John Sofranko and Professor Allen Bard for helpful discussions.

Barbara Fisher, Richard Eisenberg*
Department of Chemistry, University of Rochester
Rochester, New York 14627
Received July 3, 1980

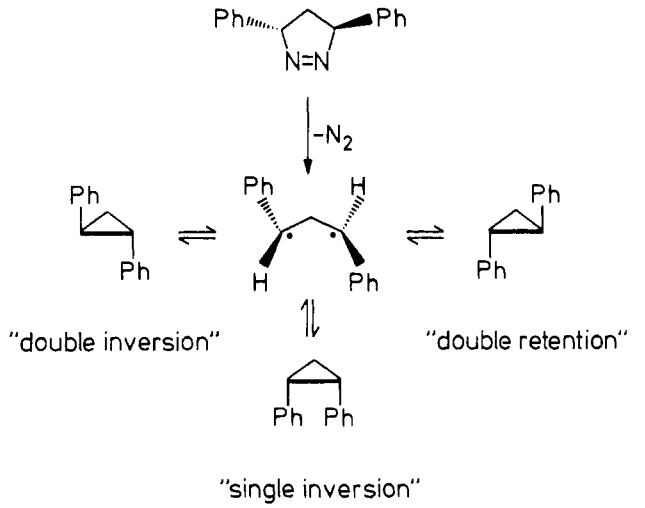
Transfer of Optical Activity in the Decomposition of (+)- and (−)-*trans*-3,5-Diphenyl-1-pyrazoline. Competing "Biradical" and "Cycloreversion" Pathways

Sir:

It is very tempting to suggest that stereomutations of cyclopropanes and the decomposition reactions of 1-pyrazolines both involve similar trimethylene intermediates (e.g., Scheme I). The stereochemical pattern of both reactions has been explained either by the implication of biradicals[1] (of varying nature[2]) or, in support of theoretical considerations,[3] via intermediate 0,0 trimethylenes (π-cyclopropanes).[4,5] Although major theoretical contributions[6] and elegant experiments[2,5,7] have greatly increased our knowledge of the involved intermediates, the outcome of new experiments seems rather unpredictable and dependent on the specific system. Studies with optically active 1-pyrazolines along this line are rather rare,[5] and we found a systematic investigation of a number of these systems rather attractive.

We report here, in the first experiments of a series, the photolysis and thermolysis of the title compounds (+)- and (−)-**1**. Both enantiomers, as well as the major reaction products (+)- and (−)-*trans*-1,2-diphenylcyclopropane (+)-**2t** and (−)-**2t**, were obtained optically pure from racemic material by direct chromatography on cross-linked triacetylcellulose[8] (Figure 1). In a typical run, saturated solutions of **1**[9] (1% in EtOH) or **2t**[10] (6% in EtOH) were injected on packed steel columns with EtOH as eluant; both the angle of rotation and the optical density were recorded continuously.[11] Due to base line separations and the use of preparative columns the pure enantiomers could be easily isolated. Their optical purities were controlled by analytical runs and their chiroptical data, rotations [(−)-**1**: $[\alpha]^{22}_{D}$ −817°, $[\alpha]^{22}_{365}$ −6680° (*c* 0.023 EtOH); (−)-**2t**: $[\alpha]^{22}_{D}$ −423°, $[\alpha]^{22}_{365}$ −1987° (*c* 0.0087 EtOH)] and molar ellipticities [(−)-**1**: $[\theta]_{332}$ −44 090° (EtOH, 1.3×10^{-3} M); (−)-**2t**: $[\theta]_{230}$ −114 021° (EtOH, 4.5×10^{-4} M)].[12]

Scheme I



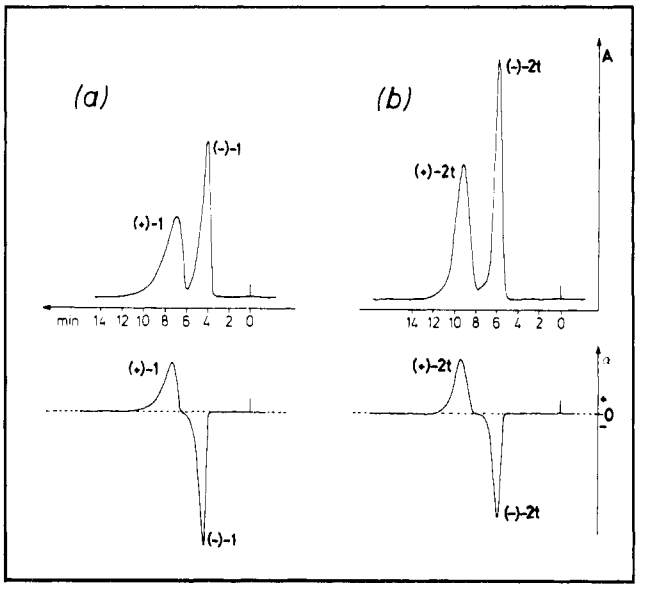


Figure 1. High-performance LC chromatograms for the separation of (a) (±)-**1**, (b) (±)-**2t** on cross-linked triacetylcellulose;[8,11] (α) angle of rotation at full lamp (Hg) intensity with filters removed; (A) absorbances at 330 nm [(±)-**1**] and 254 nm [(±)-**2t**].

Their absolute configurations were either known [(+)-/(−)-**2t**][13] or established [(+)-/(−)-**1**] by comparison of ORD and CD spectra with those of known compounds,[5a,b,14] as well as by application of an octant rule.[15]

Degassed 1.2×10^{-3} M solutions of (+)-**1**[16] in a variety of solvents were irradiated with monochromatic (330 ± 10 nm) ultraviolet light (lamp: XBO 1600 from Osram, monochromator: High Intensity Monochromator 33-86-79 from Bausch & Lomb) or thermolyzed in a constant temperature (75 ± 0.1 °C) bath until completion. Reactions were followed both by UV and CD. In a typical experiment (Figure 2) the CD maximum of (+)-**1** at 332 nm (corresponding to the n → π^* transition in **1**) decays gradually during the reaction under the formation of (−)-**2t** with

(1) For a critical review: Bergmann, R. G. *Free Radicals* **1973**, *1*, 191–237.
(2) Berson, J. A.; Pederson, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1976**, *98*, 122–143.
(3) Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475–1485.
(4) In order to accommodate the experimental data the following mechanistic proposals with their stereochemical consequences have been suggested previously:[2] (a) stereorandom trimethylene biradicals; (b) single methylene rotation; (c) double methylene rotation via 0,0 trimethylenes (π-cyclopropanes).
(5) (a) Mishra, A.; Crawford, R. J. *Can. J. Chem.* **1969**, *47*, 1515–1519. (b) Clarke, T. C.; Wendling, L. A.; Bergmann, R. G. *J. Am. Chem. Soc.* **1975**, *97*, 5638–5640. (c) For a different type of 1-pyrazoline with a remote center of asymmetry, which could, however, follow a different decomposition pathway, see: Dreibelbis, R. L.; Khatri, H. N.; Walborsky, H. M. *J. Org. Chem.* **1975**, *40*, 2074–2079.
(6) (a) Buenker, R. J.; Peyerimhoff, S. D. *J. Phys. Chem.* **1969**, *73*, 1299–1313. (b) Siu, A. K. Q.; St. John, M., III; Hayes, E. F. *J. Am. Chem. Soc.* **1970**, *92*, 7249–7252. (c) Hay, P. J.; Hunt, W. J.; Goddard, W. A., III *Ibid.* **1972**, *94*, 638–640. (d) Horsley, J. A.; Jean, Y.; Moser, C.; Salem, L.; Stevens, R. M.; Wright, J. S. *Ibid.* **1972**, *94*, 279–282.
(7) Bergmann, R. G.; Carter, W. L. *J. Am. Chem. Soc.* **1969**, *91*, 7411–7425.
(8) CEL AC-40X from Macherey-Nagel+Co, D-5160 Düren, Germany.
(9) Overberger, C. G.; Anselme, J. P. *J. Am. Chem. Soc.* **1962**, *84*, 869–870 and other papers in this series. Bandlish, B. K.; Garner, A. W.; Hodges, M. L.; Timberlake, J. W. *Ibid.* **1975**, *97*, 5856–5862. Schneider, M. P.; Strohäcker, H. *Tetrahedron* **1976**, *32*, 619–621.
(10) Beech, S. G.; Turnbull, J. H. *J. Chem. Soc.* **1952**, 4686–4690.
(11) Columns 8 mm × 250 mm; particle size 30–50 μm (7 μm has recently become available and is now being tested); flow rates 1.9 mL/min for **1**, 1.2 mL/min for **2t**; polarimeter flow cell from Hellma GmbH + Co, D-7840 Müllheim, Germany, length 100 mm, volume 57 μL; Perkin-Elmer 241 polarimeter; eluant 96% EtOH.
(12) Rotations and molar ellipticities have been determined for all enantiomers in a variety of solvents; for brevity only a few values are listed. The data compare well with the literature values for (+)-**2t**[13a] and (−)-**2t**;[13b] (+)- and (−)-**1** have been obtained here for the first time.
(13) (a) Aratani, T.; Nakanishi, Y.; Nozaki, H. *Tetrahedron* **1970**, *26*, 1675–1684; (b) Mintas, M.; Mannschreck, A.; Schneider, M. *J. Chem. Soc., Chem. Commun.* **1979**, 602–603.
(14) Snatzke, G. *Riechst., Aromen, Körperpflegem.* **1969**, *19*, 98–104.
(15) Rau, H.; Schuster, O. *Z. Naturforsch. B* **1979**, *34B*, 1519–1524.
(16) Experiments with both (+)- and (−)-**1** have been carried out; for clarity only one is used.

0002-7863/80/1502-7363$01.00/0

Table I. Chiroptical Data of (-)-2t in the Decomposition of (+)-1. Stereochemistry and Relative Importance of the "Trimethylene" and "Cycloreversion" Pathways

		(-)-2t					
		chiroptical properties, deg		optical		cycloreversion, %	
solvent	conditions[a,b]	$[\alpha]_{365}$	$[\theta]_{232}$	purity, %[c]	retention, %	exptl[d]	kinetic[e]
octane	$h\nu$	−800	−45 000	50	75	23	30
	therm	−1400	−74 000	66	83		
acetonitrile	$h\nu$	−850	−48 000	40	60	8	12
	therm	−1490	−73 000	70	85		
ethanol	$h\nu$	−906	−50 000	60	80	10(12)[f]	10
	therm	−1423	−73 000	73	87		

[a] Monochromatic irradiation at −20 °C and 330 ± 10 nm. [b] Thermolysis in a constant temperature bath at 75 °C. [c] Based on the rotational values and CD data of optically pure (-)-2t. [d] Determined under standardized conditions from (stable) 4. [e] Kinetic determination up to 30% completion: ΔA_{330} yields the disappearance of (+)-1, ΔA_{308} the formation of 3. [f] After 70% completion.

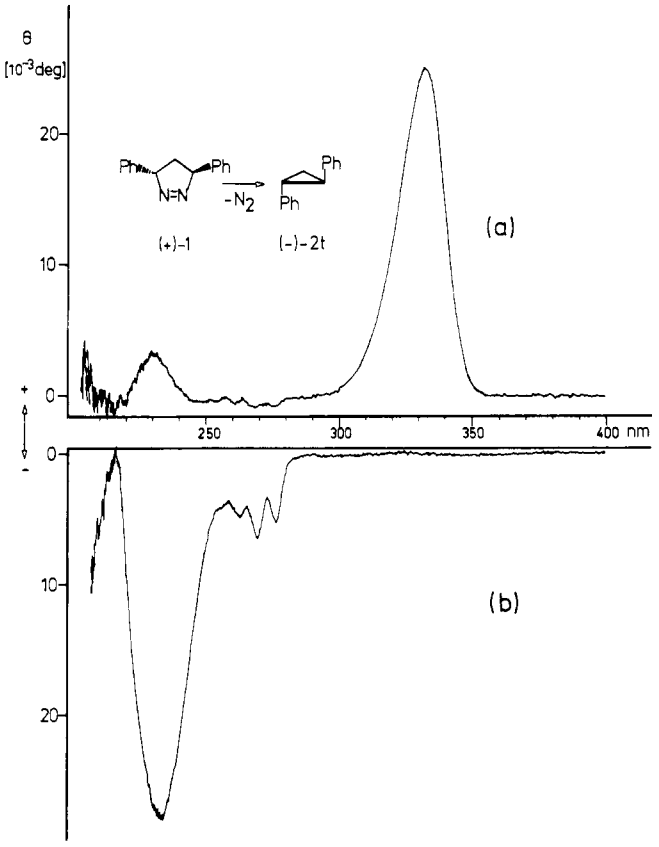
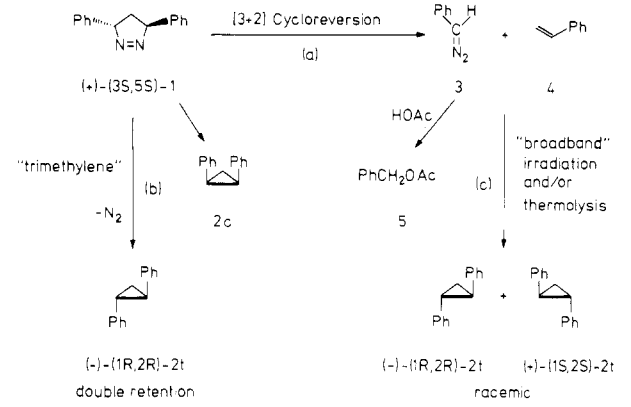


Figure 2. CD spectrum of a sample of (+)-1 (c 1.20 × 10^{-3} M, n-hexane) (a) before and (b) after irradiation with UV light (330 ± 10 nm); (b) is identical with the spectrum of (−)-2t. For solvent dependence and conditions see Table I. Thermolysis leads to similar results; cf. Table I.

a maximum at 230 nm. Both the molar ellipticities and rotational values of the resulting solutions were recorded, and the proportions of (−)-2t (~90%) and (achiral) *cis*-1,2-diphenylcyclopropane (2c) (~10%) were determined by VPC/high-performance LC. The optical purities of (−)-2t could thus be calculated (Table I) and were identical with values obtained independently in control experiments from *isolated* (−)-2t. Similarly, (−)-1 produces (+)-2t with practically identical optical purities.[16]

It has been suggested previously[17] that [3 + 2] cycloreversions may effectively compete with biradical processes in the decomposition of monocyclic 1-pyrazolines, although, to our best knowledge, a *quantitative* determination of the *primary* products of such reactions has never been achieved. Careful monochromatic irradiation of (+)-1 at −20 °C indeed revealed the formation of $PhCHN_2$ (3) and styrene (4), both clearly products of a cycloreversion process [reaction a in Scheme II].[18] Their concentrations were determined both spectroscopically and by VPC/high-performance LC [3 after trapping with HOAc as benzyl acetate (5)]. The observed amounts, a direct measure for the cycloreversion pathway (Table I), seem to be solvent dependant[18] and decrease with increasing polarity. A careful kinetic study revealed that, in spite of nearly monochromatic irradiation, the concentrations of cycloreversion products pass through a maximum during the reaction (at ~70% conversion) and decrease again with continued irradiation. The kinetically determined maximum concentrations of cycloreversion products are also listed in Table I.

Scheme II



In the thermolysis of (+)-1 the importance of cycloreversion processes cannot be estimated [see (c) in Scheme II]. Check experiments show that (+)-1 is not racemizing during thermolysis, a process which could be expected to occur via a cycloreversion–cycloaddition sequence. Thermolysis of 3 + 4 would, via a carbene route (similar to broadband irradiation), lead to racemic (±)-2t [compare (c) in Scheme II].

In summary, the decomposition of (+)-1 can be described by two independent processes as displayed in Scheme II: (a) In the photolysis of (+)-1 up to 30% of the reaction is proceeding via a cycloreversion process, which could only be detected and determined quantitatively by careful low temperature monochromatic irradiation.[19] (b) A trimethylene ("biradical") pathway (see Scheme I) occurs in which (+)-1 is clearly decomposing with high transfer of optical activity and with predominant *double retention* of configuration. Both the obtained optical purities of (−)-2t, being higher in the thermolysis than in the photolysis, and the degree of conservation of stereochemistry are the highest ever reported

(17) Rinehart, K. L.; van Auken, T. V. *J. Am. Chem. Soc.* **1960**, *82*, 5251. Rinehart, K. L.; van Auken, T. V. *Ibid.* **1962**, *84*, 3736–3743. Moore, R.; Mishra, A.; Crawford, R. J. *Can. J. Chem.* **1968**, *46*, 3305–3313. Buchwalter, S. L.; Closs, G. L. *J. Org. Chem.* **1975**, *40*, 2549–2551.

(18) A detailed study of the cycloreversion process in the decomposition of *cis*- and *trans*-3,5-diphenyl-1-pyrazolines including solvent dependence studies is presently being carried out.

(19) Broad-band irradiation would via a carbene route (see (c), Scheme II) lead to the identical ultimate products 2c and racemic 2t. The process could therefore have gone undetected in several cases, and its importance may well have been underestimated. This becomes even more important in view of the fact that in a number of cases "biradical" and "cycloreversion" processes may have rather similar energy requirements: Schneider, M.; Csacsko, B., unpublished results.

in the decomposition of a simple 1-pryazoline.[5c]

The results are in agreement with Fukui's earlier suggestions[20] and product studies with racemic **1**.[9] Regardless of the detailed nature of the involved intermediates and similar to the stereomutation of (−)-**2t**,[21] (+)-**1** must decompose via chiral intermediates (avoiding a planar 0,0 trimethylene);[3] attractive candidates[6] are 90,90 (face to face[6d,7,22] or pyramidal[6c,23]) biradicals.

We are presently investigating systems where, according to Fukui's suggestion,[20] single inversion should be expected and others where the cyclopropane work[2] suggests 0,0 trimethylene intermediates.

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft for the financial support of this work and the Fonds der Chemischen Industrie for a stipend for H.B. We also thank Professor J. A. Berson, Yale University, for stimulating discussions during the progress of this work. Helpful advice regarding the separation of enantiomers by Professor A. Mannschreck and Dr. M. Mintas, University Regensburg, is gratefully acknowledged.

(20) Inagaki, S.; Fukui, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 824–829.
(21) Crawford, R. J.; Lynch, T. R. *Can. J. Chem.* **1968**, *46*, 1457–1458.
(22) Howe, N. E.; Yankee, E. W.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 4230–4237.
(23) Jean, Y.; Salem, L. *J. Chem. Soc., Chem. Commun.* **1971**, 382–384.

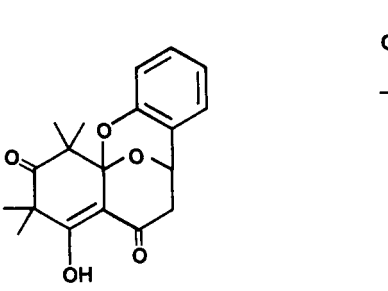
Manfred P. Schneider,* Herbert Bippi
Institut für Chemie, Universität Hohenheim
D-7000 Stuttgart-70, Germany
Received June 9, 1980

Vafzelin and Uvafzelin, Novel Constituents of *Uvaria Afzelii*

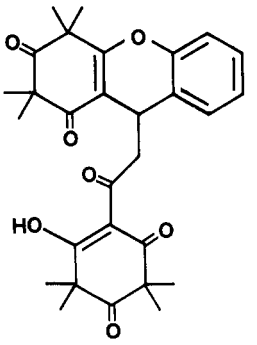
Sir:

Higher plants of the genus *Uvaria* continue to be an interesting source of biologically active secondary metabolites.[1,2] During our recent studies, we noted that an ethanolic extract of the stems of *Uvaria afzelii* Scot Elliot (Annonaceae) showed significant antimicrobial activity.[3] Fractionation of the extract was guided by an antimicrobial assay and resulted in concentration of the activity in the ethyl acetate soluble fraction of an ethyl acetate–water partition. Chromatography of the active ethyl acetate fraction over silicic acid yielded a number of fractions, and we now wish to report the structures of two novel constituents. We have given these constituents the trivial names vafzelin (**1**) and uvafzelin (**2**).[4]

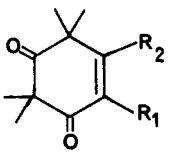
Vafzelin (**1**) was obtained as colorless prisms, mp 136–138 °C (*n*-hexane). High-resolution mass spectrometry and combustion analysis established the molecular formula of **1** as $C_{19}H_{20}O_5$. The UV spectrum showed λ_{max} (dioxane) to be 283 (ϵ 4.51 × 10^3), 250 sh (ϵ 2.62 × 10^3), and 218 nm (ϵ 3.93 × 10^3) while the IR showed bands at ν_{max} (KBr) 3415 (OH), 1725 (C=O), 1620 br (C=O), and 1595 cm^{-1} (C=C). The ^1H NMR ($CDCl_3$, 60 MHz) spectrum showed a four-proton multiplet (δ 7.27–6.53), an ABX pattern [δ 5.25 (dd, J = 1, 6 Hz), 3.20 (dd, J = 6, 18 Hz), 2.55 (dd, J = 1, 18 Hz)], and signals for four-methyl groups [δ 1.42 (6 H, s), 1.37 (3 H, s), and 1.17 (3 H, s)]. The ABX pattern and the multiplet in the aromatic region of the ^1H NMR spectrum are similar to those observed in the (*o*-hydroxylbenzyl)flavanones previously reported in *U. chamae*.[5] The ^{13}C NMR ($CDCl_3$, 15 MHz) spectrum also suggested an ortho-oxygenated alkyl substituted aromatic ring with signals at 150.2 s, 129.3 d, 125.5 d, 122.7 s, 121.4 d, and 117.1 d ppm similar to those previously reported.[6,7] Other signals in the ^{13}C NMR spectrum (211.4 s, 198.2 s, 183.7 s, 105.6 s, 53.0 s, 52.0 s, 26.1 q, 23.3 q, and 15.6 q ppm) were similar to those for syncarpic acid (**3**) and its *O*-methyl (**4**) and *C*-acetyl (**5**) derivatives.[8] The remaining three signals in the ^{13}C NMR spectrum appeared at 68.4 d (C-2), 39.2 t (C-3), and 98.7 s (C-8a) ppm. The assignment of this latter signal to a ketal carbon seemed reasonable from chemical shift theory and the fact that vafzelin (**1**) showed only three carbonyls (see **5**). The collective spectroscopic data suggested that vafzelin was composed of an *o*-hydroxycinnamoyl moiety and syncarpic acid (**3**). Since the structural evidence for **1** was largely presumptive and incomplete, a single-crystal X-ray diffraction experiment was performed.



1



2



3, R_1 = H; R_2 = OH
4, R_1 = H; R_2 = OCH_3
5, R_1 = $COCH_3$; R_2 = OH

Vafzelin crystallized in the monoclinic crystal system with a = 12.55 (2), b = 15.487 (2), c = 8.544 (1) Å, and β = 97.6 (1)°. Systematic extinctions and density considerations were uniquely accommodated by space group $P2_1/c$ with one molecule of $C_{19}H_{20}O_5$ forming the asymmetric unit. This choice, which was fully verified by subsequent refinement, requires that vafzelin be either achiral or a racemic mixture. Intensity data were collected on a fully automated four-circle diffractometer by using graphite monochromated Cu Kα (1.54178 Å) X-rays and a 1° ω scan. All 2512 unique diffraction maxima ($2\theta \leq 114°$) were collected and after correction for Lorentz, polarization, and background effects, 1631 (65%) were judged observed ($|F_o| \geq 3\sigma(F_o)$). The structure was solved uneventfully by using an automatic sign determining procedure.[9] Full-matrix least-squares refinements with anisotropic

(1) Hufford, C. D.; Lasswell, W. L., Jr.; Hirotsu, K.; Clardy, J. *J. Org. Chem.* **1979**, *44*, 4709–4710 and references therein.
(2) Edwards, J. M.; Raffauf, R. F.; LeQuesne, P. W. *J. Nat. Prod.* **1979**, *42*, 85–91 and references therein.
(3) The extract showed activity against *Staphylococcus aureus*, *Bacillus subtilis*, and *Mycobacterium tuberculosis* when assayed as previously described: Hufford, C. D.; Funderburk, M. J.; Morgan, J. M.; Robertson, L. W. *J. Pharm. Sci.* **1975**, *64*, 789.
(4) A total of 150 mg of **1** and 600 mg of **2** were obtained from 43 g of the ethyl acetate fraction using benzene and 2% ether–benzene as eluant, respectively.
(5) Lasswell, W. L., Jr.; Hufford, C. D. *J. Org. Chem.* **1977**, *42*, 1295.
(6) Hufford, C. D.; Lasswell, W. L., Jr. *Lloydia* **1978**, *41*, 151.
(7) El-Sholy, H. N.; Lasswell, W. L., Jr.; Hufford, C. D. *J. Nat. Prod.* **1979**, *42*, 264.
(8) Syncarpic acid (**3**) was also identified as a constituent of the title plant. The *O*-methyl (**4**) and *C*-acetyl (**5**) derivatives were prepared as described by Hodgson et al. [Hodgson, D.; Ritchie, E.; Taylor, W. C.; *Aust. J. Chem.* **1960**, *13*, 385]. ^{13}C NMR **3** (pyridine-d_6 ppm) 214.6 s, 189.5 s, 101.3 d, 51.95 s, and 24.9 q; **4** ($CDCl_3$) 213.2 s, 199.1 s, 178.4 s, 99.2 d, 56.3 q, 55.3 s, 48.2 s, 25.0 q, and 24.3 q; **5** ($CDCl_3$) 209.9 s, 201.6 s, 199.3 s, 196.7 s, 109.6 s, 56.8 s, 52.2 s, 27.2 q, 24.4 q, 23.9 q.

0002-7863/80/1502-7365$01.00/0