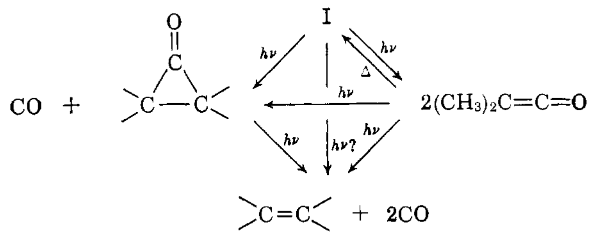
Earlier indications[1,2] of the importance of (1), which rely on the formation of a hemiketal of tetramethylcyclopropanone, are unreliable since the solvent may very well complex with I in the excited state and thus promote the monodecarbonylation reaction.[9]

The reactions in this system can be summarized as



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The Direct Preparation of 2′-O-Methyladenosine from Adenosine[1]

Sir:

Smith and Dunn[2] isolated a compound from the RNA of wheat germ and rat liver which they designated as 2′- (or 3′-) O-methyladenosine. This compound isolated from yeast soluble RNA was identified as 2′-O-methyladenosine (I) by Hall,[3] based on chromatographic comparison of hydrolysis products with authentic 2-O-methyl-D-ribose. 2′-O-Methyladenosine (I) and other 2′-O-methylribonucleoside derivatives of the naturally occurring heterocyclic bases have been found in both soluble and high molecular weight RNA from a variety of sources.[4-8]

We wish to report the first chemical synthesis of a naturally occurring 2′-O-methylpurineribonucleoside, 6-amino-2′-O-methyl-9-β-D-ribofuranosylpurine (2′-O-methyladenosine, I). Adenosine has been methylated selectively on the adenine moiety with methyl iodide in the absence of strong base to give 1-methyladenosine in good yield.[9] Szer and Shugar[10] report that excess diazomethane and uridylic acid result in a small amount of product which is methylated in the ribose moiety as well as at nitrogen 3. It has been reported[11] that adenosine methylates only very slowly in neutral aqueous media with ethereal diazomethane to give 1-methyladenosine. In an effort to obtain selective O-methylation, the reaction of diazomethane on adenosine in a homogeneous solution of water and 1,2-dimethoxyethane was studied. Under these conditions the 2′-hydroxyl was found to react preferentially to give a good yield of 2′-O-methyladenosine. To 5 g. of adenosine monohydrate dissolved in 200 ml. of warm (80°) water was added all at once, with stirring, a solution of 25 g. of diazomethane dissolved in 500 ml. of 1,2-dimethoxyethane. The clear yellow solution was allowed to cool to room temperature and was stirred overnight, at which time the color was discharged. The solution was reduced *in vacuo* to a heavy sirup. The sirup was dissolved in aqueous ethanol (80%) and evaporated *in vacuo*. This process was repeated several times with absolute ethanol to give a white foam which contained adenosine and 2′-O-methyladenosine in approximately equal quantities and a small amount of an unidentified fast moving spot, as judged by paper chromatography. The crude product was purified by column partition chromatography using the sodium borate–butanol–celite system described by Hall.[8] Fractions 5–9 were reduced to dryness to give 2.0 g. (41%) of a chromatographically pure white solid which was recrystallized from absolute ethanol to give a product (I), m.p. 200–202°; $[\alpha]^{24}\mathrm{D}$ −58.2° (c 1, H_2O). *Anal.* Calcd. for $C_{11}H_{15}N_5O_4$: C, 47.0; H, 5.34; N, 24.9. Found: C, 47.1; H, 5.67; N, 25.0. Rigorous comparison[12] of synthetic 2′-O-methyladenosine with the natural material in four solvent systems showed the products to be identical (Table I). In addition, the two samples were electrophoresed at pH 9.2 under two conditions: (1) in 0.05 *M* glycine buffer and (2) in 0.05 *M* glycine–0.05 *M* borate buffer. In both buffers the two samples migrated 5.5 cm. toward the negative pole (22 v./cm. for 4 hr.) A proton magnetic resonance spectrum in dimethyl-d_6 sulfoxide showed a sharp singlet (3H) at δ 3.78 due to the 2′-O-methyl group (TMS as an external standard). Ultraviolet absorption spectral data gave peaks at $\lambda_{\max}^{\mathrm{pH}\,1}$ 256.5 mμ (ϵ 13,800), $\lambda_{\max}^{\mathrm{MeOH}}$ 258.5 mμ (ϵ 13,700), and $\lambda_{\max}^{\mathrm{pH}\,11}$ 258.5 mμ (ϵ 13,900). Acid hydrolysis gave adenine and 2′-O-methyl-D-ribose which were identified by rigorous chromatographic comparison in three solvent systems with authentic adenine and synthetic 2′-O-methyl-D-ribose.[13] Treatment of 2′-O-methyladenosine (I) with sodium nitrite and acetic acid in the presence of a small amount of 1 *N* hydrochloric acid, after standing for 3 days at room temperature, gave 2′-O-methylinosine (II) in 58% yield. Recrystallization of II from 98% ethanol gave needles, m.p. 177–180°; $\lambda_{\max}^{\mathrm{pH}\,1}$ 248 mμ (ϵ 14,100) and $\lambda_{\max}^{\mathrm{pH}\,11}$ 251 mμ (ϵ 15,000). *Anal.* Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.3; H, 4.96; N, 19.8. Found: C, 46.5; H, 5.12; N, 20.0.

Table I

System	Solvent	*R*
1.	1-Butanol–water–concd. ammonia, 86:14:5	0.49
2.	2-Propanol–concd. HCl–water, 680:170:144	0.53
3.	2-Propanol–water–concd. ammonia 7:2:1	0.71
4.	Ethyl acetate–1-propanol–water 4:1:2	0.57

(1) Supported by Research Grant CA 04008-07 from the National Cancer Institute of the National Institutes of Health, Public Health Service.

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This work records the first selective reaction involving a 2′-hydroxyl as the major site of reaction in an unprotected naturally occurring β-D-ribofuranosyl nucleoside. The suitable blocking of the 2′-hydroxyl by a group which can be removed subsequently under adequately mild conditions has been one of the major problems of oligo- and polynucleotide chemistry.[14] The possibility that such a group (benzyl) might be introduced directly *via* phenyldiazomethane and removed later by catalytic reductive hydrogenolysis[15] is a prospect presently under active investigation in our laboratory.

The biochemical function of the 2′-O-methylnucleosides is as yet unknown.[8] Honjo and co-workers[16] have found that 2′-O-methylribonucleotides behave differently from the corresponding ribonucleotides toward a variety of enzymatic systems. Work is presently in progress to see if this selective reaction with diazomethane can be utilized for the synthesis of additional naturally occurring 2′-O-methylnucleosides of current biochemical interest.

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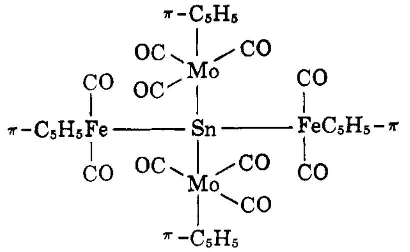
An Organometal Compound Containing Five Metal Atoms

Sir:

In a previous communication[1] we described the synthesis of an organometal carbonyl compound containing three different metals covalently bonded. We now wish to report the synthesis of a new, soluble, organometal compound (I) containing a cluster of five metal atoms—two Mo and two Fe atoms covalently bonded to a central Sn atom.



I

I, bis[π-cyclopentadienyldicarbonyliron]bis[π-cyclopentadienyltricarbonylmolybdenum]tin(IV), was prepared as follows. A tetrahydrofuran solution (40 ml.) of sodium π-cyclopentadienyltricarbonylmolybdate(−I),[2] Na[π-CpMo(CO)$_3$] (II), 10 mmoles, was prepared in a three-necked flask fitted with a stirrer, a reflux condenser, and a nitrogen inlet tube. To the yellow solution in the flask was added a THF solution (75 ml.) of dichlorobis(π-cyclopentadienyldicarbonyliron)tin(IV),[3] [π-CpFe(CO)$_2$]$_2$SnCl$_2$ (III), 5 mmoles, and the resulting red solution was stirred and refluxed for 24 hr. under an atmosphere of nitrogen. After cooling to room temperature, the solution was filtered quickly and the solvent removed from the filtrate in a rotary evaporator. Dichloromethane (75 ml.) and some pentane (20 ml.) were added to the residue. The mixture was filtered and the filtrate stored under nitrogen. A small amount of insoluble material appeared, which was filtered under carbon monoxide, and the filtrate was stored under carbon monoxide in the cold. On standing, a red-orange crystalline precipitate (0.567 g.) was obtained. The crystals were separated and recrystallized under carbon monoxide from a minimum amount of dichloromethane.

When it crystallizes in relatively larger crystals, I appears to be deep red; as small crystals, it appears orange. It does not melt, but on heating the color changes to brown between 140 and 150° and to black between 215 and 220°.

Anal. Calcd. for $C_{30}H_{20}Fe_2Mo_2SnO_{10}$: C, 37.42; H, 2.09; mol. wt., 962. Found[4]: C, 37.52; H, 2.20; mol. wt.,[5] 947.

The X-ray emission spectrum showed bands corresponding to Sn: Kβ_1 at 12.41°; Kα, Kα_1 at 14.0–14.12°; Mo: Kβ, Kβ_1 at 18.08° and Kα, Kα_1, Kα_2 at 20.29–20.41°; and Fe: Kβ_1 at 51.73° and Kα_1 at 57.47°.

The compound is air stable when dry, but in solution in the absence of carbon monoxide it decomposes rapidly. It is insoluble in pentane and water, sparingly soluble in hexane and carbon tetrachloride, and soluble in dichloromethane and acetone.

The infrared spectrum showed the absence of bridging as well as ketonic carbonyl. The spectrum in the C–O stretching region of I in dichloromethane showed the following bands (cm.$^{-1}$): 1883.3 (w), 1916.6 (sh, w), 1950 (m), 1988.8 (s), 2011 (m), and 2016.7 (sh, w).

The new compound probably has the two Mo and the two Fe atoms tetrahedrally coordinated to the Sn(IV). An X-ray study of the compound is being made by Dr. E. Corey.

We have also isolated a dark red (almost black) residue from the reaction of III and sodium tetracarbonylcobaltate(−I), NaCo(CO)$_4$. The X-ray emission spectrum showed bands corresponding to Sn, Co, and Fe. The compound was difficult to purify and has not been isolated in pure form as yet.

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