

The formation of **2** photochemically from **1** could be thought of in terms of a concerted [ $\sigma_{2a} + \pi_{2a}$ ] cycloaddition reaction;<sup>11</sup> however, such a mechanism does not account for the formation of **3**.<sup>15</sup> An alternative pathway, which can account for the production of both **2** and **3**, is an electrocyclic ring-opening reaction that breaks the C<sub>6</sub>C<sub>7</sub> 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.<sup>11,16</sup> 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 [ $\sigma_{2s} + \pi_{2s}$ ] 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.

K. E. Hine,<sup>17</sup> R. F. Childs\*

Department of Chemistry, McMaster University  
Hamilton, Ontario, Canada

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## Plant Antitumor Agents. VI. The Isolation and Structure of Taxol, a Novel Antileukemic and Antitumor Agent from *Taxus brevifolia*<sup>1,2</sup>

Sir:

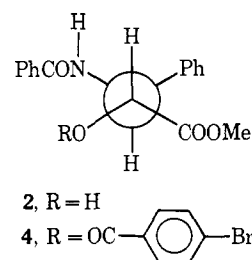
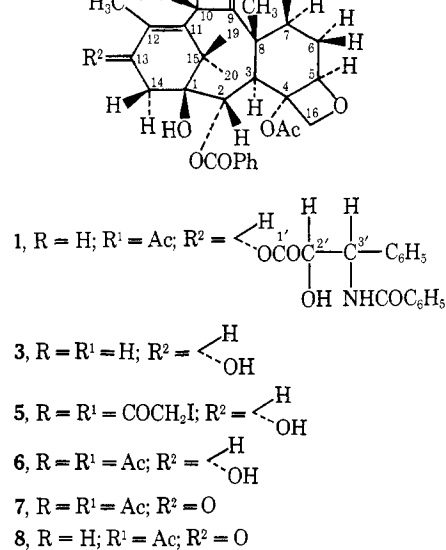
We wish to report on the structure of a novel compound named taxol (**1**), isolated from the stem bark of the western yew, *Taxus brevifolia*.<sup>3,4</sup> Taxol has potent

(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



antileukemic and tumor inhibitory properties<sup>5</sup> and is the first compound possessing the taxane<sup>6</sup> ring which has been demonstrated to have such activity.

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:<sup>7</sup> yield 0.02%; M<sup>+</sup> at *m/e* 853, calcd for C<sub>47</sub>H<sub>51</sub>NO<sub>14</sub>, 853; mp 213–216° dec; [ $\alpha$ ]<sub>D</sub><sup>20</sup> -49° (MeOH);  $\lambda_{\max}$  (MeOH) 227 nm ( $\epsilon$  29,800), 273 (1700);  $\nu_{\max}^{\text{Nujol}}$  3300–3500 (OH, NH), 1730 (ester), 1710 (ketone), 1650 (amide) cm<sup>-1</sup>. The characteristic chemical shifts<sup>8</sup> 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-

E. Perdue, New Crops Research Branch, Plant Industry 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<sub>50</sub> = 5.5 × 10<sup>-5</sup>. 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.<sup>9–11</sup>

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

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

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

Communications to the Editor



