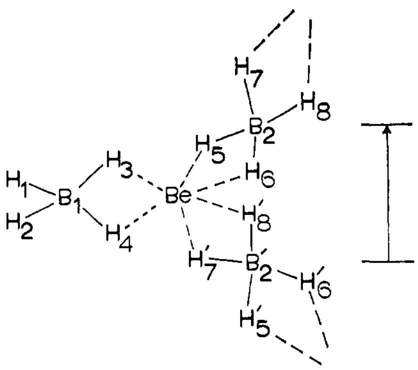
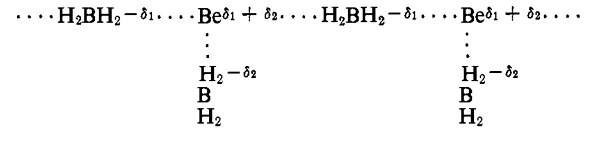


Figure 1. Schematic representation of the $Be(BH_4)_2$ structure, which can also be represented as



$$\begin{array}{cccc} \cdots H_2BH_2^{-\delta_1}\cdots & Be^{\delta_1+\delta_2}\cdots & H_2BH_2^{-\delta_1}\cdots & Be^{\delta_1+\delta_2}\cdots \\ & \vdots & & \vdots \\ & H_2^{-\delta_2} & & H_2^{-\delta_2} \\ & B & & B \\ & H_2 & & H_2 \end{array}$$

The arrow indicates the chemical repeat.

fined as $\Sigma||F_o| - |F_c||/\Sigma|F_o|$) of 0.045. Atomic coordinates are listed in Table I. Probable standard deviations are 0.01 Å for Be and B distances, and 0.03 Å for distances from these atoms to hydrogen. However, these distances to hydrogen are subject to an anomalous shortening of about 0.1 Å, because of the use of spherical atoms in the refinement (0.08 Å)[10] and because of the neglect of torsional oscillation (usually about 0.02 Å).

Table I. Coordinates for the $Be(BH_4)_2$ Crystal Structure

	x	y	z
Be	0.200	0.087	−0.003
B_1	0.164	−0.049	0.006
B_2	0.139	0.194	0.118
H_1	0.095	−0.067	0.070
H_2	0.220	−0.101	−0.048
H_3	0.207	−0.002	0.098
H_4	0.143	0.009	−0.091
H_5	0.105	0.157	0.027
H_6	0.211	0.163	0.137
H_7	0.145	0.273	0.099
H_8	0.090	0.185	0.224

Distances B_1–Be = 1.92, B_2–Be = 2.00, and B_2'–Be = 2.03 Å are comparable with 1.94 Å, the sum of covalent radii.[11] Other distances are from B_1 to H_1 (1.13 Å), H_2 (1.16 Å), H_3 (1.20 Å), and H_4 (1.21 Å); from B_2 to H_5 (1.07 Å), H_6 (1.09 Å), H_7 (1.11 Å), H_8 (1.18 Å); and from Be to H_3 (1.53 Å), H_4 (1.55 Å), H_5 (1.63 Å), H_6 (1.65 Å), H_7' (1.61 Å), and H_8' (1.59 Å). For comparison we note that BH_4^- has a B–H internuclear distance of 1.255 ± 0.02 Å in the alkali borohydrides,[12] and that the Be···H···Be bridge distance of 1.4 Å has been found in $NaO(C_2H_5)_2 \cdot (C_2H_5)_4Be_2H_2$.[13] Only B_1–H_1 and B_1–H_2 are not involved in some degree of bonding to Be. Possibly this $BH_4 \cdots$ Be interaction (for boron B_1) has some geometrical features which may be related to the unknown structure of $Be(BH_4)_2$ in the gas phase. However, the nature of bonding, *e.g.*, whether it is predominantly covalent or ionic and whether it occurs primarily between Be and B or through hydrogen bridges, must await detailed theoretical and other experimental studies.

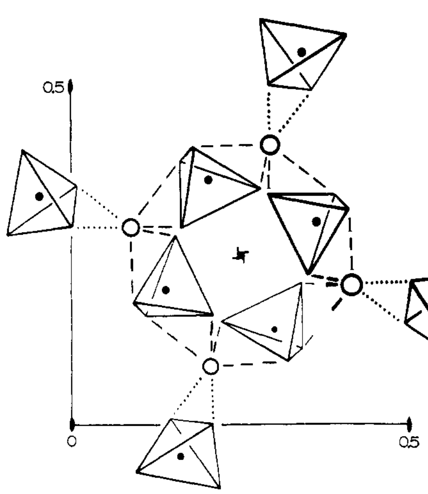


Figure 2. Portion of the unit cell, showing one helical polymeric chain around a 4_1 axis and projected along the c axis. Hydrogen arrangements are tetrahedral around B (●), and trigonal prismatic around Be (○). B–H distances are 1.14 (away from Be) and 1.20 Å (toward Be) for B_1, and 1.11 Å for the BH_4 unit within the helix. The average dotted Be···H distance is 1.54 Å, and the average dashed Be— — —H distance 1.63 Å. See text for accuracy and probable systematically short values of these distances.

Acknowledgment. We wish to thank the Office of Naval Research and the Advanced Research Projects Agency for support of this study.

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(10) T. A. Halgren, R. J. Anderson, D. S. Jones, and W. N. Lipscomb, *Chem. Phys. Lett.*, in press.

(11) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 246.

(12) P. T. Ford and R. E. Richards, *Discuss. Faraday Soc.*, 19, 230 (1955).

(13) G. W. Adamson and H. M. M. Shearer, *Chem. Commun.*, 240 (1965).

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Carbonium Ion Photochemistry. The Photoisomerization of Protonated Eucarvone[1]

Sir:

The distribution of products obtained upon irradiation of eucarvone has been shown[2] to be remarkably solvent dependent. In order to assess the importance of protonated excited states and ionic intermediates, which have been invoked[2,3] in these reactions, we have investigated the photochemistry of protonated eucarvone (**1**). We wish to report that this homolog of the protonated cyclohexa-2,4-dienones[4] undergoes a superficially similar photoisomer-

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(1) Research supported by the National Research Council of Canada.

(2) (a) G. Büchi and E. M. Burgess, *J. Amer. Chem. Soc.*, 82, 4333 (1960); J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 710 (1963); D. I. Schuster, M. J. Nash, and M. L. Kantor, *Tetrahedron Lett.*, 1375 (1964); D. I. Schuster and D. H. Sussman, *ibid.*, 1657 (1970); (b) T. Takino and H. Hart, *Chem. Commun.*, 450 (1970).

(3) O. L. Chapman, *Advan. Photochem.* 1, 353 (1963).

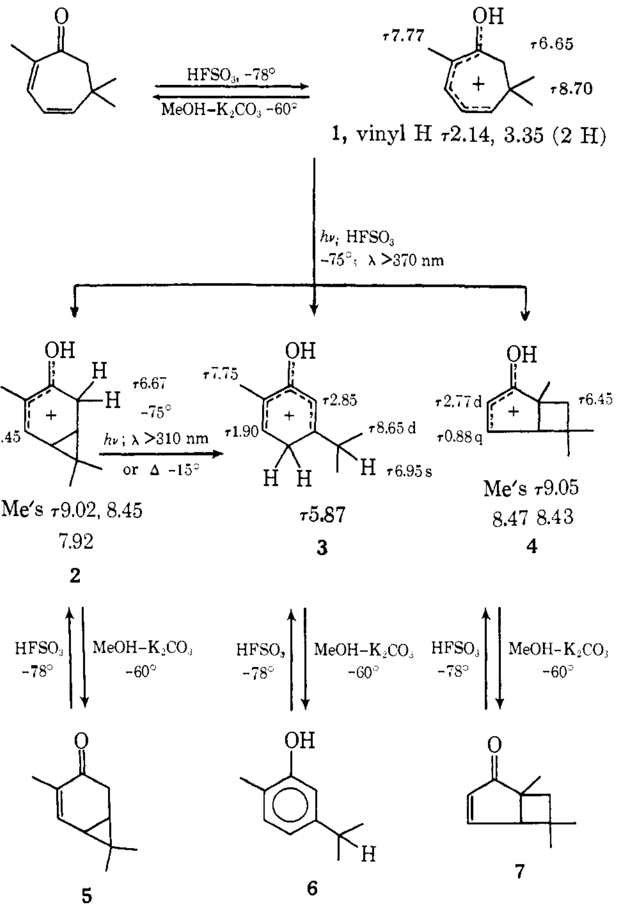
(4) B. Parrington and R. F. Childs, *Chem. Commun.*, 1581 (1970); N. Filipescu and J. W. Pavlik, *J. Amer. Chem. Soc.*, 92, 6062 (1970).

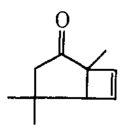
ization in FSO_3H to give predominantly the protonated bicyclo[4.1.0]heptenone (**2**).

A solution of eucarvone[5] in FSO_3H gave **1** which upon irradiation[6] of its long-wavelength absorption ($\lambda_{\max}^{H_2SO_4}$ 400 nm (ϵ 4300)) at temperatures below −75° caused it to cleanly isomerize to give **2**, **3**, and a minor product, tentatively identified as **4**. No change in the ratio of products **2** (73%), **3** (23%), and **4** (4%) could be detected by nmr during the course of the isomerization or upon continued irradiation after all **1** had been treated. Under the conditions at which the irradiations were performed, **1**, **2**, **3**, and **4** were all thermally stable.

The photoproducts were identified from their nmr spectra in acid and by quenching the cations in methanol–carbonate at −60° to give three products in good yield. These, **5**, **6**, and **7**, were separated by preparative gas chromatography and could be reprotonated with $HFSO_3$ at −78° to give **2**, **3**, and **4**, respectively. The nmr, ir, and uv spectra of **5** were identical with those reported by Takino and Hart[2b] and Zabza and Kvezynski.[7] **6** was identical in all respects with an authentic sample of carvacrol. The nmr, ir, and uv spectra of **7** were consistent with the assigned structure.

As protonation of **9** in FSO_3H at −78° gave **10**, which at −55° rearranged quantitatively ($t_{1/2} \approx 10$ min) to **4**, it would seem likely that **10** and not **4** is the initial photoproduct. Although **10** has not been observed[8] in the photolysis solution, a small amount (<1%) of a material with retention time identical with authentic **9** was detected in the quenched product.

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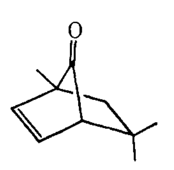
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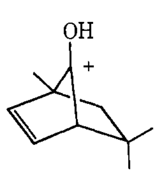
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It is instructive to compare the products found in this work with those previously obtained. If **4** does derive from **10** then the only new product obtained is **3**, which is clearly structurally related to **2** and which could be derived from a common intermediate.[9] The one outstanding difference is that whereas in all other reported photoisomerizations **8** has been the major product, no cation corresponding to protonated **8**,[10] or any rearrangement product of it, could be detected upon irradiation of **1**. As there is no evidence in the nmr spectrum of **1** of any unprotonated ketone, there can be little doubt that the photoisomerizations observed here proceed by $\pi-\pi^*$ excitation of the protonated ketone.

Ionic intermediates have been proposed[2,3] to account for the large rate accelerations observed for the disappearance of eucarvone in polar solvents and for the enhanced formation of products other than **8**. The similarity of the products in FSO_3H to those encountered in polar media would strongly support this contention. Moreover, in the protic solvents which have frequently been used it is very likely that protonation of a $\pi-\pi^*$ state would occur, giving rise to a species which, if not the same as that obtained by irradiation of the ground-state protonated ketone, undergoes similar reactions.

The major photoproduct **2** was isomerized in FSO_3H to **3** either by heating the solution to −15° ($t_{1/2}$ = 16 min) or by irradiating **2** through a Pyrex filter. The possibility that these isomerizations proceeded by an antarafacial 1,6-hydride shift from the C_5 methylene to C_7, symmetry allowed in the first excited state,[11] can be discounted, as **2** with C_5 dideuterated gave **3** with no incorporation of deuterium in the isopropyl group. A thermal 1,2-hydride shift from C_6 to C_7 is a viable alternative that is consistent with our observations. This would be a relatively high-energy process as the vacant orbital on C_7 is poorly aligned with the C_6H bond.[12] To minimize this dihedral angle it is necessary to localize charge on C_7 and rotate about the C_6C_7 bond to give a cation which could be represented as **11**.[13] Such a cation could possibly result from photochemical excitation of **2**.[14]

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[5] E. J. Corey and H. J. Burke, *J. Amer. Chem. Soc.*, 78, 174 (1956).

[6] Irradiations were performed in clear-wall nmr tubes with a Philips SP 500-W lamp and Corning Glass filter, No. 3850; nmr spectra of product cations recorded at −45°, chemical shifts referred to tetramethylammonium chloride taken as τ 6.9.

[7] A. Zabza and H. Kvezynski, *Rocz. Chem.*, 40, 463 (1966).

[8] Lack of resolution of the nmr spectra in FSO_3H at temperatures at which **10** is stable hampered observation of this 4% product

[9] In a careful study Takino and Hart[2b] have recently established that **5** is a photoproduct of eucarvone in trifluoroethanol and silica gel–cyclohexane, and that it was photolabile. We find it is also formed in 20% yield upon irradiation of eucarvone in 50% acetic acid.

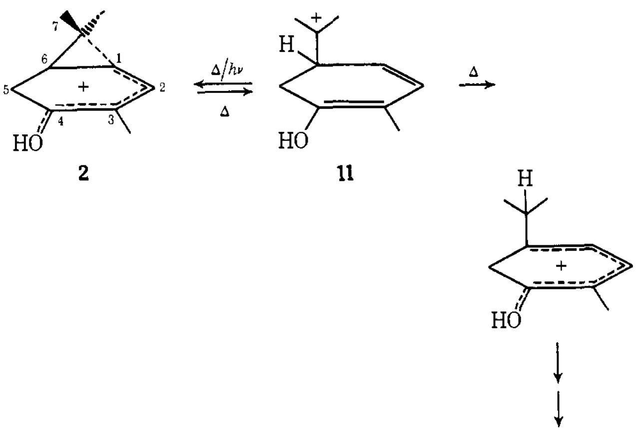
[10] Protonation of **8** with FSO_3H gives rise to a series of rearranged cations, none of which corresponds to **2**, **3**, or **4**.

[11] R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 8, 781 (1969).

[12] D. M. Brouwer and H. Hogeveen, *Recl. Trav. Chim. Pays-Bas*, 89, 211 (1969).

[13] It is not clear at this stage how best to represent the electron delocalization of **2** and to what extent the cyclopropane is involved.

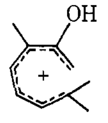
[14] H. E. Zimmerman and T. W. Flechtner, *J. Amer. Chem. Soc.*, 92, 6931 (1970).



2

11

3



12

The formation of **2** photochemically from **1** could be thought of in terms of a concerted $[_{\sigma}2_a + _{\pi}2_a]$ cycloaddition reaction;[11] however, such a mechanism does not account for the formation of **3**.[15] An alternative pathway, which can account for the production of both **2** and **3**, is an electrocyclic ring-opening reaction that breaks the C_6C_7 bond of **1** to give the open-chain cation **12**. Such a process is directly comparable to that observed upon the photoisomerization of the isoelectronic cyclohexa-1,3-dienes to the bicyclo[3.1.0]-hexenes.[11,16] While the direct isomerization of **12** to give **2** is possible, in view of the constant ratio of **2** to **3** observed in these reactions, it is attractive to consider that a cation resembling **11** might be formed either photochemically, or thermally, from **12** and that this gives the observed products, **2** and **3**.

[15] A trans ring juncture would result from the alternative $[_{\sigma}2_s + _{\pi}2_s]$ cycloaddition reaction.

[16] J. Meinwald and P. H. Mazzocchi, *J. Amer. Chem. Soc.*, **88**, 2850 (1966).

[17] Holder of National Research Council of Canada Scholarship.

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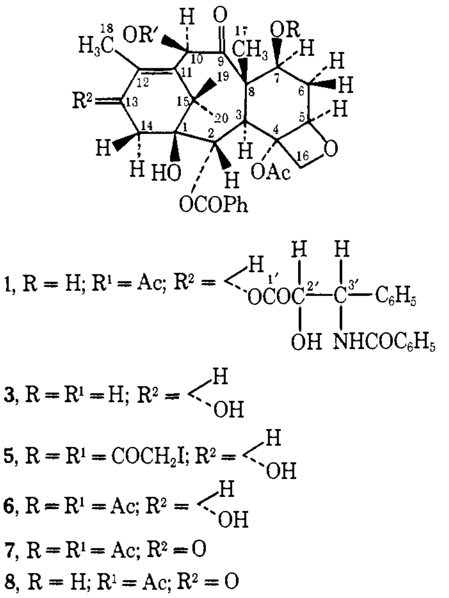
Received January 20, 1971

Plant Antitumor Agents. VI. The Isolation and Structure of Taxol, a Novel Antileukemic and Antitumor Agent from *Taxus brevifolia*[1,2]

Sir:

We wish to report on the structure of a novel compound named taxol (**1**), isolated from the stem bark of the western yew, *Taxus brevifolia*.[3,4] *Taxol has potent antileukemic and tumor inhibitory properties*[5] *and is the first compound possessing the taxane*[6] *ring which has been demonstrated to have such activity.*



1, $R = H; R^1 = Ac; R^2 = $ H, OCOC(H)(OH)–C(H)(NHCOC$_6$H$_5$)–C$_6$H$_5$ (1′, 2′, 3′)

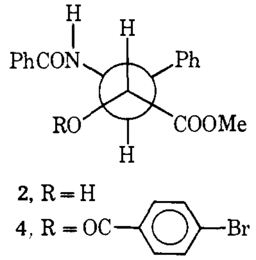
3, $R = R^1 = H; R^2 = $ H, OH

5, $R = R^1 = COCH_2I; R^2 = $ H, OH

6, $R = R^1 = Ac; R^2 = $ H, OH

7, $R = R^1 = Ac; R^2 = O$

8, $R = H; R^1 = Ac; R^2 = O$



2, R = H

4, R = OC–C_6H_4–Br

The alcohol extract of the stem bark was concentrated and partitioned between water and chloroform. Guided by assay in 9KB and various leukemia systems, three successive chromatographies of the residue from the chloroform extract on Florisil, Sephadex LH-20, and silica gel followed by crystallization from aqueous methanol gave taxol (**1**) as needles:[7] yield 0.02%; M^+ at *m/e* 853, calcd for $C_{47}H_{51}NO_{14}$, 853; mp 213–216° dec; $[\alpha]^{20}D$ −49° (MeOH); λ_{max} (MeOH) 227 nm (ϵ 29,800), 273 (1700); ν_{max}^{Nujol} 3300–3500 (OH, NH), 1730 (ester), 1710 (ketone), 1650 (amide) cm^{-1}. The characteristic chemical shifts[8] of **1** are shown in Table I.

Because of the extremely limited quantity of taxol and its evident complexity, attempts were made to prepare derivatives suitable for X-ray analysis. Al-

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[1] Previous paper in this series: M. C. Wani, J. A. Kepler, J. B. Thompson, M. E. Wall, and S. G. Levine, *Chem. Commun.*, 404 (1970).

[2] This investigation was conducted under Contract No. SA-43-ph-4322, Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health. X-Ray investigations were carried out at Duke University and were supported by a Duke Endowment Grant.

[3] A preliminary report dealing only with the isolation of 1 was presented by M. E. Wall and M. C. Wani at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., 1967; Paper No. M-006.

[4] Taxol has been isolated from several other species of the Taxus genus, including *T. Cuspidata* and *T. baccata*. We thank Dr. Robert E. Perdue, New Crops Research Branch, Plant Inudstry Station, Beltsville, Md., for obtaining the plant material.

[5] Taxol shows confirmed activity [for description of bioassay procedures and leukemia and tumor systems, *cf. Cancer Chem. Rept.*, **25**, 1 (1962)] in L-1210, P-388, and P-1534 leukemias, being highly active in the latter two systems, is also highly active as an inhibitor of WM-256 carcinosarcoma, and shows considerable cytotoxicity in 9KB assay, $ED_{50} = 5.5 \times 10^{-5}$. Less pure concentrates containing taxol were also active in Sarcoma 180 and Lewis lung tumors.

[6] B. Lythgoe, K. Nakanishi, and S. Uyeo, *Proc. Chem. Soc.*, 301 (1964).

[7] All compounds reported in this communication have been characterized spectrally (ir, uv, nmr) and analytically (elemental and mass spectrum).

[8] Spectral assignments are based on the nmr spectra of taxane derivatives reported in the literature.[9-11]

[9] M. C. Woods, K. Nakanishi, and N. S. Bhacca, *Tetrahedron*, **22**, 243 (1966).

[10] I. W. Harrison, R. M. Scrowston, and B. Lythgoe, *J. Chem. Soc. C*, 1933 (1966).

[11] D. P. Della Casa de Marcano and T. G. Halsall, *Chem. Commun.*, 1382 (1970).