additional persuasive evidence[3] for the competitive intermediacy of **10**, and the fact that the relative amounts of **15** and **17** formed from **7** and **8** are very similar is also consistent with their formation from a common intermediate. Finally, the temperature dependence of the rates of carbene-derived and diradical-derived product observed in the parent system[1] is also found in the dimethyl series.[11]

In summary, our results are best rationalized by the postulate that pyrazolines of general structure **1** undergo dual pathway decomposition.[12] The major route involves rate-determining carbene formation, followed by rapid reaction of this material to give characteristic hydrogen-shifted and insertion products. The minor route involves direct nitrogen loss and subsequent bicyclopentane formation, presumably *via* substituted 1,3-diradicals.

Acknowledgments. We are grateful to the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

(11) A plot of the log of the ratio of radical-derived to carbene-derived products is linear and gives ΔE_a = 5.24 kcal/mol and $\Delta\Delta S^{\ddagger}$ = +3.38 eu.

(12) Once again, for the reasons stated in footnote 11 in ref 1, we consider an open-chain diazo compound, formed *via* retro-1,3-dipolar reaction of **7** and **8**, the most likely source of carbene **10**.

(13) National Science Foundation Predoctoral Fellow, 1970–present.

(14) (a) Alfred P. Sloan Foundation Fellow, 1970–1972; (b) Camille and Henry Dreyfus Foundation Teacher–Scholar Grant Awardee, 1970–1975.

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Multiple Mechanisms in the Thermal and Photochemical Decomposition of 2,3-Diazabicyclo[3.1.0]hex-2-enes

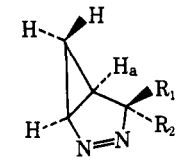
Sir:

We report the synthesis and decomposition of several bicyclic azo compounds designed as precursors to "cyclopropylmethylene" diradicals[1] of the type **1**. We believe that the results reported here (as

1

in the accompanying communications)[2] provide notable exceptions to the generally observed reaction modes of bicyclic azo compounds.

Addition of cyclopropene[3] to a pentane solution of diazoethane at −78° yielded a 60:40 mixture of *exo*- and *endo*-4-methyl-2,3-diazabicyclo[3.1.0]hex-2-ene (**2a** and **2b**, respectively) as a pale yellow oil. The epimeric mixture was separated by preparative vpc (10 ft × 3/8 in., glass, UC-W98, 20% on HMDS Chromosorb W; 55°). Compound **2a** exhibits the following spectral characteristics: *m/e* 96 (4%), 68 ($M^+ - N_2$, 42%),



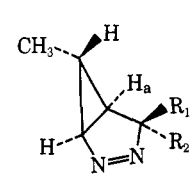
2a, $R_1 = H_b$; $R_2 = CH_3$
2b, $R_1 = CH_3$; $R_2 = H_c$

67 (base peak); nmr (60 MHz, CCl_4 containing 2% $CHCl_3$) δ 4.66 (1 H, mult), 4.24 (1 H, d of q, J = 7.3, 3.0 Hz), 2.8–0.9 (2 H, complex mult), 1.33 (3 H, d, J = 7.3 Hz), −0.19 (1 H, mult); ir ν_{max}^{film} 1515 (N=N), 1030 cm^{-1}; uv λ_{max}^{hexane} 328 nm (ε 335). Compound **2b** shows: *m/e* 96 (5%), 68 (37%), 67 (base); nmr (60 MHz, CCl_4 containing 2% $CHCl_3$) δ 5.0–4.5 (2 H, complex mult), 1.60 (1 H, mult), 1.47 (3 H, d, J = 7.3 Hz), 0.89 (1 H, mult), −0.17 (1 H, mult); ir ν_{max}^{film} 1514, 1028 cm^{-1}; uv λ_{max}^{hexane} 330 nm (ε 149). The 220-MHz nmr spectra of **2a** and **b** are pseudo-first-order and can be satisfactorily analyzed, establishing the indicated stereochemistry unequivocally; in **2a** the vicinal H_a–H_b coupling constant is 1.3 Hz, whereas $J_{H_a-H_c}$ is 6.5 Hz in **2b**.[4]

Sealed tube pyrolysis (vapor or liquid phase) of **2a** at 119°, or irradiation (3130 Å, pentane), resulted in clean formation of *trans*-1,3-pentadiene (*t*-**3**) (98%) and *cis*-1,3-pentadiene (*c*-**3**) (2%).[5] Decomposition of **2b** under identical conditions produced 3% *t*-**3** and 97% *c*-**3**. No change in product ratios was observed on thermolysis of **2a** or **b** in apparatus packed with glass helices. The ratio of the first-order rate constants for pyrazoline disappearance at 119°, k_{2a}/k_{2b}, was found to be 30, while quantum yields for 3130-A induced pyrazoline decomposition were 0.75 (**2a**) and 0.53 (**2b**).[6]

The unusual rate ratio and product selectivity exhibited by pyrazolines **2** suggest that mechanisms other than diradical may obtain. We have prepared pyrazolines **4** to gain further mechanistic insight.

Addition of diazoethane to 3-methylcyclopropene[7] at −78° afforded *exo*-4,*exo*-6-dimethyl-2,3-diazabicyclo-[3.1.0]hex-2-ene (**4a**) and the endo 4 epimer **4b**. The



4a, $R_1 = H_b$; $R_2 = CH_3$
4b, $R_1 = CH_3$; $R_2 = H_c$

stereochemistry assigned at C_4 is supported by the nmr spectra (100 MHz): in **4a**, $J_{H_a-H_b}$ = 2.3 Hz, and $J_{H_a-H_c}$ = 7.1 Hz (**4b**). All other spectral characteristics of **4** are consistent with the proposed structure.

Pyrolysis or photolysis of **4a** or **b** gave mixtures of C_6H_{10} hydrocarbons (Scheme I). The nature of the decomposition products strongly suggests the intervention of carbenes **5a** and **5b**, visualized as arising *via* the mechanism shown in Scheme I. We have pre-

(1) (a) R. Srinivasan, *J. Amer. Chem. Soc.*, **90**, 4498 (1968); (b) J. Saltiel, L. Metts, and M. Wrighton, *ibid.*, **92**, 3227 (1970).

(2) (a) D. H. White, P. B. Condit, and R. G. Bergman, *ibid.*, **94**, 1348 (1972); (b) R. A. Keppel and R. G. Bergman, *ibid.*, **94**, 1350 (1972).

(3) G. L. Closs and K. D. Krantz, *J. Org. Chem.*, **31**, 638 (1966).

(4) We wish to thank Professor Robert S. Cooke for assistance in analyzing the 220-MHz spectra of **2**.

(5) The dienes were identified by spectral and vpc comparison with authentic samples. The absolute diene yield was 86%.

(6) Blue fluorescence (λ_{max} 430 nm) with an onset at 365 nm (~78 kcal/mol) was observed from a degassed pentane solution of a 3:2 mixture of **2a** and **2b**.

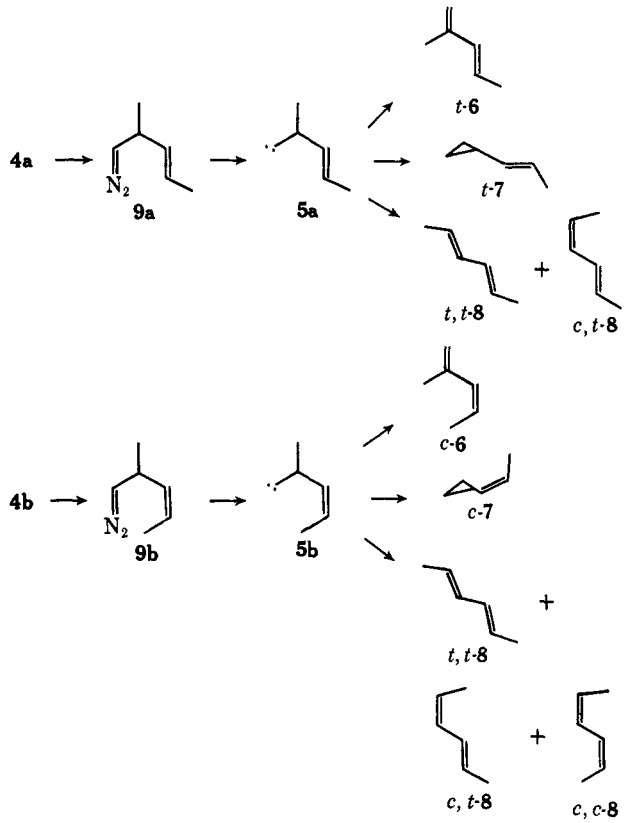
(7) R. Köster, S. Arora, and P. Binger, *Angew. Chem., Int. Ed. Engl.*, **9**, 810 (1970).

Table I. Product Distributions Observed on Decomposition of **4a**, **4b**, and **10**

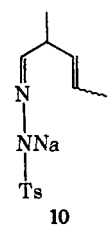
Compd	Decomp conditions	Products, %[a,b]						
		t-6	*c*-6	*t*-7	*c*-7	*t,t*-8	*c,t*-8	*c,c*-8
4a	Δ, 149°	65.1		4.9		12.3	17.7	
	Δ, 162°	63.8		9.0		9.6	17.5	
	Δ, 175°	60.4		14.4		10.0	15.3	
	Δ, 190°	56.4		23.4		7.8	12.8	
	hν, 313 nm	57.7		5.8		15.0	21.5	
4b	Δ, 149°		55.9		4.9	6.3	5.8	27.1
	Δ, 161°		51.9		9.0	5.3	3.5	25.3
	Δ, 178°		47.2		19.5	4.4	4.3	24.6
	Δ, 188°		43.6		27.1	2.3	4.8	22.2
	hν, 313 nm		47.6		23.5	4.6	12.4	11.9
10	Δ, 200°[c]	61.6	13.3	3.6	0.5	9.7	8.8	2.6

[a] All products have been identified by comparison of ir, nmr, and mass spectra with those of authentic samples. Preparative pyrolysis of a mixture of **4a** and **4b** afforded a 71% isolated yield of hydrocarbons. [b] Products are stable to the reaction conditions employed. [c] No significant changes in product ratios from **10** were found in the range 180–240°.

Scheme I



pared the appropriate *p*-toluenesulfonylhydrazone precursor **10**[8] to carbenes **5** and decomposed tetraglyme



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suspensions of the sodium salt in the hot (200°) vpc injector port.[9] Product distributions obtained from pyrolysis of **10** at 200° and from **4a** and **4b** at several temperatures are shown in Table I. The large dependence of the pyrazoline product distribution on pyrolysis temperature is extremely complex. However, several points can be made. First, the products of **10** exhibit no variation with temperature (180–240°), suggesting that the origin of the pyrazoline temperature effect is not in the carbenes derived from the aliphatic diazo compounds **9**. Also, we find that at none of the temperatures examined (135–200°) does the pyrazoline product distribution correspond completely to that observed from **10**. In particular, the relatively large amounts of *c,t*-**8** obtained from **4a** and *c,c*-**8** from **4b** may implicate a competitive diradical or concerted path leading to hexadienes of retained pyrazoline C-4 configuration but inverted at the initial C-6 center. In order to account for the observed increase in cyclopropylpropenes (**7**) at elevated temperatures we must invoke a third mechanistic alternative, which we envision as a direct route to a highly energetic carbene without the intermediacy of ring-opened diazo compounds **9**. Preferential insertion into an α-methyl C–H bond leads to **7**.

The observations reported here unambiguously implicate carbene formation as a major decomposition path in the diazabicyclo[3.1.0]hex-2-ene system. A similar retro-1,3-dipolar addition has been described by Franck-Neumann[10] in the photolysis of 1,5-dicarbomethoxy-6,6-dimethyl-2,3-diazabicyclo[3.1.0]-hex-2-ene. Also, such a mechanism may account for the minor amounts of cleavage products observed photochemically by van Auken and Rinehart[11] and McGreer,[12] and thermally by Crawford[13] in monocyclic pyrazoline systems. We conclude that this novel reaction mode must be considered to be competitive with simple N_2 extrusion in strained bicyclic pyrazoline systems, and may also obtain in some unstrained monocyclic systems.

(8) The carbene precursor was prepared from a mixture of isomeric 2-methylpent-3-enals and judged to be approximately 82–86% trans by nmr. Full synthetic details will be presented later.

(9) G. M. Kaufman, J. A. Smith, G. G. Vander Stouw, and H. Schechter, *J. Amer. Chem. Soc.*, 87, 935 (1965).

(10) M. Franck-Neumann and C. Buchecker, *Tetrahedron Lett.*, 2659 (1969).

(11) T. V. van Auken and K. L. Rinehart, Jr., *J. Amer. Chem. Soc.*, 84, 3736 (1962).

(12) D. E. McGreer, N. W. K. Chiu, M. G. Vinje, and K. C. K. Wong, *Can. J. Chem.*, 43, 1407 (1965).

(13) R. J. Crawford and A. Mishra, *J. Amer. Chem. Soc.*, 88, 3963 (1966). Of the pyrazolines reported by Crawford, only 4,4-dimethyl-Δ¹-pyrazoline exhibits such cleavage.

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(14) NDEA Fellow, 1969–present.
(15) (a) Alfred P. Sloan Foundation Fellow, 1970–1972; (b) Camille and Henry Dreyfus Foundation, Teacher–Scholar Grant Awardee, 1970–1975.

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Datiscoside, a Novel Antileukemic Cucurbitacin Glycoside from *Datisca glomerata*[1,2]

Sir:

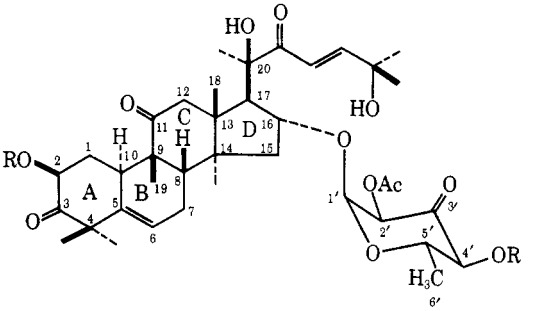
We wish to report on the isolation and structural elucidation of datiscoside (**1**), a novel antileukemic[3] principle from *Datisca glomerata* Baill. The structure of datiscoside was determined by X-ray crystallographic analysis of the di-*p*-iodobenzoate **3**, thereby establishing for the first time unambiguously the configurations of the cucurbitacins at C-20, assigned previously on biogenetic grounds, and at C-2, for which contradictory arguments have been presented in the literature.[4,5]

Alcoholic extracts of the roots of *D. glomerata*[6] showed significant inhibitory activity *in vivo* against Walker 256 intramuscular carcinosarcoma in the rat and the P-388 lymphocytic leukemia in the mouse and *in vitro* against cells derived from human carcinoma of the nasopharynx (KB). Fractionation of the alcoholic extract was guided by the 9KB assay. Successive solvent partitions and chromatography on SilicAR CC-7 yielded fractions from which were crystallized datiscoside (**1**), $C_{38}H_{54}O_{12}$[7] (mp 174–175°; $[\alpha]^{23}D$ +26° (*c* 1.04, $CHCl_3$); uv max (MeOH) 231 nm (ϵ 11,600); ir (KBr) 2.90, 5.73, 5.80, 5.92, 6.17, 8.10, and 9.30 μ; nmr ($CDCl_3$) τ 2.96 (1 H, d, J = 15 Hz), 3.52 (1 H, d, J = 15 Hz), 4.24 (1 H, m), 4.75 (2 H, s), 5.51 (1 H, s), 7.89 (3 H, s), 8.47–8.80 (21 H, 7 × CH_3), 8.91 (3 H, s), and 8.99 (3 H, s); *m/e* 624, 498, 481, 458, 455, 403, 385, 369, 219, 144, 127, 126, 112, 111, 105, 100, and 96) and cucurbitacin D (**2**), identified by comparison of its properties with those reported in the literature.[8]

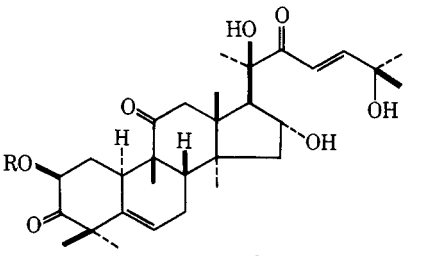
(1) Tumor Inhibitors. LXXII. Part LXXI: C. H. Smith, J. Larner, A. M. Thomas, and S. M. Kupchan, submitted for publication.
(2) Supported by grants from the National Cancer Institute (CA-11718 and CA-11760) and the American Cancer Society (T-275 and T-541), and a contract with Chemotherapy, National Cancer Institute (NIH 71-2099).
(3) Datiscoside showed confirmed *in vivo* activity against P-388 leukemia and WM-256 intramuscular carcinosarcoma and cytotoxicity (ED_{50} = 0.16 μg/ml) against cells derived from the human carcinoma of the nasopharynx (KB). Cytotoxicity (KB) and *in vivo* activity were assayed by the procedures described in *Cancer Chemother. Rep.*, **25**, 1 (1962).
(4) D. Lavie and B. S. Benjaminov, *J. Org. Chem.*, **30**, 607 (1965).
(5) G. Snatzke, P. R. Enslin, C. W. Holzapfel, and K. B. Norton, *J. Chem. Soc. C*, 972 (1967); *cf.* D. H. R. Barton, C. F. Garbers, D. Giacopello, R. G. Harvey, J. Lessard, and D. R. Taylor, *ibid.*, 1050 (1969); J. R. Bull and P. R. Enslin, *Tetrahedron*, **26**, 1525 (1970).
(6) The roots were collected in California in July 1962. The authors acknowledge with thanks receipt of the dried plant material from Dr. R. E. Perdue, Jr., U.S.D.A., in accordance with the program developed by Chemotherapy, National Cancer Institute.
(7) Elemental formulas were confirmed by concordant elemental analyses.
(8) P. R. Enslin, *J. Sci. Food Agr.*, **5**, 410 (1954); P. R. Enslin, R. Rehm, and D. E. A. Rivett, *ibid.*, **8**, 673 (1957).

Elemental analysis and spectral data for datiscoside (**1**) supported assignment of a cucurbitacin-like nucleus to which a highly oxygenated substituent was attached. A glycoside structure appeared likely, but the nmr spectrum and relatively nonpolar characteristics were not indicative of a common sugar derivative. Initial attempts at acid hydrolysis led to extensive decomposition,[9] but treatment of **1** with 2 N H_2SO_4 at 70° for 11 hr did afford cucurbitacin D (**2**) in low yield. This result served to interrelate datiscoside (**1**) with other known cucurbitacins as well, since cucurbitacin D had been correlated with cucurbitacins B, E, and I.[10]

Unequivocal proof of the structure, stereochemistry, and absolute configuration of datiscoside was achieved by X-ray crystallographic analysis of datiscoside di-*p*-iodobenzoate (**3**), mp 215–216°. Crystals of the di-*p*-



1, R = H
3, R = *p*-iodobenzoate



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iodobenzoate are orthorhombic with space group $P2_12_12_1$ and a = 19.609 (7), b = 31.485 (17), and c = 8.743 (3) Å, Z = 4. The asymmetric unit contains, in addition, two molecules of water of hydration. The calculated density is 1.475 g cm^{-3}, in reasonable agreement with the observed value of 1.49 (1) g cm^{-3}.

Intensity data were collected by counter diffractometry using monochromatic Cu Kα radiation. The iodine atoms were located from a three-dimensional Patterson synthesis, and the carbon and oxygen atoms were found from three successive three-dimensional electron-density syntheses calculated using the heavy atom method of phase determination. The atomic parameters were refined by the block-diagonal least-squares method using anisotropic thermal parameters for the iodine atoms only and isotropic parameters for the light atoms. Taking into account the anomalous dispersion terms for the iodine atoms ($\Delta f'$ = −1.03, $\Delta f''$ = 7.0), the parameters for the absolute configuration shown in Figure 1 yielded R = 0.100 for the 1627 independent significant reflections measured. A structure factor calculation with coordinates appropriate to

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(10) D. Lavie, Y. Shvo, D. Willner, P. R. Enslin, J. M. Hugo, and K. B. Norton, *Chem. Ind. (London)*, 951 (1959).