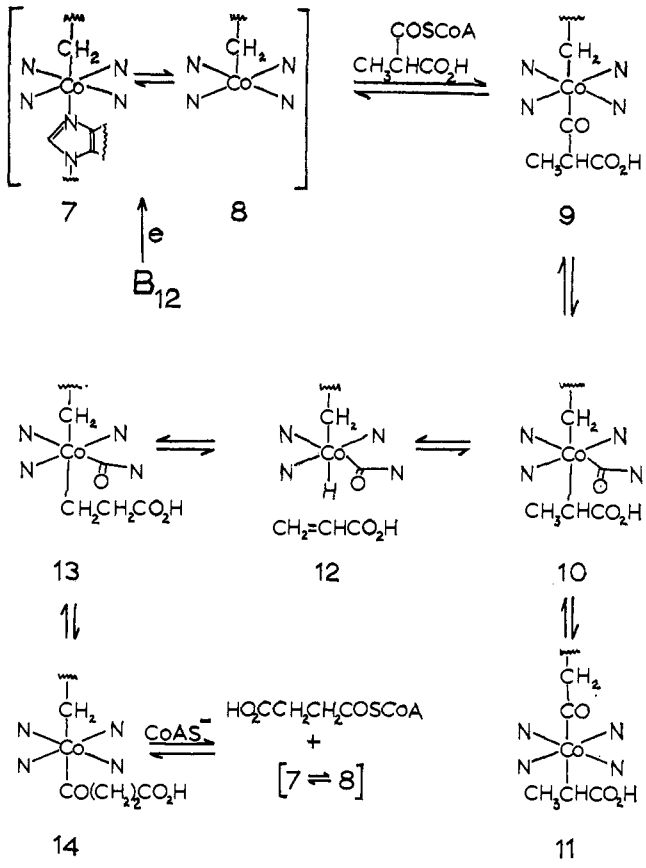

SCHEME 3

may be similarly reduced to a nucleophilic species (**7** ⇌ **8**) which may then be acylated by methylmalonyl CoA to form methylmalonyl coenzyme B_{12} (**9**). The second stage of the proposed mechanism is initiated by an intramolecular transcarbonylation (**9** ⇌ **10** ⇌ **11**) wherein no over-all ligand loss from cobalt occurs. Theoretical justification of this lies in the above discussed decarbonylation of acyl metal carbonyls and in the ready formylation of primary and secondary amines by metal carbonyls.[8,18] The flexibility of the strained corrin

$$R_2N\text{-}\underset{i}{M(CO)_n} \xrightarrow{CO} R_2N\underset{ii}{COM(CO)_n} \longrightarrow R_2NCHO$$

ring system must play a large part in this transcarbonylation. Inspection of models reveals that one of the hydropyrrole rings may become approximately perpendicular to the plane of the other three. This affords a means of lengthening the cobalt nitrogen distance to accommodate the carbonyl group of **10** which would not be available in a rigid prophyrin ring system. The remainder of the mechanism is straightforward and parallels Scheme 2. Transient loss of acrylic acid from **10** to produce **12**, re-addition of **12** to acrylic acid in the opposite sense to produce **13**, recarbonylation of **13** to produce succinyl B_{12} **14** and cleavage of **14** by CoA will produce succinyl CoA and regenerate a molecule of reduced coenzyme B_{12}.

The proposed mechanism is completely consistent with results obtained from labeling experiments and in addition predicts a reduced form of coenzyme B_{12} as the active agent and the intermediacy of acyl derivatives of the coenzyme.

Among other biochemical transformations which require coenzyme B_{12} are the isomerization of propylene glycol to propionaldehyde[20,21] and the interconversion of glutamic and β-methylaspartic acid.[22,23] The last of these (Scheme 4) is superficially similar to the methylmalonyl–succinyl CoA rearrangement. However, from labeling experiments[23] (an over-all 1,2 shift of the glycine residue) and the observation that more

$$HO_2CCH_2CH_2\overset{\pm}{C}HNH_3CO_2H \rightleftharpoons HO_2C\overset{\pm}{C}HCHNH_3CO_2H$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad CH_3$$

SCHEME 4

than one enzyme is necessary for this reaction,[23] the assumption that these two rearrangements are mechanistically closely related is not warranted at present.

(18) This reaction, which frequently occurs under quite mild conditions, probably proceeds *via* intermediates i and ii.[19]

(19) H. W. Sternberg and I. Wender, Abstracts of Papers, International Conference on Coördination Chemistry, London, April, 1959.

(20) A. M. Brownstein and R. H. Abeles, *J. Biol Chem.*, **236**, 1199 (1961).
(21) R. H. Ables and H. A. Leed, Jr., *ibid.*, **236**, 2347 (1961).
(22) A. Munch-Petersen and H. A. Barker, *ibid.*, **230**, 649 (1958).
(23) H. A. Barker, *Fed. Proc.*, **20**, 956 (1961).

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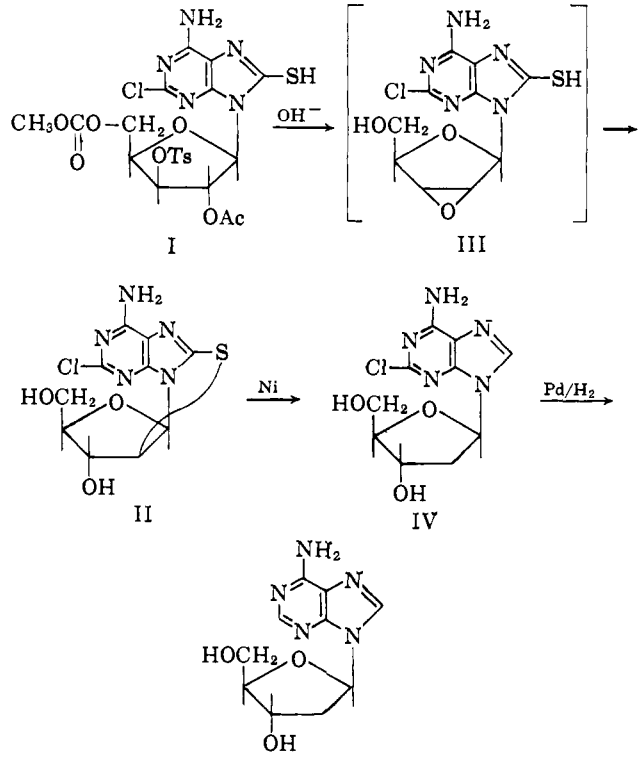
A New Type of "Cyclonucleoside" Derived from 2-Chloro-8-mercapto-9-β-D-xylofuranosyladenine

Sir:

We wish to report a new type of compound, "8,2′-cyclonucleoside," in the purine series and a synthesis of 2′-deoxyadenosine *via* a route involving this compound.

In the purine nucleoside series the cyclonucleoside salt has been reported by Clark, *et al.*,[1] though the cyclonucleoside derived from 2-keto or thioketopyrimidine has been reported[2] by many investigators. The configurational similarity of the 8-hydroxy or 8-mercapto group of purine nucleoside to the 2-keto



(1) V. M. Clark, A. R. Todd and J. Zussman, *J. Chem. Soc.*, 2959 (1951).
(2) A. M. Michelson and A. R. Todd, *ibid.*, 816 (1955); D. M. Brown, D. B. Parihar and A. R. Todd, *ibid.*, 3035, 4242 (1958); G. Shaw and R. N. Warrener, *ibid.*, 50 (1959); J. F. Codington, R. Fecher and J. J. Fox, *J. Am. Chem. Soc.*, **82**, 2792 (1960); *ibid.*, **83**, 1889 (1961), N. C. Jung and J. J. Fox, *ibid.*, **83**, 3060 (1961).

group of pyrimidine[3] led us to attempt the synthesis of 8,2′-cyclonucleoside.

2′-*O*-Acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl-D-xylofuranosyl chloride[4] was condensed with 2,8-dichloroadenine chloromercury salt in refluxing xylene to give 2,8-dichloro-9-(2′-*O*-acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl)-β-D-xylofuranosyladenine, m.p. 160–162° (*Anal.* Calcd. for $C_{21}H_{21}O_9N_5Cl_2S$: C, 42.85; H, 3.60; N, 11.90. Found: C, 42.56; H, 3.79; N, 11.90. $\lambda_{max}^{0.1\,N\,HCl}$ 263 mμ, $\lambda_{max}^{0.1\,N\,NaOH}$ 263 mμ. Paper chromatography: R_f 0.90 (1-butanol: water = 86:14). This material was converted to its 8-mercapto derivative by the reaction with one equivalent of thiourea. Although 2-chloro-8-mercapto-9-(2′-*O*-acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl)-β-D-xylofuranosyladenine (I) was obtained in the form of a hard glass (yield 68.2%), evidence for its assigned structure was obtained by paper chromatography (R_f 0.90 (1-butanol: water = 86:14)) and spectrophotometric analysis ($\lambda_{max}^{0.1\,N\,HCl}$ 302, 310 mμ; λ_{max}^{EtOH} 302, 310 mμ, $\lambda_{max}^{0.1\,N\,NaOH}$ 300 mμ).

Refluxing of I in methanol containing sodium methoxide for 12 min. gave a compound having m.p. 228–229° dec. $\lambda_{max}^{0.1\,N\,HCl}$ 277 mμ, $\lambda_{max}^{0.1\,N\,NaOH}$ 277 mμ. *Anal.* Calcd. for $C_{10}H_{10}O_3N_5ClS.0.5H_2O$: C, 36.99; H, 3.38; N, 21.56. Found: C, 36.66; H, 3.82; N, 20.80. Paper chromatography [R_f 0.42 (water, pH 10.0), R_{Ad}[5]]. From spectrophotometric, chromatographic and elemental analytical data, the resulting compound was concluded to be 2-chloro-8-mercapto-8,2′-anhydro-D-xylofuranosyladenine (II) and not the presumed intermediate 2′,3′-anhydronucleoside (III). This was further supported by the fact that II has no ν_{max}^{Nujol} at 863 cm.$^{-1}$, which has been assigned to the epoxide group.[4]

The structure of II confirmed by the desulfurization of compound II with Raney nickel, which afforded 2-chloro-2′-deoxyadenosine (IV) [R_f 0.52 (water, pH 10.0), $\lambda_{max}^{0.1\,N\,HCl}$ 265, $\lambda_{max}^{0.1\,N\,NaOH}$ 265 mμ]. Hydrogenation of compound IV over palladized charcoal as a catalyst gave 2′-deoxyadenosine [R_f 0.35 (1-butanol–water = 86:14), 0.50 (water, pH 10.0); $\lambda_{max}^{0.1\,N\,HCl}$ 258, $\lambda_{max}^{0.1\,N\,NaOH}$ 260 mμ]. This material was compared directly with the authentic 2′-deoxyadenosine[6] and 3′-deoxyadenosine[7]

Sample	Hydrolysis product	R_f[a]	Spray I[b]	Spray II[c]
Natural 2′-deoxy-adenosine	2-Deoxyribose	0.21	Pink ++	Pink +
Synthetic 2′-deoxy-adenosine	2-Deoxyribose	.21	++	+
3′-deoxyadenosine	3-Deoxyribose	.41	+	+++

[a] Paper chromatography, 1-butanol–acetic acid–water = 4:1:5, after equilibration overnight, upper layer was used. [b] Cysteine–sulfuric acid reagent: J. G. Buchanan, *Nature*, **168**, 1091 (1951). [c] Aniline hydrogen phthalate reagent: S. M. Partridge, *Nature*, **164**, 443(1949).

These results clearly show that the resulting deoxynucleoside is 2′-deoxyadenosine and not the 3′-isomer. Thus it must be concluded that the 8,2′-cyclic bond was formed by the nucleophilic attack of the 8-mercapto group on the 2′-carbon atom of the epoxide linkage in III.

(3) M. Wilkins. "Nucleoproteins," R. Stoops, Ed., Solvay Inst. Chem., 11th Chemical Conference, Interscience, New York, N. Y., 1959, p. 48.

(4) C. D. Anderson, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 3967 (1959).

(5) R_{ad} stands for a value obtained from R_f divided by R_f of adenosine.

(6) Purchased from Sigma Chemical Co. St. Louis, Mo.

(7) Unpublished experiments by A. Yamazaki and M. Ikehara.

It is hoped that 8,2′-cyclonucleoside will be useful in transforming the sugar moiety of purine nucleosides in a manner similar to that which has been used so successfully in the pyrimidine series.[8] Experiments along this line are now in progress in our Laboratory.

(8) J. J. Fox and I. Wempen, *Advan. Carbohydrate Chem.*, **14**, 283 (1959).

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Evidence for Chain Transfer in the Autoxidation of Hydrocarbons Retarded by Phenol

Sir:

Peroxy radical–antioxidant complexes have been postulated by Hammond, *et al.*,[1] to be intermediates in the inhibition of the autoxidation of hydrocarbons. Despite numerous attempts to establish the existence of such complexes,[2–4] no direct evidence has yet been obtained for their existence and, at the same time, no plausible alternative mechanism has yet been proposed.

The postulation of these complexes was based on the kinetic evidence that the rate of oxygen absorption during the oxidation of tetralin in the presence of phenol or N-methyl aniline followed the kinetic relation

$$-\frac{dO_2}{dt} \propto \frac{[Ri]^{1/2}}{[\text{inhibitor}]^{1/2}}$$

where R_i is the rate of radical production from azobis-(2-methyl propionitrile) (AIBN). This postulation, however, assumed that the rate was first order with respect to hydrocarbon concentration.

In the present work it has now been demonstrated that the dependence of the rate of oxygen absorption with respect to the concentration of the hydrocarbon is not first order. Data are presented in Fig. 1 for the initial rate of oxygen absorption by chlorobenzene solutions of phenol, AIBN, and tetralin. When phenol was absent, the rate was first order with respect to hydrocarbon concentration, demonstrating that the rate of formation of radicals from AIBN did not vary with hydrocarbon concentration. However, when phenol was added, the rate became $^3/_2$ order with respect to the hydrocarbon. Similar results were obtained using 9,10-dihydroanthracene as the substrate. Thus

$$-\frac{dO_2}{dt} \propto \frac{[R_i]^{1/2}\,[RH]^{3/2}}{[\text{phenol}]^{1/2}}$$

The kinetic chain lengths in these experiments ranged from 4 to 30.

A mechanism which can account for the observed kinetics follows

$$R' - N = N - R' \xrightarrow{k_1} 2aR'\cdot + N_2 \quad R_i = 2ak_1[AIBN] \quad (1)$$

$$R'\cdot + O_2 \xrightarrow{k_2} R'O_2\cdot \quad (2)$$

$$R'O_2\cdot \text{ (or } RO_2\cdot) + RH \xrightarrow{k_3} R'O_2H + R\cdot \quad (3)$$

$$R\cdot + O_2 \xrightarrow{k_4} RO_2\cdot \quad (4)$$

$$RO_2\cdot + AOH \xrightarrow{k_5} RO_2H + AO\cdot \quad (5)$$

$$AO\cdot + RH \xrightarrow{k_6} AOH + R\cdot \quad (6)$$

$$RO_2\cdot + AO\cdot \xrightarrow{k_7} \text{inert products} \quad (7)$$

where AOH is phenol, AO· is the phenoxy radical and RH is tetralin. If one makes the usual steady state

(1) G. S. Hammond, C. S. Boozer, C. E. Hamilton, and J. N. Sen, *J. Am. Chem. Soc.*, **77**, 3238 (1955).

(2) K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

(3) J. R. Thomas and C. A. Tolman, *J. Am. Chem. Soc.*, **84**, 2930 (1962).

(4) J. R. Thomas, *ibid.*, **85**, 591, 593 (1963).