solvent was stirred for 10 min with ether (50 mL) and mixed with pentane (50 mL). The mixture was cooled overnight at –20 °C, and the product precipitated was filtered and used further without purification: yield, 11 g (38%); ^{1}H NMR ($CDCl_3$) δ 0.81 (d, 6 H, isopropyl-CH_3), 1.4-1.8 (m, 1 H, isopropyl-CH), 2.05–3.15 (m, 5 H, CH_2, CH), 2.44 (s, 3 H, CH_3), 7.32–7.90 (m, 4 H, aromatic).

b. 3-Isopropylcyclobutanone. A horizontal glass tube filled with anhydrous K_2CO_3 was attached to a 100-mL three-necked flask by way of a stopcock. The flask was equipped with an inside thermometer, nitrogen inlet tube, and a magnetic stirring bar. A cold trap was attached to the horizontal glass tube which was connected to an oil pump via a stopcock. 1-Isocyano-3-isopropyl-1-tosylcyclobutane (40 mmol, 11.1 g) was taken in the flask and dissolved in sulfolane (40 mL) at 50 °C. The whole apparatus was evacuated at 50 °C for 15 min, the stopcock to the pump was closed, and the apparatus was filled with nitrogen. The cold

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5244 *J. Am. Chem. Soc., Vol. 107, No. 18, 1985*

Hanack and Auchter

trap was cooled in liquid nitrogen, and the three-necked flask was immersed in a water bath. As soon as the temperature inside the three-necked flask dropped to 25 °C, a mixture of 2.16 mL (120 mmol) of water and 2.14 mL (140 mmol) of concentrated H_2SO_4 was added in one portion to the vigorously stirred solution. During this process, the temperature increased to 60 °C. The water bath was removed, the stopcock to nitrogen cylinder was closed, and the stopcock to the oil pump was opened carefully. The mixture was heated to 120 °C within 1 h, during which time the 3-isopropylcyclobutanone formed was pumped into the cold trap at 0.1–1 Pa. The treatment was continued for 2 h more. The product in the cold trap was freed from traces of water by drying with molecular sieves (4 Å) and is pure enough for further purposes; yield, 3.4 g (75%); ^{1}H NMR (CDCl$_3$) δ 1.10 (d, 6 H, isopropyl-CH$_3$), 1.53–1.90 (m, 1 H, isopropyl-CH), 1.92–2.42 (m, 1 H, 4-ring-CH), 2.65–3.40 (m, 4 H, 4-ring-CH$_2$).

2,4-Dimethylcyclobutanone. This was synthesized from 2,4-dibromopropane[27] analogous to 3-isopropylcyclobutanone described above. The overall yield is 20%: ^{1}H NMR (CDCl$_3$, 400 MHz, cis–trans mixture, 3:1), (cis) 1.12 (d, 6 H, CH$_3$), 1.12, 2.45 (2m, 1 H each, CH$_2$), 3.1 (m, 2 H, 2 × CH), (trans) 1.18 (d, 6 H, CH$_3$), 1.80 (m, 2 H, CH$_2$), 3.2 (m, 2 H, 2 × CH).

Synthesis of Substituted 1-Cyclobutenyl Nonaflates. General Procedure. To a magnetically stirred solution of 6 g (29.2 mmol) of 2,6-di-*tert*-butyl-4-methylpyridine (33)[28] in dry dichloromethane (80–90 mL) was added with the aid of a syringe 13.3 g (22.8 mmol) of nonafluorobutanesulfonic acid anhydride[3] at room temperature. After the solution was stirred for 5 min, the appropriate cyclobutanone (20 mmol) was injected with a syringe and the progress of the reaction was monitored by GC. The reaction time varied between 2 and 7 days, whereby the formerly colorless mixture got darker slowly due partly to polymerization. When the GC analysis showed no increase in the formation of the product, the solvent was removed in a rotary evaporator and the residue was digested in dry pentane. The insoluble pyridinium nonaflate was filtered through a fritted-glass funnel and washed with a small quantity of pentane. The filtrate was concentrated, and the residue was chromatographed on a short silica gel column cooled to −10 °C to −20 °C using pentane as the eluent, whereby the nonaflate was obtained in short retention time. After removal of the solvent, the residue was condensed in a cold trap at 10^{-2}–1 Pa. The less volatile nonaflates must be heated carefully with a heat regulable hot gun. Excess heating decomposes the nonaflates. The reaction time and yield for the synthesis of different 1-cyclobutenyl nonaflates together with the spectroscopic data for the new nonaflates are given below. All nonaflates are colorless liquids with characteristic odor.

1-Cyclobutenyl Nonaflate (1):[5] Reaction time, 3 days; yield, 12%.
3-Methyl-1-cyclobutenyl Nonaflate (30):[5] 3 days; 22%.
3-Cyclopropyl-1-cyclobutenyl Nonaflate (31):[5] 3 days; 16%.
3-Isopropyl-1-cyclobutenyl Nonaflate (19): 3 days; 40%; ^{1}H NMR (CDCl$_3$) δ 0.90, 0.92 (2d, 6 H, isopropyl-CH$_3$), 1.37–1.68 (m, 1 H, isopropyl-CH), 2.22–2.54 (m, 2 H, ring CH + CH$_2$), 2.93 (dd, 1 H, ring CH$_2$), 5.47 (br s, 1 H, C=CH); ^{13}C NMR (CDCl$_3$) δ 19.8 (C-6, C-7), 31.5 (C-5), 37.8, 41.8 (C-3, C-4), 119.2 (C-2), 139.9 (C-1); IR 3060, 3040, 2900, 2870, 1625, 1430, 1350, 1245, 1205, 1145, 1035, 1010, 925 cm^{-1}; MS, m/e 394 (6%, M$^+$), 351 (3), 315 (3), 287 (10), 219 (10), 131 (14), 111 (14), 95 (21), 94 (35), 79 (100), 68 (50), 68 (85), 67 (3), 55 (42). Anal. Calcd for C$_{11}$H$_{11}$F$_9$O$_3$S: C, 33.51; H, 2.81. Found: C, 33.38; H, 2.85.

2-Methyl-1-cyclobutenyl Nonaflate (28)[5] **and 4-Methyl-1-cyclobutenyl Nonaflate (20):** 3 days; 50%. The reaction of 2-methylcyclobutanone with nonafluorosulfonic acid anhydride gave a mixture of 95% **28** and 5% **20**. Pure 2-methyl-1-cyclobutenyl nonaflate (28) can be obtained with some loss by column chromatography. A small amount of 4-methyl-1-cyclobutenyl nonaflate (20) was obtained pure by preparative GC. **20:** ^{1}H NMR (CDCl$_3$) δ 1.23 (d, 3 H, CH$_3$), 1.77, 2.43 (2m, 1 H each, CH$_2$), 3.14–3.28 (m, 1 H, CH), 5.38 (br s, 1 H, C=CH); MS, m/e 366 (7%, M$^+$), 301 (10), 219 (3), 131 (10), 69 (57), 68 (53), 55 (100%, C$_4$H$_7^+$).

2-Cyclopropyl-1-cyclobutenyl Nonaflate (29): 7 days; 10%; GC purity 93%; ^{1}H NMR (CDCl$_3$) δ 0.54–0.87 (m, 4 H, cyclopropyl-CH$_2$), 1.45–1.75 (m, 1 H, cyclopropyl-CH), 1.88–1.95 (m, 2 H, C-CH$_2$), 2.70–2.77 (m, 2 H, CH$_2$CONf); IR 3090, 3020, 2980, 2940, 2860, 1710, 1420, 1350, 1240, 1205, 1140, 1030, 1005, 985 cm^{-1}; MS, m/e 392 (7%, M$^+$), 364 (1), 219 (7), 131 (9), 109 (14), 81 (100), 79 (63).

2,3-Dimethyl-1-cyclobutenyl Nonaflate (21): 4 days; 7%; GC purity 80%; ^{1}H NMR (CDCl$_3$) δ 1.12 (d, 3 H, 3-CH$_3$), 1.64–1.79 (m, 3 H, 2-CH$_3$), 2.19–2.49, 2.85–3.08 (2m, 2 H and 1 H each, CH, CH$_2$); IR

2970, 2940, 2880, 1720, 1425, 1355, 1245, 1205, 1145, 1080, 1070, 1035, 1020, 895 cm^{-1}; MS, m/e 380 (13%, M$^+$), 301 (13), 219 (4), 131 (11), 69 (100).

Bicyclo[3.2.0]hept-6-en-6-yl Nonaflate (23): 3 days; 18%. From the cyclobutanone **85**, exclusively this isomer was formed: ^{1}H NMR (CDCl$_3$) δ 0.95–1.95 (m, 6 H, CH$_2$), 2.92 (dd, 1 H, CHC=), 3.48 (dd, 1 H, CHCONf), 5.25 (br s, 1 H, C=CH); IR 2960, 2870, 1630, 1430, 1355, 1300, 1250, 1150, 1000, 950, 910 cm^{-1}; MS, m/e 392 (13%, M$^+$) 310 (4), 219 (3), 131 (5), 109 (46), 93 (30), 91 (61), 81 (100). Anal. Calcd for C$_{11}$H$_9$F$_9$O$_3$S: C, 33.68; H, 2.31. Found: C, 33.49; H, 216.

Bicyclo[4.2.0]oct-1(8)-en-8-yl Nonaflate (24): 3 days; 47%. The reaction of cyclobutanone **76** with nonafluorobutanesulfonic acid anhydride as described above gave a mixture of **24** and **25** in a ratio of 98:2, from which **24** was separated by column chromatography at −20 °C: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.95–1.08 (m, 1 H), 1.20–1.35 (m, 2 H), 1.68–1.80 (m, 1 H), 1.80–1.93 (m, 2 H), 2.08–2.18 (m, 2 H), 2.43–2.53 (m, 2 H), 2.92 (m, 1 H); IR 2970, 2890, 1730, 1435, 1360, 1255, 1210, 1150, 1110 cm^{-1}; MS, m/e 406 (22%, M$^+$), 219 (8), 106 (69), 95 (100), 81 (92). Anal. Calcd for C$_{12}$H$_{11}$F$_9$O$_3$S: C, 35.48; H, 2.73. Found: C, 35.45; H, 2.50.

Bicyclo[4.2.0]oct-7-en-7-yl Nonaflate (25). About 1 g of a mixture of **24** and **25** was chromatographed over silica gel using pentane as the eluent at +10 °C, whereby the reactive nonaflate **24** decomposed completely while ca. 20 mg of **25** could be obtained pure with a short retention time: ^{1}H NMR (CDCl$_3$, 400 MHz) 1.35–1.82 (m, 8 H, CH$_2$), 2.63 (m, 1 H, CHC=C), 3.21 (m, 1 H, CHCONf), 5.46 (s, 1 H, C=CH).

Bicyclo[6.2.0]decenyl Nonaflate (26 and 27): 2.5 days; 43%. A mixture of **26** and **27** was formed in the ratio of 70:30, which was separated as in the case of **24/25**. **26:** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.25–2.15 (m, 12 H, 8-ring-CH$_2$), 2.25–2.97 (m, 2 H, 4-ring-CH$_2$), 2.93 (1 H, CH). **27:** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.2–1.9 (m, 12 H, 8-ring-CH$_2$), 2.53 (m, 1 H, CHC=C), 3.03 (m, 1 H, CHCONf), 5.33 (s, 1 H, C=CH). **26/27:** MS, m/e 434 (8%, M$^+$), 392 (3%, M$^+$ − C$_3$H$_6$), 219 (1), 204 (11), 190 (19), 81 (89), 67 (100).

2,4-Dimethyl-1-cyclobutenyl Nonaflate (22): 7 days; 17%; GC purity 90%; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.20 (d, 3 H, 4-CH$_3$), 1.68, 2.33 (2m, 1 H each, CH$_2$), 1.75 (m, 3 H, 2-CH$_3$), 3.10–3.18 (m, 1 H, CH); GC/MS, m/e 380 (23%, M$^+$), 301 (2), 219 (3), 131 (9), 119 (7), 81 (43), 69 (100).

Kinetic Measurements. To a thermostated apparatus equipped with magnetic stirrer, automatic buret, and electrode[15] containing 35 mL of 80% trifluoroethanol, 5 μL of appropriate 1-cyclobutenyl nonaflate was added. The nonafluorobutanesulfonic acid produced during the solvolysis was titrated automatically at pH 5 with a 0.015 N standard sodium hydroxide solution in 80% TFE.

Solvolysis Products. Analytical Method. Ten microliters of appropriate nonaflate dissolved in 500 μL of solvent containing 1.1–1.5-fold excess of triethylamine was placed in a small glass vial equipped with a magnetic bar and closed with a septum. The vial was kept at 25–70 °C according to the reactivity of the nonaflate, and the contents were allowed to solvolyze. The progress of the reaction and the product composition was determined by gas chromatography. The solvolysis products were identified as far as possible by comparing their GC retention times with authentic samples as well as GC/MS.[5,7,10,11,20,29]

Half-Preparative Method. An appropriate 1-cyclobutenyl nonaflate (0.25–1 g) was solvolyzed in 8–12 mL of TFE containing 1–2-fold excess of triethylamine. When the solvolysis was completed (GC control), the solvent was distilled off by using a small Vigreux column. Then the volatile products of the solvolysis were condensed in a cold trap at 0.1 Pa. The condensed products were diluted with chloroform, if necessary, and separated by preparative GC and identified by ^{1}H NMR and GC/MS spectra. The separation of products was achieved, in part, only after two successive gas chromatographys over columns packed with the same or different materials. The identity of the isolated solvolysis products with the products found from the analytical solvolysis was proved after identifying the products by spectra and repeating the capillary GC analysis with both samples. Spectroscopic data of products thus identified are assembled below.

3-Isopropyl-1-(2,2,2-trifluoroethoxy)cyclobutene (47b): ^{1}H NMR (CDCl$_3$) δ 0.87, 0.89 (2d, 3 H each, isopropyl-CH$_3$), 1.23–1.54 (m, 1 H, isopropyl-CH), 2.02–2.24 (m, CH and part of CH$_2$), 2.69 (dd, 1 H, part of CH$_3$), 4.08 (q, 2 H, CH$_2$CF$_3$), 4.71 (d, 1 H, C=CH, J = 0.9 Hz); GC/MS, m/e 194 (31%, M$^+$), 179 (30), 151 (100%, M$^+$ − C$_3$H$_7$), 68 (73).

5-Methyl-4-(2,2,2-trifluoroethoxy)-1-hexyne (49b): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.929, 0.934 (2d, 6 H, 2 × CH$_3$), 1.93 (m, 1 H,

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CHCH$_3$), 1.99 (t, 1 H, C≡CH), 2.41 (dd, 2 H, CH$_2$CH), 3.33 (dt, 1 H, CHOCH$_2$CF$_3$), 3.87, 4.03 (2dq, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 194 (1%, M$^+$), 179 (8), 155 (100%, M$^+$ – C$_3$H$_3$).

4-Isopropyl-1-(2,2,2-trifluoroethoxy)cyclobutene (66): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.87, 0.94 (2d, 6 H, isopropyl-CH$_3$), 1.68 (m, 1 H, isopropyl-CH), 2.09 (dd, 1 H, part of CH$_2$), 2.73 (m, 1 H, ring CH), 3.47 (br s, 1 H, part of CH$_2$), 4.06 (q, 2 H, CH$_2$CF$_3$), 4.58 (br s, 1 H, C=CH); GC/MS, *m/e* 194 (23%, M$^+$), 179 (100%, M$^+$ – CH$_3$).

4-Methyl-5-(2,2,2-trifluoroethoxy)-1-hexyne (68, Two Diastereomers): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.98/1.00 (d, 3 H, CH$_3$), 1.14/1.15 (d, 3 H, CH$_3$), 1.76–1.86/1.73–1.83 (m, 1 H, 4-H), 1.939/1.942 (t, 1 H, 1-H), 2.27, 2.38/2.11, 2.33 (2m and 2ddd, 2 H, CH$_2$), 3.46/3.61 (m, 1 H, 5-H), 3.7–3.9 (m, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 194 (1%, M$^+$), 127 (100%, M$^+$ – C$_5$H$_7$), 179 (10).

4-Methyl-4-(2,2,2-trifluoroethoxy)-1-hexyne (69): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.89 (t, 3 H, CH$_2$CH$_3$), 1.26 (s, 3 H, CCH$_3$), 1.61, 1.66 (2dq, 1 H each, CHCH$_3$), 2.00 (t, 1 H, C≡CH), 2.28, 2.38 (m, 2 H, CHC≡CH), 3.7–3.9 (m, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 194 (M$^+$, not found), 179 (17), 165 (42%, M$^+$ – C$_2$H$_5$), 155 (100%, M$^+$ – C$_3$H$_3$).

5-Methyl-5-(2,2,2-trifluoroethoxy)-1-hexyne (70): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.19 (s, 6 H, 2 × CH$_3$), 1.66–1.84 (m, 2 H, 4-H), 1.91 (t, 1 H, C≡CH), 2.09–2.28 (m, 2 H, 3-H), 3.68 (q, 2 H, CH$_2$CF$_3$), GC/MS, *m/e* 194 (1%, M$^+$) 179 (27), 141 (100%, M$^+$ – C$_4$H$_5$).

2,3-Dimethyl-1 (2,2,2-trifluoroethoxy)cyclobutene (51): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.05 (d, 3 H, 3-CH$_3$), 1.58 (m, 3 H, 2-CH$_3$), 1.96 (m, 1 H, part of CH$_2$), 2.23 (m, 1 H, CH-CH$_3$), 2.77 (m, 1 H, part of CH$_2$) 4.13 (q, 2 H, CH$_2$CF$_3$), GC/MS, *m/e* 180 (100%, M$^+$), 165 (73), 140 (7), 127 (13).

2,4-Dimethyl-1-(2,2,2-trifluoroethoxy)cyclobutene (53): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.13 (d, 3 H, 4-CH$_3$), 1.47 (m, 1 H, part of CH$_2$), 1.66 (m, 3 H, 2-CH$_3$), 2.14 (m, 1 H, part of CH$_2$), 2.82 (m, 1 H, CHCH$_3$), 4.20 (2dq, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 180 (90%, M$^+$), 179 (43), 185 (90), 67 (100).

5-(2,2,2-Trifluoroethoxy)-2-hexyne (55): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.27 (d, 3 H, CHCH$_3$), 1.77 (t, 3 H, C≡CCH$_3$), 2.22–2.33 and

2.36–2.47 (2m, 1 H each, CH$_2$), 3.67 (tq, 1 H, CHCH$_3$), 3.87 (2dq, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 180 (37%, M$^+$), 165 (33), 127 (100%, M$^+$ – C$_4$H$_5$).

8-(2,2,2-Trifluoroethoxy)bicyclo[4.2.0]oct-1(8)-ene (75): ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.86–1.00 (m, 1 H), 1.15–1.20 (m, 2 H), 1.65–1.78 (m, 2 H), 1.80–1.90 (m, 1 H), 1.90-2.04 (m, 2 H), 2.14, 2.37 (2dd, 1 H each, 4-ring-CH$_2$), 2.64 (dt, 1 H, bridgehead-CH), 4.17 (q, 2 H, CH$_2$CF$_3$); GC/MS, *m/e* 206 (57%, M$^+$), 191 (35), 177 (30), 165 (10), 152 (2), 127 (16), 107 (30), 91 (57), 79 (71), 43 (100).

10-(2,2,2-Trifluoroethoxy)bicyclo[6.2.0]dec-1(10)-ene (77): GC/MS, *m/e* 234 (M$^+$, absent), 219 (10), 206 (12), 205 (13), 193 (13), 191 (33), 178 (14), 177 (13), 165 (100), 153 (14), 152 (16), 139 (57).

6-(2,2,2-Trifluoroethoxy)bicyclo[3.2.0]hept-6-ene (83): ^{1}H NMR (CDCl$_3$) δ 0.75-1.80 (m, ring-CH$_2$), 2.77 (m, 1 H, CHCO), 3.23 (m, 1 H, CHC=C), 4.05 (q, 2 H, CH$_2$CF$_3$), 4.43 (br s, C=CH); GC/MS, *m/e* 192 (59%, M$^+$), 177 (100), 164 (39), 109 (34), 93 (43), 91 (38), 81 (63).

trans-2-Ethynyl-1-(2,2,2-trifluoroethoxy)cyclopentane (84): GC/MS, *m/e* 192 (M$^+$, absent), 191 (32%, M$^+$ – H), 177 (24), 152 (46), 139 (61), 93 (88), 91 (100).

7-(2,2,2-Trifluoroethoxy)bicyclo[4.2.0]oct-7-ene (88): GC/MS, *m/e* 206 (9%, M$^+$), 191 (15), 178 (13), 177 (55), 165 (10), 164 (6), 67 (100).

trans-2-Ethynyl-1-(2,2,2-trifluoroethoxy)cyclohexane (89): GC/MS, *m/e* 206 (M$^+$, absent), 191 (29), 178 (27), 177 (23), 165 (28), 139 (100).

9-(2,2,2-Trifluoroethoxy)bicyclo[4.2.0]oct-7-ene (90): GC/MS, *m/e* 234 (13%, M$^+$), 219 (10, 205 (15), 192 (35), 191 (72), 180 (49), 177 (88), 67 (100).

trans-2-Ethynyl-1-(2,2,2-trifluoroethoxy)cyclooctane (91): GC/MS, *m/e* 234 (M$^+$, absent), 233 (2), 205 (7), 191 (25), 165 (61), 139 (49), 91 (85), 79 (100).

Ground Term Splitting of High-Spin Co²⁺ as a Probe of Coordination Structure. 1. Dependence of the Splitting on Coordination Geometry[1a]

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Abstract: The sign and magnitude of the splitting between the two lowest Kramers doublets (Δ) of high-spin Co²⁺ in a variety of structurally defined, small molecule coordination complexes is determined. The range of values of Δ is found to be <13 cm⁻¹ in tetracoordinate sites, ~20–50 cm⁻¹ in pentacoordinate sites of trigonal-bipyramidal or square-pyramidal geometry, and ≥50 cm⁻¹ in hexacoordinate sites. It is shown on the basis of group theoretical arguments and estimates of the zero-field splitting derived by second-order perturbation theory that the observed range of values of Δ correlates well with that predicted by theory. On this basis, it is suggested that the splitting between the two lowest Kramers doublets of high-spin Co²⁺ may provide a diagnostic signature of coordination geometry.

Except for diffraction techniques, there are no methods to determine directly the structure of metal ion coordination complexes. This circumstance is particularly true upon substitution of metal ions into metalloproteins and enzymes as spectroscopic probes, for evaluation of the coordination environment generally rests heavily on the assumption that the metal ion binding site

remains isostructural with that defined by X-ray crystallographic studies of the native enzyme. High-spin Co²⁺ has been employed as a spectroscopic probe of Zn²⁺ metalloenzymes since it usually can be incorporated into the apoenzyme to regenerate catalytic activity.[2] However, the spectroscopic complexities of high-spin Co²⁺ with respect to the orbital degeneracy of the ground state and coupling of excited state terms with changes in coordination environment have resulted only in qualitative characterization of

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