Table I. Reduction Products (% Yields)[a] Formed by Action of Transition Metal–Reducing Agent Combinations on N_2, KCN, $C_6H_{11}NC$, and n-$C_4H_9C{\equiv}CH$

Transition metal (0.01 mol) –reducing agent	N_2	KCN[b]		n-$C_4H_9C{\equiv}CH$[b]
$Mo(acac)_3$–NaNp (1:6)		$NoCH_4$	C_6H_{12} (22)	
$MoCl_5$–Mg[c,d]	NH_3			$CH_3(CH_2)_3CH{=}CH_2$ (10), n-C_6H_{14} (13)
$Fe(acac)_3$–NaNp (1:6)		CH_4 (5)	C_6H_{12} (13)	
$FeCl_3$–Mg[c,d]	NH_3	No CH_4; C_2H_{4-6}	CH_4 (2.6), C_6H_{12}, C_2H_{4-6} (trace)	$CH_3(CH_2)_3CH{=}CH_2$ (33), n-C_6H_{14} (5)
$TiCl_3$–Mg[e]	NH_3	No CH_4; C_2H_{4-6} (trace)	CH_4 (6.4), C_6H_{12}, C_2H_{4-6} (trace)	
Cp_2TiCl_2–NaNp (1:6)[f]	NH_3	CH_4 (0.7); C_2H_6 (12)		
(Nitrogenase)	NH_3	CH_4 (major prod); CH_3NH_2; C_2H_{4-6} (trace)	CH_4, C_2H_{4-6} (trace) (from CH_3NC and C_2H_5NC)	$RCH{=}CH_2$

[a] Yields based on metal derivatives. [b] THF solution (20–40 ml) for 2–5 days at room temperature with 1 mol of reactant. [c] M. E. Vol'pin, A. A. Belyi, and V. B. Shur, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2225 (1965). [d] M. E. Vol'pin and V. B. Shur, *Nature (London)*, **209**, 1236 (1966). [e] For $TiCl_4$–Mg fixation results, see *c* and *d* above. [f] E. E. van Tamelen, G. Boche, S. W. Ela, and R. B. Fechter, *J. Amer. Chem. Soc.*, **89**, 5707 (1967).

induced reduction of acetonitrile, although principally involving cyanide loss,[11] did lead to formation of small amounts (0.2–2%) of ethane, the product of the enzyme reaction; in addition some ammonia and primary amine were detected.

As in nitrogenase reactions,[1] all organic substrate studies herein inhibit the fixation of N_2 by the transition metals employed. Acetylene reductions were restricted to the use of transition metal–Mg combinations, since it was noted that sodium metal or sodium naphthalenide alone caused conversion to ethylene.[12] Because the transition metals herein are in themselves effective hydrogenation catalysts, "overreduction" of an acetylene to alkane is not surprising. In preliminary runs, compounds of cobalt and chromium were found to give, under the conditions described herein, results similar to those found with iron, molybdenum, and/or titanium.

Although no one transition metal–reducing agent combination mimics all the nitrogenase phenomena, all of the latter can be simulated by the group as a whole. The entire body of results demonstrates that the characteristic reactions of nitrogenase carried out on organic substrates are not so unusual that they cannot be realized nonenzymically by a representative group of specific transition metal compounds. It seems likely that in the enzyme system particular transition metal derivatives are utilized, not so much for their chemical novelty as for their compatibility with other cellular constituents. The rate of the complete reductive cleavage of the N_2 triple bond may be greatly accelerated so as to preclude other, undesirable reaction courses—evidently possible as indicated by the behavior of substrates other than N_2—with such selectivity conceivably a result of the combined effect of molybdenum and iron. Also, it is apparent from this study that, in an overall sense, closer simulation of nitrogenase behavior is achieved with iron than with molybdenum, in accordance with the view expressed by some[1] that iron is the coordinating species in the enzymic process.[13]

(11) C. Bjorklund and H. Rudler, unpublished observations to be reported more fully elsewhere.

(12) H. Normant, *Bull. Soc. Chim. Fr.*, 354 (1960); 859 (1965); and observations made in this study.

(13) For related commentary, see references in footnotes 9 and 10.

Although it is true that the titanium based, abiological catalytic fixation of N_2 is operated in aprotic media, the very site of the biological process also might be water free, by virtue of protection offered by the enzyme structure. Also, strong reducing agents (*e.g.*, naphthalene radical anion or Mg) are employed in the laboratory fixations; but the utilization of probably 12–15 mol of ATP[1] for reduction of each mole of N_2 to ammonia would allow a high reduction potential for the enzymic reaction. Finally, in the enzymic N_2 fixation process, *molybdenum* may be substituted by *vanadium*,[14,15] an elemental neighbor of *titanium*. In view of the foregoing, we believe that the Ti(II)–based room temperature–atmospheric pressure catalytic N_2 fixation process[16] represents an instructive transition metal model for the biochemical phenomenon. However, further elucidation of the obscure and probably complicated enzymic and nonenzymic transformations described herein must await more detailed and incisive experimentation.

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(16) (a) E. E. van Tamelen, G. Boche, and R. Greeley, *J. Amer. Chem. Soc.*, **90**, 1677 (1968); (b) E. E. van Tamelen and D. A. Seeley, *ibid.*, **91**, 5194 (1969).

E. E. van Tamelen,* H. Rudler, C. Bjorklund
Department of Chemistry, Stanford University
Stanford, California 94305
Received March 22, 1971

Alkali Sensitivity of 3-Methylpyrimidine Nucleosides

Sir:

After the first and only successful isolation of 3-methyluridine from an *enzymatic hydrolysate of soluble*

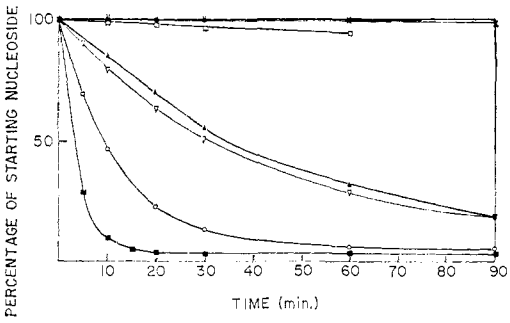


Figure 1. Kinetics of the alkaline breakdown of N_3-methylnucleosides as a functon of base strength and time (37°): ■—■—■—, 2×10^{-3} *M* N_3-methyl-2′,3′-*O*-isopropylideneuridine in 0.3 *N* KOH; ⊙—⊙—⊙—, 2×10^{-3} *M* N_3-methyl-2′,3′-*O*-isopropylideneuridine in 0.1 *N* KOH; ×—×—×—, 2×10^{-3} *M* N_3-methyl-2′,3′-*O*-isopropylidene-5′-*O*-methyluridine in 0.1 *N* KOH; ▲—▲—▲—, 10^{-3} *M* N_3-methyluridine in 1.0 *N* KOH; ▽—▽—▽—, 10^{-3} *M* N_3-methyl-2′-deoxyuridine in 1.0 *N* KOH; □—□—□—, 1–2 × 10^{-3} *M* N_3-methylthymidine in 1.0 *N* KOH; ●—●—●—, 2×10^{-3} *M* 2′-*O*-isopropylideneuridine in 0.5 *N* KOH. The percentage of remaining nucleoside is calculated from the absorbance after neutralization with hydrochloric acid.

RNA,[1] subsequent attempts to isolate 3-methyluridines from *alkaline hydrolysates* of yeast tRNA failed.[2] In this communication we show that 3-methyluridine is extremely labile to alkali and would not survive the conditions of standard basic hydrolysis (0.3 *M* alkali at 37° overnight) usually applied to RNA.

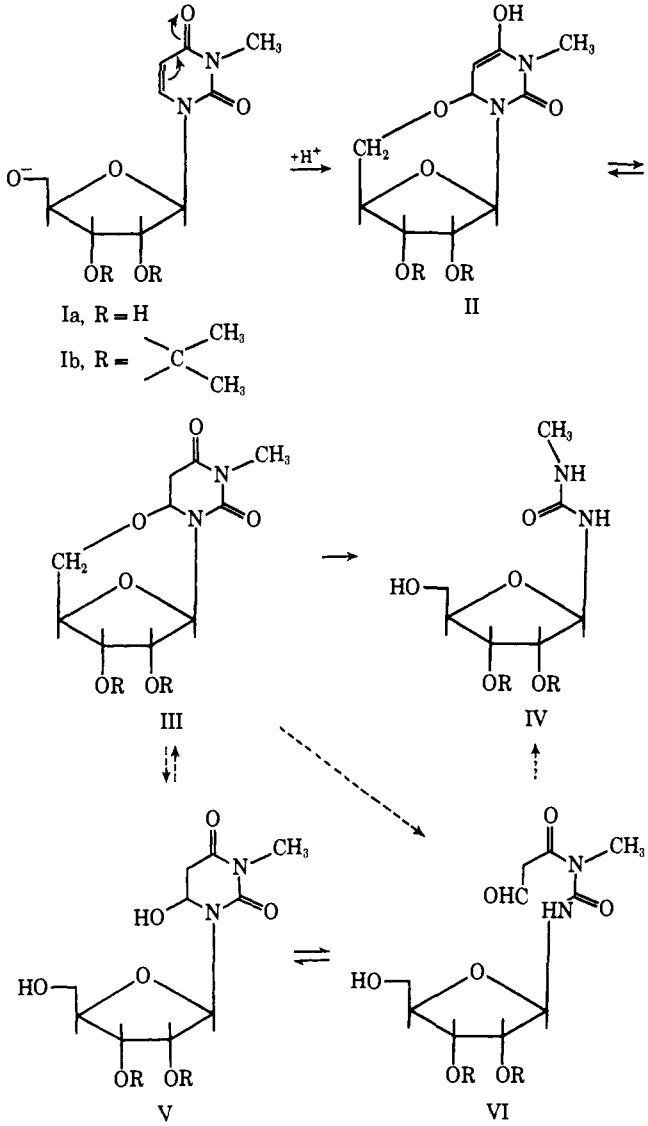
In a typical kinetic experiment (Figure 1) a solution of the 3-methylpyrimidine nucleoside (1–2 × 10^{-3} mol) was incubated at 37° with potassium hydroxide of varying strength, and the optical density measured, after neutralization, as a function of time. The alkaline breakdown was strongly accelerated, when the 2′,3′-hydroxyls were protected by the isopropylidene group. In contrast to 3-methyluridine, 3-methylthymidine nucleosides were much more stable under identical conditions, and only 25.4% degradation was observed after 10 hr.

A 0.1 *M* solution of 3-methyl-2′,3′-isopropylideneuridine (Ib) in 0.5 *N* KOH at 40° lost all uv absorption (λ 260 nm) after 30 min. From the resulting solution, after purification over Amberlite IRC-50 (H^+ form) and after cellulose column chromatography, a crystalline riboside, mp 163–164°, was obtained, which on the basis of nmr data ((in $CDCl_3$) 6.18 (s) (C_1'), 5.00 (C_3'), 4.51 (C_2'), 3.17 (-NHCH_3), and 1.33 and 1.52 ppm (>CMe_2)), and acid hydrolysis to *N*-methylurea, was identified as 3-methylurea riboside IV by direct comparison with an authentic sample.

This surprisingly smooth breakdown was inhibited by the methylation of the 5′-hydroxyl group of Ib (Figure 1). This finding suggests a 6,5′ interaction for which there are several precedents.[3] The dihydropyrimidine (II → III) resulting from such an addition to the anti conformation I[4] is unstable to alkali[5] and breaks down to several possible products, III, IV, V, and VI. The three-carbon fragment, presumably formylacetic acid, lost on the way to 3-methylurea riboside IV, apparently undergoes rapid polymerization in the alkaline medium. We were unable to trap and isolate it as propane-1,3-diol in the presence of borohydride.[6,7]

The kinetics of nucleophilic addition and ring opening could also be followed by the characteristic changes in the nmr spectrum of 3-methyl-2′,3′-isopropylideneuridine in D_2O–NaOD. As the alkaline breakdown progressed, the *N*-methyl signal at 3.29 ppm and the olefinic protons at 5.93 and 7.78 ppm decreased. A new methyl signal (2.75) for the N_3-methylureido moiety is observed in addition to a transient signal at 8.29 characteristic of an aldehyde proton of an intermediate of type VI.

The much greater alkali stability of thymidine shows the strong effect that a 5 substituent has also on the ground-state reactivity of the 5,6 unsaturation, previously exemplified in the excited state by greater or



complete resistance to photohydration,[8] photolysis,[9] or photoreduction.[10] This unexpected easy "*ground-state*

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(8) *Cf.* K. C. Smith and P. C. Hanawalt, "Molecular Photobiology," Academic Press, New York, N. Y., 1969, p 59 ff.
(9) Y. Kondo and B. Witkop, *J. Amer. Chem. Soc.*, **90**, 3258 (1968).
(10) Y. Kondo and B. Witkop, *ibid.*, **91**, 5264 (1969).

hydration" of 3-methyluridine is remarkable, because the comparable *photohydration* has an energy requirement of *ca.* 40 kcal/mol.[11] The rate enhancement must be due to a new kind of intramolecular 6,5′ interaction only observable after alkylation of the N-3 position. The conformational requirements for maximum effect are quite strict: while 3-methyl-2′,3′-isopropylideneuridine is very alkali labile, the analogous 2′,3′-cyclic phosphate, which differs by bond angles, ring strain, and opportunity for 3′,5′ interaction, was found to be surprisingly stable.

Incubation of 3-methylnucleotides and poly-3-methylnucleotides with alkali showed that poly-3-methyluridylic acid and 3-methyluridine dinucleotide were broken down slowly in 0.1 *N* NaOH aqueous solution as compared to 3-methyl-2′,3′-*O*-isopropylideneuridine. Apparently depolymerization precedes base degradation. Since nucleophilic reactions are greatly promoted by addition of DMSO,[12,13] considerable rate enhancement of the base-catalyzed degradation of poly-3-methyluridylic acid was observed in a mixture of water–DMSO (40:60 v/v). DMSO accelerates both depolymerization of poly-3-methyluridylic acid and nucleophilic attack by base. Alkaline hydrolysis of N-methylated polyuridylic acid to mononucleotides has met with difficulties before[14] and in the light of these findings may not be possible.

In view of the importance of methylation in the process of viral infection[15] the possible base lability of 3-methyluridine and other methylated pyrimidines and purines[1] becomes a matter of interest and concern.

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(16) Associate in the Visiting Program of the U. S. Public Health Service, 1966–1970.
(17) NATO Research Fellow, 1969–1970.

Yoshikazu Kondo,[16] Jean-Louis Fourrey,[17] B. Witkop*
National Institute of Arthritis and Metabolic Diseases
National Institutes of Health, Bethesda, Maryland 20014
Received September 19, 1970

High-Resolution Boron Nuclear Magnetic Resonance. I. Pentaborane(9)

Sir:

The ^{11}B nmr spectra of boron hydrides usually show well-resolved splitting of peaks due to coupling between boron and terminal hydrogens. Except for diborane(6) and tetraborane(10) additional fine structure is usually not observed in the separate resonances.[1] This paucity of fine structure has been attributed to quadrupole relaxation effects of the ^{11}B nucleus.[2,3]

However, Williams *et al.*,[4] speculated that the broadness of the lines in that portion of the ^{11}B nmr spectrum representing the resonance of the apex boron of pentaborane(9) (I) was not due to nuclear quadrupole broadening but resulted from unresolved boron–boron coupling. More recently, the measurement of ^{10}B and ^{11}B spin–lattice relaxation times in diborane(6) and pentaborane(9) led to the conclusion that the ^{11}B nmr line widths should be only several hertz at room temperature and that the observed line widths were, in all likelihood, due to complex unresolved splittings.[5]

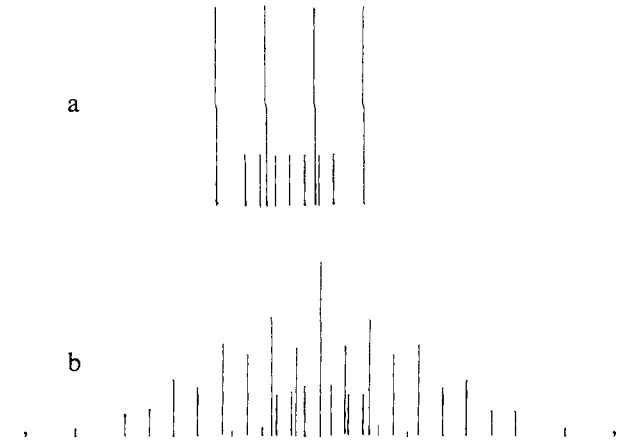
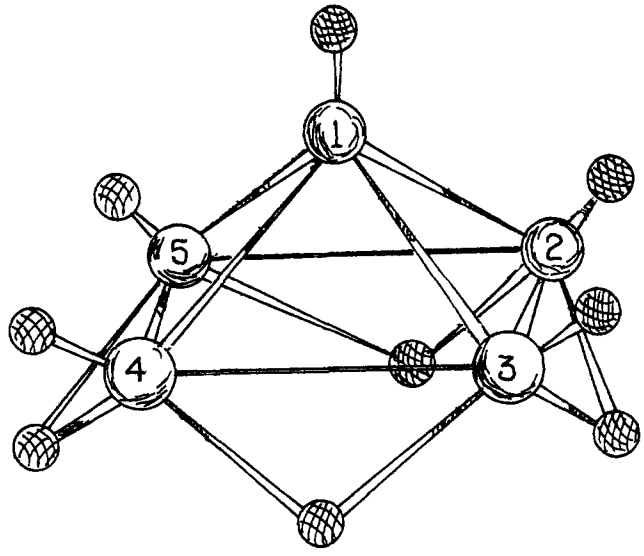


Figure 1. Predicted ^{11}B nmr spectrum of B_5H_9 assuming a value of $J_{^{11}B^{11}B}$ of 20 Hz: (a) basal boron resonance; (b) apex boron resonance.



I, B_5H_9

It is therefore of interest to reexamine the ^{11}B nmr spectrum of pentaborane(9) under high-resolution conditions in order to critically evaluate the hypothesis stated above. In order to obtain high-resolution ^{11}B spectra it is necessary to remove *all* proton coupling to boron, since the B_5H_9 spin system is very complicated. Assuming a particular value for $J_{^{11}B^{11}B}$ and that the ^1H noise-decoupled[6] spectrum of isotopically normal B_5H_9 will be first order, one can easily arrive at the predicted spectra shown in Figure 1. Figure 1a depicts the spectrum of the basal borons which are deshielded with respect to the resonance of the apex boron, Figure 1b, by 40.8 ppm It is essential to note that by assuming a

(1) For example, see G. R. Eaton and W. N. Lipscomb, "NMR Studies of Boron Hydrides and Related Compounds," W. A. Benjamin, New York, N. Y., 1969, and references therein.
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