phosphate donor such as adenosinetriphosphate. With the purified phosphohexokinase, K_s values for the various nucleotides have been determined as follows: ATP, 3×10^{-5} *M;* ITP, 7×10^{-5} *M;* and UTP, 3.3×10^{-5} *M*. The maximum velocity is only slightly greater with ATP than with the other nucleotides. ADP does not enhance the rate of phosphorylation in the presence of UTP. These results make it highly unlikely that nucleoside diphosphokinase[10] and ADP participate in the phosphorylation of fructose-6-phosphate by UTP or ITP with the purified muscle phosphohexokinase.

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ALKALOIDS OF *RAUWOLFIA SERPENTINA* BENTH. III.[1] RESCINNAMINE, A NEW HYPOTENSIVE AND SEDATIVE PRINCIPLE

Sir:

The interest in Rauwolfia therapy for the treatment of hypertension has prompted extensive chemical investigations[2] of the Indian plant *Rauwolfia serpentina* Benth in a search for its physiologically active principles. Recently the isolation and structural elucidation of reserpine, an alkaloid possessing pronounced sedative and hypotensive activity, has been reported.[3]

Extensive pharmacological[4] and clinical[4] comparison between reserpine and an alkaloidal extract[5] of *Rauwolfia serpentina* indicated, however, that reserpine could not account for all of the hypotensive and sedative activity of this fraction. As a result of further chemical studies we now wish to report on another highly active alkaloid, **rescinnamine**, the 3,4,5-trimethoxycinnamic acid ester of methyl reserpate.

The isolation of rescinnamine from its natural source was effected by subjecting the benzene soluble portion of the alkaloidal extract,[5] after removal of reserpine by crystallization from methanol, to chromatographic separation on acid washed alumina. An amorphous fraction was obtained which readily crystallized from benzene yielding rescinnamine as fine needles, m.p. 238–239° (vac.), $[\alpha]^{24}\text{D}$ -97 ± 2 (*c* 1.0, in $CHCl_3$). Analytical data indicated the empirical formula $C_{35}H_{42}O_9N_2$: Calcd. C, 66.23; H, 6.67; N, 4.41; OCH_3, 29.34; mol. wt., 634.71. Found: C, 66.24; H, 6.62; N, 4.45; OCH_3, 28.81; equiv. wt., 636[6]; pK'_a, 6.4.[6]

On basic hydrolysis with 0.75 *N* sodium hydroxide in methanol–water, rescinnamine yielded 3,4,5-trimethoxycinnamic acid and reserpic acid. The 3,4,5-trimethoxycinnamic acid (m.p. 126.5–127°) gave no depression of melting point on admixture with an authentic sample. The infrared spectra and ultraviolet spectra were identical. Calcd. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92; OCH_3, 39.08. Found: C, 60.46; H, 5.95; OCH_3, 38.94[7]; methyl ester, m.p. 96.5–97°.[8]

Reserpic acid, isolated as its hydrochloride, was identified by comparison of its hydrochloride and methyl ester derivatives with authentic samples prepared from reserpine.

The infrared spectrum (nujol) of rescinnamine is similar to that of reserpine in the region of the shorter wave lengths (2.5–7 μ) with the exception of a more intense band at 6.19 μ, which may be attributed to the conjugated double bond of 3,4,5-trimethoxycinnamic acid. The ultraviolet spectrum showed $\lambda_{\max}^{\text{alc}}$ (log ϵ): 229 mμ (4.73), 302 mμ (4.39); $\lambda_{\min}^{\text{alc}}$ (log ϵ): 258 mμ (3.88). The band at 302 mμ is a summation of the α,β-disubstituted 6-methoxyindole and 3,4,5-trimethoxycinnamate chromophores.

Pharmacological tests on rescinnamine show it to have hypotensive, bradycardic and sedative activity similar to that of reserpine. More complete data on these evaluations will be published elsewhere by Dr. G. E. Cronheim.

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[1] Papers I and II, THIS JOURNAL, **75**, 4867 (1953); **76**, 1332 (1954).

[2] For a comprehensive review of earlier work see Asima Chatterjee (nee Mookerjee), "Fortschritte der Chemie Organischer Naturstoffe," Vol. 10, Springer-Verlag, Vienna, Austria, 1953, pp. 390–417.

[3] *Cf.* L. Dorfman, A. Furlenmeier, C. F. Huebner, R. Lucas, H. B. MacPhillamy, J. M. Mueller, E. Schlittler, R. Schwyzer and A. F. St. Andre, *Helv. Chim. Acta*, **37**, 59 (1954), and references cited therein.

[4] This work was carried out by the biological sciences and clinical sections of this Laboratory.

[5] This work was carried out on an alkaloidal extract of *Rauwolfia serpentina*, generically designated "alseroxylon," which is available from Riker Laboratories, Inc., Los Angeles, California.

[6] Potentiometric titration in 75% dimethylformamide–water with 0.01 *N* HCl.

[7] Microanalyses by Dr. Adalbert Elek.

[8] H. P. King and Wei-Yuan Huang, THIS JOURNAL, **71**, 1836 (1949).

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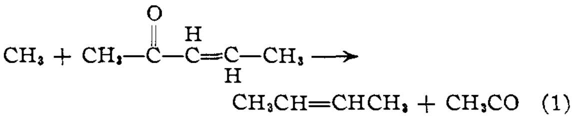
RECEIVED APRIL 1, 1954

A VAPOR-PHASE FREE RADICAL ADDITION-ELIMINATION: REPLACEMENT OF ACETYL BY METHYL[1]

Sir:

We have obtained substantial evidence for a vapor-phase free radical "addition–elimination reaction," (1) in which a methyl radical adds to the olefinic double bond of *trans*-methyl propenyl ketone and an acetyl radical is eliminated. At temperatures above 120° the acetyl radical formed in (1) rapidly dissociates and the following over-all chain sequence is believed to occur



$$CH_3 + CH_3\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}\overset{H}{C}\text{=}\underset{H}{C}\text{—}CH_3 \longrightarrow CH_3CH\text{=}CHCH_3 + CH_3CO \quad (1)$$

$$CH_3CO \longrightarrow CH_3 + CO \quad (2)$$

The results of the following experiments can best be explained by assuming the existence of this new type of radical process.[2]

A. Photolyses of *trans*-Methyl Propenyl Ketone at 2380 Å.—2-Butene was found to be the major hydrocarbon product from all direct photolyses of *trans*-methyl propenyl ketone at 2380 Å. and various temperatures, pressures and intensities.

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[1] The authors gratefully acknowledge the support of the Atomic Energy Commission through contract AT(11-1)-89, Project No. 4.

[2] For a recent review of reactions of methyl radicals see A. F. Trotman-Dickenson, *Quart. Rev.*, VII, 198 (1953).