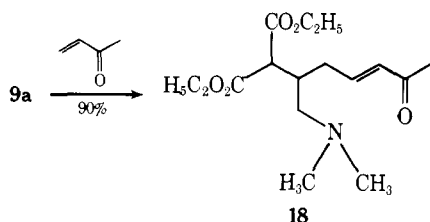


the resulting yellow solution for 2 min, providing **16** in 94% yield.¹²

A typical experimental procedure follows. To a solution of 0.33 g (1.26 mmol) of LTP in 20 mL of THF (distilled from lithium aluminum hydride) under nitrogen was added 170 μ L (1.3 mmol) of dimethylallylamine. A yellow precipitate immediately formed and redissolved after about 1 min to produce a red solution. To this solution was added 0.23 g (1.26 mmol) of sodiodiethylmalonate in 4 mL of THF. The color of the solution immediately faded to yellow-orange. Stirring at room temperature was continued for 6 h, and the mixture was diluted with chloroform. The chloroform solution was washed with water, dried, and evaporated to leave 0.45 g of yellow crystalline complex **9a**, which was recrystallized from benzene/hexane to provide analytically pure material.

Although complexes **9a-f** and **11a-f** are insensitive to air and moisture and are amenable to shelf storage for months, they are also sufficiently reactive, under appropriate conditions, to allow replacement of palladium by carbon moieties. For example, treatment of **9a** with methyl vinyl ketone in refluxing benzene containing triethylamine¹⁶ gives adduct **18**¹¹ in 90% yield.¹²



We foresee considerable synthetic utility in carbopalladation and subsequent transformations. We are actively investigating the range of allylic substrates amenable to these reactions, the further applicability of palladocycles to formation of new carbon-carbon bonds, and the stereochemistry of the nucleophilic addition-reduction sequence. Applications of this chemistry to the synthesis of natural products are in progress. The results of these studies will be reported in due course.

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- David Ross Predoctoral Fellow, 1975-1977.

Robert A. Holton,*¹⁷ Richard A. Kjonaas¹⁸

R. B. Wetherill Laboratory of Chemistry
Purdue University, West Lafayette, Indiana 47907

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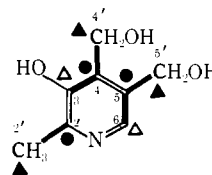
Biosynthesis of Vitamin B₆ The Incorporation of [1,3-¹³C₂]Glycerol¹

Sir:

Radioactivity from specifically ¹⁴C-labeled glycerol is incorporated nonrandomly into pyridoxol (Scheme I). Chemical degradation showed one third of the activity of pyridoxol derived from [2-¹⁴C]glycerol to be located at each of C-2, C-4, and C-5, accounting for all radioactivity in the sample.² These three carbon atoms were free of activity when [1-¹⁴C]glycerol served as the precursor.^{2,3} It was established that one fifth of the activity within pyridoxol derived from this substrate resides at each of C-2', C-4', and C-5'.³ The only uncertainty which remains concerns the mode of distribution of the unaccounted two fifths of activity from [1-¹⁴C]glycerol among the two carbon atoms of pyridoxol, C-3 and C-6. We have resolved this uncertainty by determining the quantitative distribution of ¹³C in pyridoxol derived from [1,3-¹³C₂]glycerol by ¹³C NMR spectrometry.

A 2-L culture of *E. coli* B, strain WG2, was incubated in the presence of [1,3-¹³C₂]glycerol containing 90% isotopic enrichment at each terminal carbon atom (Merck Sharp & Dohme, Montreal, Canada) (1 g). This tracer served as the sole carbon source. Culture conditions and the procedure for the isolation of pyridoxol hydrochloride were as previously described.³ In the carrier dilution procedure of the isolation, 3.80 mg of unlabeled pyridoxol hydrochloride was added. All reisolated pyridoxol hydrochloride (2.0 mg) was transferred to a standard melting point tube (90 mm \times 1 mm i.d.) and dissolved in D₂O (30 μ L). The proton noise-decoupled (without NOE) carbon-13 spectrum⁴ of this solution (\sim 0.4 M) was determined on a JEOL PS-100 NMR spectrometer, operating in the pulse Fourier transform mode. The natural abundance

Scheme I



* Mode of incorporation of glycerol into pyridoxol. Sites of activity derived from [1-¹⁴C]glycerol (▲, △) (relative specific activity \sim 20%) and from [2-¹⁴C]glycerol (●) (relative specific activity \sim 33%) shown by degradation (▲, ●) or inferred (△, ○).

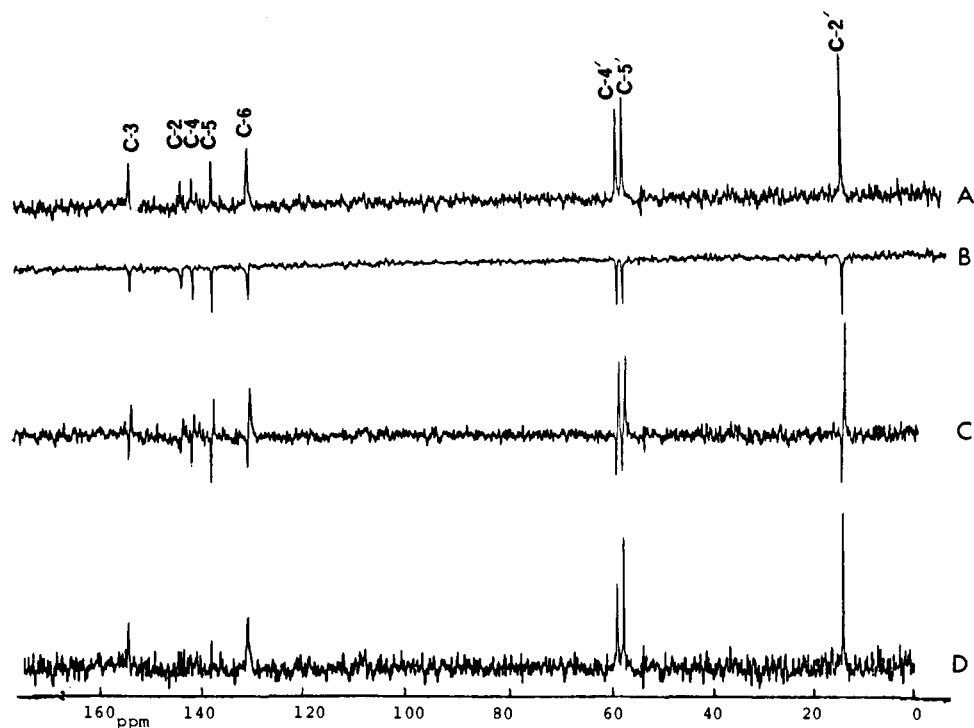


Figure 1. A, proton noise decoupled (PND) spectrum of ^{13}C -enriched sample of pyridoxol hydrochloride (2.0 mg/30 μL) derived from $[1,3\text{-}^{13}\text{C}_2]$ glycerol; B, inverted PND spectrum of natural abundance sample of pyridoxol hydrochloride (2.4 mg/30 μL); C, offset sum of spectra A and B; D, difference spectrum.

Table I. Incorporation of $[1,3\text{-}^{13}\text{C}_2]$ Glycerol into Pyridoxol

Pyridoxol carbon atom	chemical shift, ppm	Pyridoxol (natural abundance ^{13}C)		Pyridoxol enriched in ^{13}C , from $[1,3\text{-}^{13}\text{C}_2]$ glycerol		Ratio of relative peak integrals, enriched sample/natural abundance sample	Relative percent excess ^{13}C above natural abundance at individual C atoms
		Measured peak integral	Relative peak integral (C-2 = 1.00)	Measured peak integral	Relative peak integral (C-2 = 1.00)		
C-2'	16.5	1000	2.20 ± 0.25	1000	8.70 ± 0.97	3.95 ± 0.63	20 ± 5
C-5'	59.0	807	1.77 ± 0.20	825	7.18 ± 0.80	4.06 ± 0.64	21 ± 5
C-4'	60.1	795	1.75 ± 0.20	762	6.63 ± 0.74	3.79 ± 0.61	19 ± 5
C-6	131.8	751	1.65 ± 0.18	730	6.35 ± 0.71	3.85 ± 0.60	20 ± 5
C-5	138.8	603	1.33 ± 0.15	176	1.53 ± 0.17	1.15 ± 0.18	1 ± 2
C-4	142.5	440	0.97 ± 0.11	118	1.03 ± 0.11	1.06 ± 0.16	0 ± 2
C-2	144.7	455	1.00 ± 0.11	115	1.00 ± 0.11	1.00 ± 0.16	0
C-3	154.7	341	0.75 ± 0.08	321	2.79 ± 0.31	3.72 ± 0.59	19 ± 5

spectrum of a 2.4-mg sample of pyridoxol hydrochloride was determined under identical conditions.

Comparison of the spectrum of pyridoxol derived from $[1,3\text{-}^{13}\text{C}_2]$ glycerol with the natural abundance spectrum⁵⁻⁸ demonstrated enhancement of the signals at C-2', C-3, C-4', C-5', and C-6 of the labeled material, as expected. This is visually demonstrated by a difference spectrum (Figure 1D) which was obtained by superposition of the spectrum of the enriched sample on the inverted and slightly offset spectrum of the natural abundance sample, followed by computer operations which nullify one of the nonenriched carbon signals (e.g., that of C-2) and treat the other signals proportionately. The resultant difference spectrum shows positive peaks only for ^{13}C -enriched carbon atoms. It is evident that C-2', C-5', C-4', C-6, and C-3 are enriched with ^{13}C , whereas C-5, C-4, and C-2 are not.

However, to resolve the remaining uncertainty in the mode of incorporation of glycerol into pyridoxol, the extent of enrichment at each of these carbons had to be determined. This was accomplished by normalizing the peak integrals (Table I) for each carbon atom of both the enriched pyridoxol and the natural abundance sample, using as a standard the integral of

any one of the carbon atoms, C-2, C-4, or C-5, which are known^{2,3} not to incorporate tracer from C-1 of glycerol. The ratio (normalized peak integral of C-x in the enriched sample)/(normalized peak integral of C-x in the natural abundance sample) provides a quantitative comparison of the ^{13}C enrichment at each of C-2' (20%), C-3 (19%), C-4' (19%), C-5' (21%), and C-6 (20%), and shows that each of these centers is equally enriched in ^{13}C in the pyridoxol derived from $[1,3\text{-}^{13}\text{C}_2]$ glycerol. In confirmation of earlier results with ^{14}C , C-2, C-4, and C-5 of pyridoxol receive no enrichment from this precursor (Table I).⁹

With the present data, unequivocal assignment is possible of the origin of all carbons atoms of pyridoxol, from glycerol as the carbon source, and the evidence is now complete for the specific precursor-product relationship between glycerol and pyridoxol which we put forward on the basis of the previous results.^{2,3}

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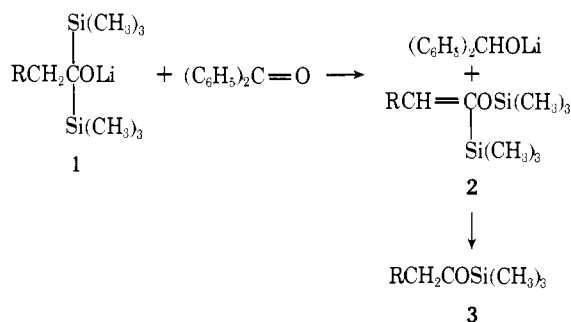
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 (10) Department of Pathology.

Robert E. Hill,*¹⁰ Iwao Miura, Ian D. Spenser
 Departments of Pathology and Chemistry
 McMaster University
 Hamilton, Ontario L8S 4M1
 and Department of Chemistry, Columbia University
 New York, New York 10027
 Received April 1, 1977

Reactions of Lithium Alkoxide of 1,1-Bis(trimethylsilyl)alkan-1-ol with Benzophenone. A Novel Way to Silyl Enol Ether of Acylsilane

Sir:

Much attention has been focused on the preparation of acylsilane because of its interesting spectral behavior.¹ Among the various methods reported hitherto, the most effective one involves an acyl anion equivalent such as 2-lithio-1,3-dithiane² or 1-ethoxyvinyl lithium.³ We wish to report herein an effective method for the preparation of silyl enol ether⁴ or its parent acylsilane.⁵ We have recently reported that 1,1-bis(trimethylsilyl)alkan-1-ol can be prepared effectively from the corresponding trimethylsilyl carboxylate through reductive silylation,⁶ and its lithium alkoxide has proved to be an efficient base for specific generation of ketone⁷ or ester enolate.⁸ In the course of further studies on the reaction with carbonyl compounds, it has been found that this type of alkoxide **1** is easily



oxidized with benzophenone to afford the silyl enol ether of the corresponding acylsilane **2**, accompanied by the precipitation of lithium alkoxide of benzhydrol. The following procedure is illustrative. The lithium alkoxide of 1,1-bis(trimethylsilyl)-3-phenylpropan-1-ol was prepared by treating the alcohol (280 mg, 1.0 mmol) with an equimolar amount of butyllithium in *n*-hexane (2 mL). To the resulting solution was added an *n*-hexane (2 mL) solution of benzophenone (182 mg, 1.0 mmol) and it was stirred for 2 days at room temperature. During this period, the lithium alkoxide of benzhydrol was deposited. The reaction mixture was quenched with water and was extracted with ether. From the ether extracts, the trimethylsilyl enol ether of 3-phenylpropionyltrimethylsilane⁹ (207 mg, 74%) and benzhydrol (140 mg, 76%) were isolated by TLC separation, along with the recovered alcohol (38 mg, 14%) and benzophenone (40 mg, 22%). If desired, 3-phenylpropionyltri-

Table I. Reactions of Lithium Alkoxide of 1,1-Bis(trimethylsilyl)alkan-1-ol with Benzophenone^{a,b}

RR'CHC(SiMe ₃) ₂ OLi		→	RR'C=COSiMe ₃	→	RR'CHCOSiMe ₃
1			2		3
R	R'		Yield of 2 (3 ^c)		Recovery of 1
C ₄ H ₉	H		64 (61)		24
C ₆ H ₁₃	H		67 (63)		18
C ₆ H ₅ CH ₂	H		74 ^d (70)		14
C ₆ H ₅ CH ₂	H		67 ^e		25
C ₆ H ₅ CH ₂	H		33 ^f (31 ^{f,g} , 64 ^{f,h})		0
CH ₂ =CH(CH ₂) ₇	H		69 (62)		15
(CH ₃) ₂ CH	H		56 (52)		6
(CH ₃) ₃ CCH ₂ CH(CH ₃)	H		54 (51)		12
C ₄ H ₉	C ₂ H ₅		30 ⁱ		9

^a The reaction was performed in *n*-hexane under refluxing for 14 h, unless otherwise noted. In all of the reactions, benzhydrol was obtained in the yield almost comparable with that of **2**. ^b Satisfactory spectral and elemental analyses were obtained on all new compounds. ^c Acylsilane was obtained by quenching the reaction mixture with 6 N hydrochloric acid. ^d The reaction was carried out in *n*-hexane at room temperature for 2 days. ^e The reaction was carried out in benzene at room temperature for 1 day. ^f The reaction was carried out in THF at room temperature for 2 hr. ^g 3-Phenylpropanoic acid was also formed in 33%. ^h The reaction mixture was treated with anhydrous cupric chloride before quenching with hydrochloric acid. ⁱ The carboxylic acid was also formed in 24%.

methylsilane was obtained in 70% yield by treating the reaction mixture with 6 N hydrochloric acid, followed by TLC purification.

As shown in Table I, silyl enol ether or its parent acylsilane is generally obtained in good conversion yield (~80%) from the alcohol of type $\text{RCH}_2\text{CH}_2\text{C}(\text{SiMe}_3)_2\text{OH}$, while introduction of a substituent into the α or β position decreases the yield of conversion and an appreciable amount of the corresponding carboxylic acid is also formed.

Employment of the nonpolar solvent such as *n*-hexane or benzene appears to be crucial to complete this oxidation reaction. For example, when THF was used as the solvent in the reaction of the lithium alkoxide of 1,1-bis(trimethylsilyl)-3-phenylpropan-1-ol, the reaction mixture became a dark-green solution immediately, probably owing to the formation of benzophenone ketyl radical, from which, on quenching with hydrochloric acid, the corresponding acylsilane was isolated in only 31% yield, accompanied by the concomitant formation of 3-phenylpropanoic acid (33%). The yield of the acylsilane was contrarily raised to 64% yield with little formation of the carboxylic acid when an excess amount of anhydrous cupric chloride was added to the reaction mixture and it was stirred for 1 h at 0 °C.¹⁰ These results have revealed that the precursor of the carboxylic acid can be converted effectively into the acylsilane through the reaction with cupric chloride.

Similar reactions with other carbonyl compounds¹¹ such as benzaldehyde or benzalacetophenone were also attempted, but the former was almost inert toward this oxidation reaction,¹² and the reaction with the latter resulted in the formation of complex mixture.

On the mechanistic point of view, the following observations have strongly suggested intermediary existence of radical species:¹³ (1) while benzaldehyde is unattacked by the alkoxide,¹² a stable radical such as galvinoxyl oxidizes the alkoxide to give **2**, which may exclude an alternative ionic mechanism (Scheme I) and (2) characteristic color of benzophenone ketyl radical is developed through the reaction. The reaction can be explained reasonably by assuming one-electron-transfer process.¹⁴ Thus, one-electron transfer takes place initially between benzophenone and the carbanionic intermediate **4**, which is