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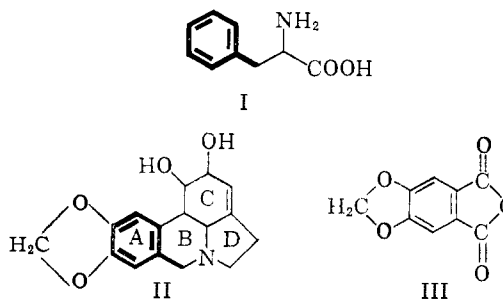
NATHAN L. BAULD

RECEIVED JULY 30, 1962

THE BIOGENETIC ORIGIN OF THE C<sub>6</sub>-C<sub>1</sub> UNIT OF LYCORINE<sup>1</sup>

Sir:

It has been shown experimentally that the phenolic compounds 2-C<sup>14</sup>-tyrosine,<sup>2-4</sup> 3-C<sup>14</sup>-tyrosine<sup>5,6</sup> and 2-C<sup>14</sup>-tyramine<sup>7</sup> are directly incorporated into rings C and D of the *Amaryllidaceae* alkaloids. In addition, 1-C<sup>14</sup>-norbelleadine,<sup>8,9</sup> 1,1'-C<sup>14</sup>-norbelleadine<sup>10</sup> and partially methylated derivatives of norbelleadine<sup>11</sup> are able to serve as intermediates in the biosynthesis of these alkaloids. The purpose of this report is to provide information about the nature of the precursor(s) of the C<sub>6</sub>-C<sub>1</sub> unit of the *Amaryllidaceae* alkaloid, lycorine (II, heavy bonds).



man<sup>13</sup> and carbon atom-5 was isolated as the dime-done derivative according to the procedure of Humber, *et al.*<sup>14</sup>

The percentage incorporation of 2- and 3-C<sup>14</sup>-phenylalanine and the specific activities of lycorine and its degradation product, hydrastic anhydride (Table I), show that 3-C<sup>14</sup>-phenylalanine can serve as the precursor of the C<sub>6</sub>-C<sub>1</sub> unit of lycorine, *but only one phenylalanine unit is utilized in the biosynthesis of lycorine* (II, heavy bonds). However, this incorporation of phenylalanine into

TABLE I  
INCORPORATION OF RADIOACTIVE COMPOUNDS INTO LYCORINE AND RELATIVE ACTIVITIES OF DEGRADATION PRODUCTS<sup>a</sup>

	Injected <sup>b</sup>		Incorporated <sup>c</sup>		Lycorine		Hydrastic anhydride		Carbon atom-5 of lycorine <sup>d</sup>	
	Mg.	mμc.	mμc.	%	Specific activity, mμc./mM	Relative activity	Specific activity, mμc./mM	Relative activity	Specific activity, mμc./mM	Relative activity
3-C <sup>14</sup> -DL-Phenylalanine	20	13,000	48.0	0.37	92.5	100	87.0	94		
3-C <sup>14</sup> -DL-Phenylalanine	12	9,850	17.5	0.18	5.81	100	4.9	84		
2-C <sup>14</sup> -DL-Phenylalanine	15	25,000	0.0	0.0	0.0					
3-C <sup>14</sup> -DL-Tyrosine	4	11,000	20.0	0.18	9.2	100	0.0	0		
2-C <sup>14</sup> -Tyramine	4	15,600	158.0	1.01	32.4	100	0.0	0		
H <sup>3</sup> -Protocatechuic aldehyde	66	6,650	15.0	0.23	7.4					
2-C <sup>14</sup> -DL-Tyrosine	12	20,800	44.8	0.22	11.1	100			8.41	76

<sup>a</sup> Samples were counted in a Packard Tri-Carb Scintillation Counter in toluene or ethanol-dioxane-naphthalene scintillator solutions. <sup>b</sup> All radioactive compounds were injected into the corm with the exception of 2-C<sup>14</sup>-phenylalanine. This was injected into the stem. <sup>c</sup> Based on incorporation after recrystallization of lycorine to constant specific activity. <sup>d</sup> Isolated as the formaldehyde dimedone derivative.

The labeled compounds were injected at three separate time intervals into *Narcissus incomparabilis* Mill. The alkaloids were extracted from all of the tissue.<sup>12</sup> The amounts of radioactive compounds administered, incorporation into lycorine, the degradation of lycorine to hydrastic anhydride (III) and the isolation of carbon atom-5 as formaldehyde are shown in Table I. The lycorine was degraded to hydrastic anhydride according to the procedure of Warnhoff and Wild-

lycorine does not proceed *via* tyrosine. This can be seen by (1) the lack of incorporation of 2-C<sup>14</sup> phenylalanine into rings C and D of lycorine (Table I) and (2) the tyrosine isolated, after hydrolysis of the plant protein from the phenylalanine experiments, was not radioactive. On the other hand, 3-C<sup>14</sup>-tyrosine can be incorporated into lycorine only as a C<sub>6</sub>-C<sub>2</sub> unit (rings C and D of II). Similar results, on the incorporation of 3-C<sup>14</sup>-tyrosine to haemanthamine, haemanthidine and tazettine have been reported by Wildman, Fales and Battersby<sup>5</sup> and Jeffs.<sup>6</sup> Since the haemanthamine from the 3-C<sup>14</sup>-phenylalanine experiment appears to be radioactive, it may well be that this aromatic amino acid is the C<sub>6</sub>-C<sub>1</sub> precursor for the pyrrolo-phenanthridine and 5,10b-ethanophenanthridine alkaloids. Experiments are in progress to demonstrate these inter-relationships.

The conversion of phenylalanine to the dihydroxylated, C<sub>6</sub>-C<sub>1</sub> precursor of lycorine, without going through tyrosine, might be explained on the

(1) This work was supported by a grant-in aid from the National Science Foundation.

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basis of the recent report on the enzymatic conversion of phenylalanine to phenylserine followed by cleavage with threonine aldolase to give benzaldehyde and glycine.<sup>15</sup> If a similar enzyme were functioning in *N. incomparabilis*, it may be possible for phenylalanine  $\rightarrow$  phenylserine  $\rightarrow$  protocatechuic aldehyde without going through tyrosine. The protocatechuic aldehyde then would be the C<sub>6</sub>-C<sub>1</sub> fragment. To test this possibility, H<sup>3</sup>-protocatechuic aldehyde was injected into four plants, and 0.23% of the tritium was incorporated into the lycorine (recrystallized four times) (Table I). The exact location of the tritium is currently being determined. Protocatechuic acid-C<sup>14</sup> is not incorporated.<sup>16</sup> On the basis of the above results, it appears that the two aromatic amino acids, phenylalanine and tyrosine, give rise to protocatechuic aldehyde and tyramine which serve as the C<sub>6</sub>-C<sub>1</sub> and C<sub>6</sub>-C<sub>2</sub> units, respectively, in the biosynthesis of lycorine. Tyrosine or tyramine can not replace phenylalanine as the C<sub>6</sub>-C<sub>1</sub> fragment and phenylalanine can not replace tyrosine or tyramine as the C<sub>6</sub>-C<sub>2</sub> unit.

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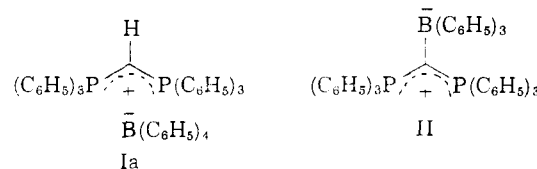
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### PHOTOCHROMISM IN MESOMERIC PHOSPHONIUM SALTS<sup>1</sup>

Sir:

We wish to report preliminary results on the photochromism of mesomeric phosphonium salts. When white crystals of triphenylphosphonium methylenetriphenylphosphorane tetraphenylboron, Ia, are irradiated by sunlight or an ultraviolet lamp, an orange-red color rapidly develops.

was synthesized and found also to be photochromic, white crystals becoming yellow on irradiation. Other salts of type I, including tri-



phenylphosphonium methylenetriphenylphosphorane tetrafluoroborate, Ib, and iodide, Ic, change color more slowly than Ia. Colors resulting from ultraviolet irradiation are listed in Table I, together with analytical data. Color changes were observed in air or nitrogen at room temperature, and were not reversed by heating to 100°. When the source was removed, the intensity of the color slowly diminished to a pale yellow.

Infrared and ultraviolet spectra of the compounds were unchanged by irradiation. Characteristic infrared bands (KBr pellet) attributed to the mesomeric cation occur as a triplet of increasing intensity at 1027, 1010, and 988 cm<sup>-1</sup>. Ultraviolet  $\lambda_{\max}$  (acetonitrile) occur at 267 m $\mu$  ( $\epsilon = 7200-10,800$ ). For Ia, continuous absorption with no peaks occurs in acetonitrile in the visible region ( $\epsilon = 1, 7, \text{ and } 51 \text{ at } 600, 500 \text{ and } 400 \text{ m}\mu$ , respectively).

The mesomeric compounds were prepared from triphenylphosphonium methylenetriphenylphosphorane bromide,<sup>2</sup> Id, which is not photochromic. Id was obtained by treating methylenebis-(triphenylphosphonium bromide) with aqueous sodium carbonate<sup>2</sup> or lithium butyl in ether. Metathesis reactions of Id, in methanol or water, yielded triphenylphosphonium methylenetriphenylphosphorane tetraphenylboron, Ia, tetrafluoroborate, Ib, and iodide, Ic. The inner salt II was synthesized by the addition of triphenylboron to hexaphenyl-

TABLE I  
MESOMERIC PHOSPHONIUM SALTS

Compound	Empirical formula	M.p., <sup>a</sup> °C.	Irradiated color	Elemental analyses, % <sup>b</sup>				
				C	H	P	B	X <sup>c</sup>
Ia	C <sub>81</sub> H <sub>51</sub> P <sub>2</sub> B	205-208	Orange-red	85.5	6.0	7.2	1.3	..
				85.3	6.1	7.4	1.0	..
Ib	C <sub>27</sub> H <sub>31</sub> P <sub>2</sub> BF <sub>4</sub>	259.5-260.5	Yellow	71.2	5.0	9.95	1.7	12.2
				71.5	5.55	10.0	1.5	12.0
Ic	C <sub>37</sub> H <sub>31</sub> P <sub>2</sub> I	253-254	Yellow	66.9	4.7	9.3	..	19.1
				67.2	4.7	9.4	..	19.0
Id	C <sub>37</sub> H <sub>31</sub> P <sub>2</sub> Br	274-275	White	72.0	5.0	10.0	..	13.0
				71.9	5.2	10.1	..	13.2
II	C <sub>55</sub> H <sub>45</sub> P <sub>2</sub> B	253-255	Yellow	84.8	5.8	7.95	1.4	..
				85.1	5.9	7.7	1.5	..

<sup>a</sup> Melting points are corrected. <sup>b</sup> Calculated values are listed on the upper line; found values on the lower. <sup>c</sup> X values are for halogen as indicated in empirical formulas.

With a Hanovia Lamp (Model 30600), at a distance of four centimeters, the change occurs in four seconds. E.p.r. measurements show that unpaired electrons are present in the orange-red material, but not in the white crystals. The corresponding inner salt, triphenylphosphonium(triphenylboronyl)methylenetriphenylphosphorane, II,

carbodiphosphorane,<sup>2</sup> obtainable from Id by reactions with potassium,<sup>2</sup> sodium hydride or lithium butyl. Proton and P<sup>31</sup> n.m.r. spectra are consistent with the assigned mesomeric structures. For Ia, B<sup>11</sup> resonance was observed at +25 p.p.m. relative to trimethyl borate in methylene chloride. For the inner salt II it was necessary to utilize

(1) This work was supported in part by the Office of Naval Research.

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