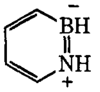
borazaropyridine (II) are chemically very stable,[5] unlike those of I; this suggested that five-membered heteroaromatic rings containing boron might also be stabilized by additional heteroatoms. We wish to report a new synthesis of such a system, 5,1,3,4-boratriazarole (III), which seems to show stability of a high order and which can be regarded as an analog of imidazole or pyrazole.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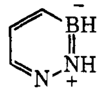
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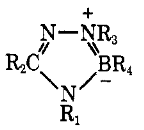
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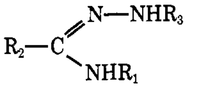
IV

One derivative of III had been reported previously, *i.e.*, the tetraphenylboratriazarole (III, $R_1 = R_2 = R_3 = \text{Ph}$) which was obtained in 5% yield by pyrolysis of a mixture of 2,5-diphenyltetrazole with the pyridine adduct of 2,5-diphenylboron azide.[6] We have now found that compounds of this type can be prepared quite generally and in good yield by heating a boronic acid derivative (RBX_2, where X = Cl, OCH_3, OC_2H_5, OH, or NMe_2) with the corresponding acid amidrazone (IV) in boiling benzene. Volatile products (HCl, $NHMe_2$) were removed by passing dry nitrogen through the reaction mixture while liquid ones (H_2O, ROH) were eliminated with a Dean-Stark moisture trap. The structures of the products were indicated by elemental analysis,[7] by the method of synthesis, and by the identity of the tetraphenyl derivative, as indicated by its melting point and infrared spectrum, with the compound prepared by Paetzold.[6] The mass spectra showed in each case a very strong peak corresponding to the mass number expected for the molecular ion from III. The compounds so far prepared are listed in Table I with their melting points.

Table I. 5,1,3,4-Boratriazaroles

	R_1	R_2	R_3	R_4	Mp, °C[a]	% yield[b]
IIIa	H	CH_3	H	C_6H_5	147–149	63
b	H	CH_3	CH_3	C_6H_5	130–131	64
c	C_6H_5	H	H	C_6H_5	149–150	59
d	H	2-Pyridyl	H	C_6H_5	166–167	81
e	C_6H_5	H	C_6H_5	C_6H_5	164–165	35
f	C_6H_5	C_6H_5	H	C_6H_5	222–223	95
g	C_6H_5	C_6H_5	C_6H_5	C_6H_5	198–200	65
h	C_6H_5	C_6H_5	H	*n*-Bu	107	50

[a] In sealed capillary, under nitrogen; uncorrected. [b] Based on starting amidrazone; reported yields before preparation of analytical samples.

While these boratriazaroles are destroyed by boiling with strong acid or alkali (*e.g.*, 10% HCl or NaOH) they are stable to hydrolysis under milder conditions. Thus contrary to the statement by Paetzold,[6] IIIg is unchanged by prolonged (2 weeks) exposure to air and is recovered unchanged on addition of water to a solution of it in ethanol. Moreover, IIId is formed by heating a dilute aqueous solution of the amidrazone and phenylboronic acid, a remarkable tribute to its stability; we know of no other case where an aminoborane has been formed by reaction of an amine with a boronic acid in aqueous solution. Several of these compounds are recovered on solution in acid followed by neutralization; this last observation suggests, however, that they may in fact have undergone reversible hydrolysis.

The aromatic nature of these compounds is further indicated by their mass spectra in which 99% of the total ionization is concentrated in the peak corresponding to the parent molecular ion; a relatively large peak was also observed corresponding to the doubly charged molecular ion, a feature which seems to be characteristic of "borazaromatic" compounds.[8] Since acid amidrazones (IV) can be prepared readily by procedures which allow introduction of an almost arbitrary selection of substituents,[9] the way seems open to the synthesis of a wide variety of compounds of possible biological interest.

We also tried to synthesize hydroxy analogs of III (*i.e.*, with R_2 = OH) by heating phenylboron dichloride with derivatives of semicarbazide. While products were obtained which showed mass spectra compatible with the expected 2-hydroxy-5,1,3,4-boratriazaroles, their instability to hydrolysis by traces of water or alcohol has so far prevented their isolation in a state pure enough for elemental analysis. The infrared spectrum of the triphenyl derivative showed a strong carbonyl band, indicating that it exists as the amide tautomer.

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(5) J. Namtvedt and S. Gronowitz, *Acta Chem. Scand.*, **22**, 1373 (1968).

(6) P. I. Paetzold, *Z. Anorg. Allg. Chem.*, **326**, 64 (1963).

(7) All new compounds gave satisfactory elemental analyses.

(8) M. J. S. Dewar and P. Rona, unpublished work.

(9) D. G. Neilson, R. Roger, J. W. M. Heattie, and L. R. Newlands, *Chem. Rev.*, **70**, 151 (1970).

(10) National Institutes of Health Postdoctoral Fellow.

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Received January 22, 1971

The Total Synthesis of (±)-Vindorosine

Sir:

Pentacyclic, highly functionalized *Aspidosperma* alkaloids are of special interest because two representatives, namely, vindoline and 1-demethyl-1-formylvindoline, are structural components of the oncolytic double alkaloids vincaleukoblastine and leurocristine. Vindorosine[1] which cooccurs with the two antitumor agents in *Vinca rosea* Linn. does not seem to have been detected in double alkaloids yet. It was proposed[1] to be 11-demethoxyvindoline (**1**), based mainly on comparison of its nmr and ORD spectra with those of vindoline (**2**).[2]

Outlined below is a synthesis of vindorosine (**1**) confirming its structure which should be applicable also to the preparation of related alkaloids.

Condensation of 1-methyltryptamine with 1-chloro-3-ketobutene-1 in ethanol solution containing triethylamine provided the liquid hydrogen bonded *cis*-enamino ketone **3** (92%): ir ($CHCl_3$) 3000, 1640, 1560 cm^{-1};

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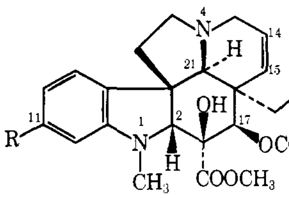
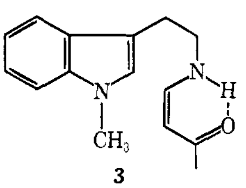
(1) B. K. Moza and J. Trojánek, *Collect. Czech. Chem. Commun.*, **28**, 1427 (1963).

(2) The correct gross structure of vindoline was determined by M. Gorman, N. Neuss, and K. Biemann (*J. Amer. Chem. Soc.*, **84**, 1058 (1962)) while the correct stereoformula follows from the X-ray analysis of leurocristine methiodide performed by J. W. Moncrief and W. N. Lipscomb (*Acta Crystallogr.*, **21**, 322 (1966)).



1, R = H
2, R = OCH$_3$

nmr (CDCl$_3$) δ 4.90 (d, 1, J = 7 Hz), 6.52 (d of d, 1, J = 7, 12 Hz), and 9.8 (broad s, 1). Attempts to cyclize this amine failed but the N-acetyl *trans*-enamino ketone **4** (64%) (mp 128–130°; nmr (CDCl$_3$) δ 5.69 (d, 1, J = 14 Hz), 8.04 (d, 1, J = 14 Hz)), prepared by acetylation with acetic anhydride–triethylamine in hot benzene, when heated in boron trifluoride etherate at 90° for 27 min gave the tetracyclic indoline **5** (38%) (mp 195–197°; ir (CHCl$_3$) 1720, 1640, 1605 cm^{-1}; uv (C$_2$H$_5$OH) 251 (ε 9200), 301 (ε 3400) nm). From the nonbasic portion of the reaction mixture the tetrahydro-β-carboline **7**, mp 118–120°, with typical indole uv absorption, was isolable in 20% yield. Exposure of the indole **7** to boron trifluoride[3] under identical conditions gave a maximum of 8% of the indoline **5** demonstrating that the indoline is formed directly from its precursor **4** by electrophilic C-3 substitution followed by nucleophilic enol addition to C-2 of the resulting indolenine.[4] The oily amine **6** (92%) available from the amide **5** by hydrolysis with hot 10% aqueous hydrochloric acid contains two epimerizable centers of asymmetry (β,β′-diamino ketone!) and inspection of molecular models indicates the most stable diastereomer to have the stereochemistry indicated in **6**.



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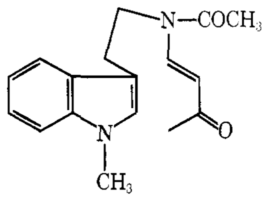

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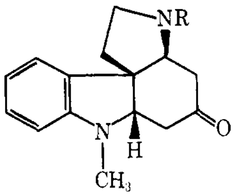
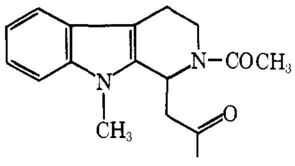


5, R = COCH$_3$
6, R = H



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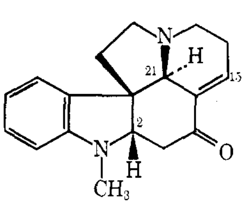
Condensation of the secondary amine **6** with acrolein was carried out in methanol solution with added sodium methoxide. The resulting mixture of epimeric ketols was not separated in preparative runs but dehydrated directly with boron trifluoride in acetic acid at room temperature to give the pentacyclic ketone **8** (40%): mp 152–154°; ir (CHCl$_3$) 1690, 1625, 1605 cm^{-1}; uv (C$_2$H$_5$OH) 245 (ε 16,000) and 302 (ε 3700) nm; nmr (CDCl$_3$) δ 3.61 (d of d, J = 4, 11 Hz, C-2), 4.12 (narrow m, C-21), 7.0 (d of d with fine splitting, J = 2.5, 5 Hz, C-15). Ethylation of the α,β-unsaturated ketone **8** with ethyl iodide in *tert*-butyl alcohol-1,2-dimethoxyethane containing potassium *tert*-butoxide[5] yielded the β,γ-unsaturated ketone **9** (44%): mp 156–159°; ir (CHCl$_3$) 1700 cm^{-1}; nmr (CDCl$_3$) δ 5.50 (d with fine splitting, J = 10 Hz, C-15), 5.77 (d of d with fine splitting, J = 5, 10 Hz, C-14). In agreement with the configuration assigned, the nmr spectra of **9** and all substances to be described exhibit the high-field three-proton triplet at δ 0.4 previously encountered in the spectrum of vindoline (**2**) and attributed to long-range shielding of the methyl protons by the benzene ring. Condensation of the ketone **9** with dimethyl carbonate in the presence of sodium hydride[6] furnished a mixture of the keto ester **10** and its enol tautomer (100%), from which the pure keto form **10** could be isolated by crystallization: mp 148–151°; ir (CHCl$_3$) 1735, 1710 cm^{-1}.



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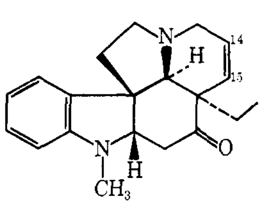

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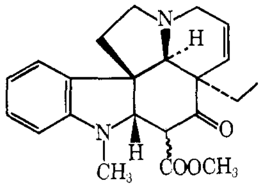

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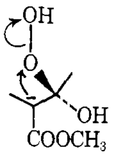

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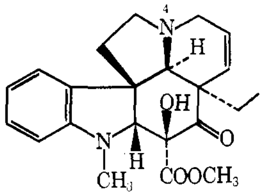
12



13

Solutions of the β-keto ester **10** in *tert*-butyl alcohol–1,2-dimethoxyethane containing potassium *tert*-butoxide were stable to oxygen at −35° but addition of 85% hydrogen peroxide caused oxidation. The resulting hydroxy keto ester **13** (31%), mp 174–176°, in addition to bands at 1760, 1740, and 1715 cm^{-1} had broad ir absorption at 3100–2300 cm^{-1} previously encountered in the spectrum of vindoline (**2**) and attributed to hydrogen bonding between the hydroxy group and N-4.[2,7] Overall course and stereochemical outcome of this oxidation can be rationalized by assuming intermediates **11** and **12**. Reduction of the ketone **13** with a limited amount of lithium aluminum hydride in tetrahydro-

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(3) J. Harley-Mason and W. R. Waterfield, *Tetrahedron*, **19**, 65 (1963); J. E. D. Barton and J. Harley-Mason, *Chem. Commun.*, 298 (1965).

(4) Experimental work and theory on electrophilic substitution in indoles were summarized by A. H. Jackson and A. E. Smith, *Tetrahedron*, **24**, 403 (1968). See also J. R. Williams and L. R. Unger, *Chem. Commun.*, 1605 (1970).

(5) J. M. Conia, *Bull. Soc. Chim. Fr.*, 690 (1954); R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957).

(6) U. T. Bhalerao, J. J. Plattner, and H. Rapoport, *J. Amer. Chem. Soc.*, **92**, 3429 (1970).

(7) W. H. Hargrove, *Lloydia*, **27**, 340 (1964).

furan at −70° gave a mixture of substances separable by thin-layer chromatography. Acetylation of the slower moving diol in excess acetic anhydride containing sodium acetate at room temperature yielded a monoacetate (60%), mp 182–185°, whose ir ($CHCl_3$) and mass spectra were indistinguishable from those of natural vindorosine (**1**). Identity was confirmed by thin-layer chromatography using two different solvent combinations.

Acknowledgment. The authors are grateful to the National Institutes of Health for financial support and to Dr. N. Neuss, Eli Lilly and Company, for a sample of natural vindorosine.

(8) National Institutes of Health Predoctoral Fellow, 1969–1971.

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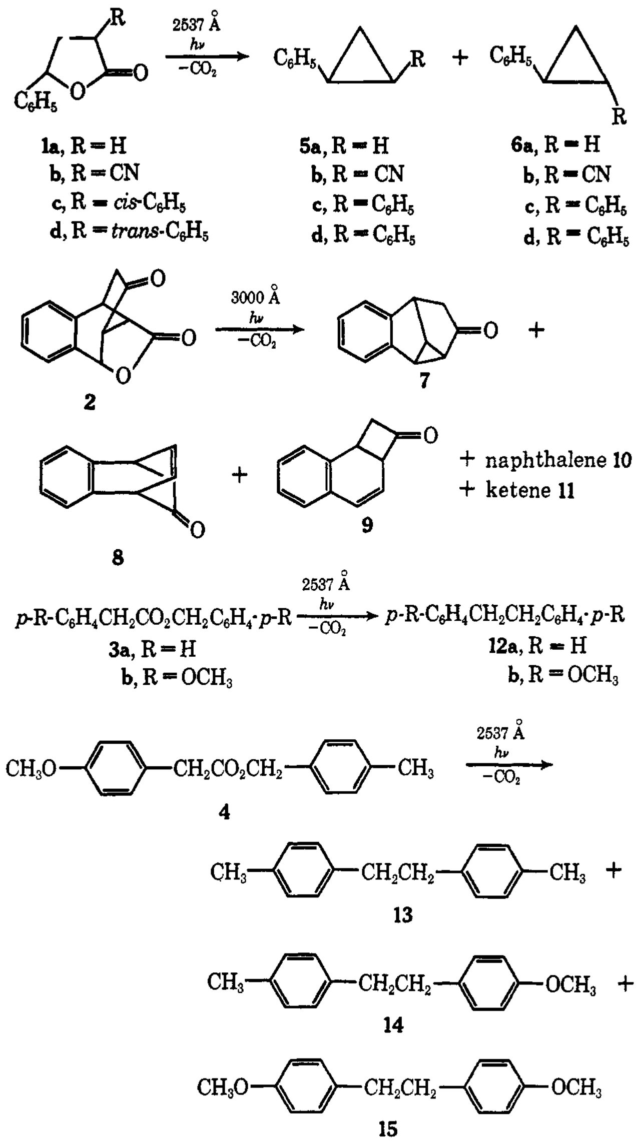
Photodecarboxylation of Benzyl Esters[1,2]

Sir:

Recent reports[3–6] on the photoelimination of carbon dioxide from lactones and esters have prompted us to report our results that carbon dioxide extrusion is a general photochemical process for γ-phenyl-γ-butyrolactones (*e.g.*, **1** and **2**, Scheme I) and for their acyclic analogs (*e.g.*, benzyl esters **3** and **4**). In previous communications,[7,8] we reported an efficient photodecarboxylation of lactone **2**. Although efficient loss of carbon dioxide has been observed for a dihydrosantonin[3] and for simple γ-butyrolactones in the vapor phase,[4] carbon dioxide loss is ordinarily a minor pathway in the solution photochemistry of lactones[5] and esters.[6]

The model compounds chosen for study are shown in Scheme I.[9] Qualitative and quantitative results of photolysis of the model compounds are shown in Table I and Scheme I.[10] For all γ-phenyl-γ-butyrolactones studied, the efficiency of carbon dioxide loss is good, with $\Phi_{dis} = 0.03$–0.18. However, in contrast to γ-phenyl-γ-butyrolactone (**1a**) ($\Phi_{CO_2} = 0.020$), the α- and β-phenyl isomers decarboxylate very inefficiently ($\Phi_{CO_2} \leq 0.001$) indicating that efficient carbon dioxide loss requires phenyl substitution at the γ position.

Scheme I. Products from Photolysis of Benzyl Esters



A priori either stepwise or unsymmetrical concerted mechanisms for the transformation are possible. To study the mechanistic pathway further, the *cis*- and *trans*-α,γ-diphenyl-γ-butyrolactones (**1c** and **d**) were prepared and photolyzed. The results are clearly inconsistent with a completely concerted loss of carbon dioxide with cyclopropane formation, since the zero-time quantum yields for appearance of *cis*- and *trans*-

Table I. Quantum Yields[a] for Photolysis of Esters

Ester	λ, Å	Φ_{dis}[b,c]	Φ_{CO_2}[c,d]	% yield[e]
1a	2537	0.026	0.020	
1b	2537	0.092	0.100	77
1c	2537	0.045	0.026	51
1d	2537	0.051	0.027	51
2	3000	0.18	0.15	38
3a	2537	0.033	0.031	57
3b	2537	0.25	0.19	

[a] Direct irradiation, dioxane solvent. [b] Obtained by quantitative vpc. [c] Quantum yields at 20–30% conversion. [d] Trapped with tared Ascarite–Anhydrone scrubber. [e] Yield of radical coupling products based on the disappearance of ester at *ca.* 50% conversion.

(1) We wish to acknowledge support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, and a General Research Grant from the University of Kansas.

(2) Presented in part at the Midwest Regional Meeting of the American Chemical Society, Lincoln, Neb., 1970.

(3) G. W. Perold and G. Ourisson, *Tetrahedron Lett.*, 3871 (1969).

(4) I. S. Krull and D. R. Arnold, *ibid.*, 1247 (1969), and references therein.

(5) R. Simonaitis and J. N. Pitts, Jr., *J. Amer. Chem. Soc.*, **91**, 108 (1969), and references therein.

(6) J. S. Bradshaw, E. L. Loveridge, and L. White, *J. Org. Chem.*, **33**, 4127 (1968), and references therein.

(7) R. S. Givens and W. F. Oettle, *Chem. Commun.*, 1164 (1969).

(8) R. S. Givens and W. F. Oettle, *J. Amer. Chem. Soc.*, in press.

(9) We thank Drs. R. N. Johnson and I. J. Miller for details of the synthesis and isolation of the diphenyl lactones; see R. N. Johnson, J. B. Lowry, and N. V. Riggs, *Tetrahedron Lett.*, 5113 (1967). Details will be given in our full paper.

(10) Products **5–8**, **10**, and **12–15** were identified by comparison of spectral and physical properties with known samples; **9** was identified by analysis of the nmr, ir, and mass spectra, by nmr double irradiation studies, and by elemental analysis. Ketene **11** was trapped as ethyl acetate (R. S. Givens, W. F. Oettle, R. L. Coffin, and R. G. Carlson, *J. Amer. Chem. Soc.*, in press).