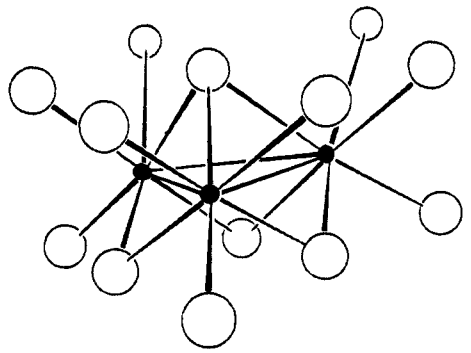

Figure 2. The structure of the Mo_3O_{13} unit that occurs in $Zn_2Mo_3O_8$ and related compounds.

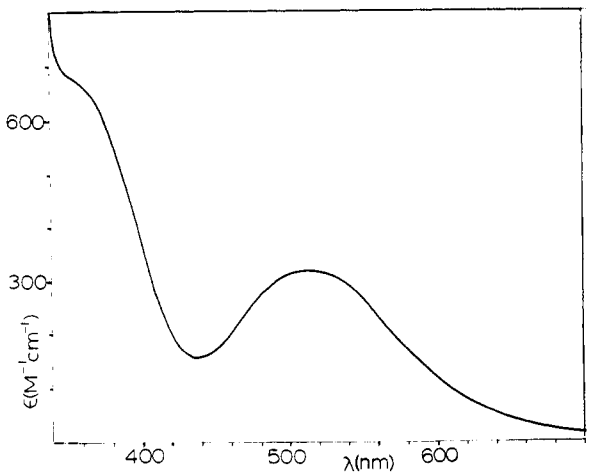

Figure 3. Absorption spectrum of $[Mo_3O_4(C_2O_4)_3(H_2O)_3]^{2-}$.

symmetry-based molecular orbital treatment leads naturally to the conclusion that the metal atoms are linked by single bonds since the occupied MO's having metal-metal character give the electron configuration a^2e^4. The Mo-Mo distance in $Zn_2Mo_3O_8$ (2.524 Å[11]) is not very different from the one found here.

Ardon and co-workers[3a,b] have presented evidence that the Mo^{IV} aquo ion is dinuclear, with a charge of +4 and, hence, most likely $[(H_2O)_4Mo(\mu\text{-}O)_2Mo(H_2O)_4]^{4+}$. Thus, in the presence of oxalate a structural transformation occurs. It is true that both species, Ardon's and ours, are red, but the spectra are different, as a comparison of Figure 3 with the spectrum of the aquo ion[3a] will show. The formation of the trinuclear oxalato ion is irreversible and this new species is stable indefinitely in aqueous solution without reverting to the Ardon species.

The compound described here is the first example of a structurally characterized complex containing Mo^{IV} *isolated from aqueous solution of molybdenum(IV)*. It is also one of the most stable and easily prepared Mo^{IV} complexes known. It suggests that the aqueous (and other) chemistry of this oxidation state of molybdenum may be more extensive than previously supposed.[12]

Supplementary Material Available: A table of atomic positional and thermal parameters, a more complete list of interatomic distances and angles, and a list of structure factors (16 pages). Ordering information is given on any current masthead page.

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Received May 8, 1978

Interaction of Vicinal and Nonvicinal Amino-Hydroxy Group Pairs in Aminoglycoside-Aminocyclitol Antibiotics with Transition Metal Cations. Selective N Protection

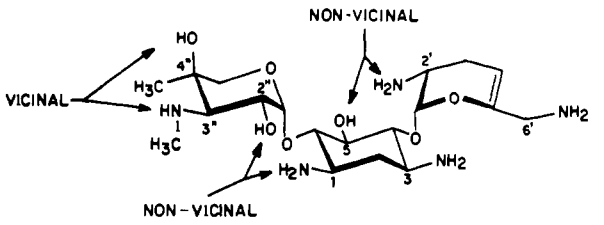
Sir:

We wish to report a novel, general, and high yielding method of selective N protection of aminoglycoside-aminocyclitol antibiotics via divalent transition metal complexing of vicinal and nonvicinal amino-hydroxy group pairs.[1]

We define a nonvicinal amino-hydroxy group pair as one in which the two groups might be located on different rings, yet are in proximity owing to a unique stereochemical consequence as a result of conformational preference about the glycosidic linkage and possible further stabilization of the conformation by hydrogen bonding between the two groups.[2-5]

It was thought that, under suitable conditions, both vicinal and nonvicinal amino-hydroxy group pairs might form reversible complexes with divalent transition metal cations, the extent to which these cation complexes are formed being dependent on the type and amount of transition metal, availability of the pair for complexing, stability of the complex, and nature of the solvent. Conventional N blocking of amino groups not complexed in a similar manner would then lead to, after removal of the metal, selectively N-protected derivatives.

Treatment of sisomicin (**1**) with cobaltous acetate tetrahydrate (3 equiv) in Me_2SO (0.005 mol %) for 30 min, fol-



SISOMICIN (1)

lowed by acetic anhydride (3 equiv), and subsequent removal of the metal with hydrogen sulfide afforded 3,2′,6′-tri-*N*-acetylsisomicin (**4**) in 95% yield.[6] The results of similar selective 3,2′,6′-tri-N protection of sisomicin (**1**) and related antibiotics using a variety of N-blocking agents and transition metal salts are given in Table I. As seen, for the antibiotics listed in Table I, Co^{2+} ions appear to give best yields of the tri-N-blocked products.[6]

0002-7863/78/1500-5253$01.00/0

Table I. Some 3,2′,6′-Tri-N-Protected Aminoglycoside-Aminocyclitol Antibiotics Prepared via 1,2″ and 3″,4″ Complexing with Transition Metal Salts

compd	no.	reagent[a]	$M^{2+}(^{-}OAc)_2$	product no.	% yield
sisomicin	**1**	Ac_2O	3Co	**4**	95
		Ac_2O	2Cu + 2Ni	**4**	85
5-episisomicin	**6**	Ac_2O	2Cu + 2Ni	**7**	88
sisomicin	**1**	CBZ-NOP	2Cu + 2Ni	**8**	70
		CBZ-NOP	3Co	**8**	95
		PMZ-S-DMP	3.6Co	**9**	88
		TCEC-NOS	7Co	**10**	80
		TCEC-NOS	3Co	**10**	95
gentamicin C_{1a}	**11**	CBZ-NOP	3Cu + 3Ni	**12**	81
		TCEC-NOS	2Cu + 2Ni	**13**	78
gentamicin C_2	**14**	CBZ-NOP	3Cu + 3Ni	**15**	81
gentamicin C_1	**16**	CBZ-NOP	3Cu + 3Ni	**17**	74
5-episisomicin	**6**	TCEC-NOS	3.4Co	**18**	95
		PMZ-S-DMP	3.4Co	**19**	88

[a] *N*-(Benzyloxycarbonyloxy)phthalimide, CBZ-NOP; *S*-(*p*-methoxybenzyloxycarbonyl)-4,6-dimethylpyrimidinethiol, PMZ-S-DMP; *N*-(2,2,2-trichloroethoxycarbonyloxy)succinimide, TCEC-NOS.

Table II. Some 3,6′-Di-N-Protected Aminoglycoside-Aminocyclitol Antibiotics Prepared via 1,2″ and 3″,4″ Complexing with Transition Metal Salts

compd	no.	reagent[a]	$M^{2+}(-OAc)_2$	product no.	% yield
gentamicin B	**2**	PMZ-S-DMP	3Co	**20**	95
		CBZ-NOP	3Co	**21**	91
		CBZ-NOP	2Cu + 2Ni	**21**	85
		CBZ-NOP	3Cu	**21**	66
kanamycin A	**3**	PMZ-S-DMP	6.4Ni	**22**	95
		CBZ-NOP	6.4Ni	**23**	88
3′,4′-dideoxygentamicin B	**24**	CBZ-NOP	2Cu + 2Ni	**25**	90
2′,3′-dideoxygentamicin B	**26**	CBZ-NOP	3Co	**27**	86

[a] Abbreviations are explained in Table I, footnote *a*.

Similarly, gentamicin B (**2**) and kanamycin A (**3**), which do not have an amino group at the 2′ position, were converted into a number of the corresponding 3,6′-di-N-protected derivatives in yields ranging between 88 and 95%. In the case of kanamycin A, Ni^{2+} appeared to give best yields of the di-N-blocked derivatives (Table II).

In the above reactions, when the amount of the transition metal was limited to just 3″,4″ complexing and the amount of the N-protecting agent increased to 4 or 3 equiv, high yields of 1,3,2′,6′-tetra-N-blocked or 1,3,6′-tri-N-blocked (when there is no amino group at the 2′ position) derivatives could be prepared. However, best conditions were achieved with cobalt or copper acetate (0.5–1 equiv) in methanol for simple acylations. For example, treatment of **1** or **2** with copper acetate in methanol followed by acetic anhydride, 4 and 3 equiv, respectively, afforded, after the usual workup, 1,3,2′,6′-tetra-*N*-acetylsisomicin (**28**) and 1,3,6′-tri-*N*-acetylgentamicin B (**29**) in near-quantitative yields.[1,7]

As an example of selective 6′-N protection, treatment of kanamycin A (**3**) and gentamicin B (**2**) with cupric chloride in Me_2SO, followed by *N*-benzyloxycarbonyloxyphthalimide (1 equiv), afforded, after removal of the metal, solely the corresponding 6′-N-protected derivatives **30** and **31**, respectively.[1,7]

An unexpected, but highly useful reaction was discovered when sisomicin (**1**) was reacted with 6 equiv of nickelous acetate (or chloride) in methanol prior to treating with the usual blocking agents (2 equiv). The products were 2′,6′-di-N-protected sisomicins. For example, reaction of **1** as mentioned above with *N*-(2,2,2-trichloroethoxycarbonyloxy)succinimide gave, after workup with ammonia, 2′,6′-di-*N*-(2,2,2-trichloroethoxycarbonyl)sisomicin (**32**) in 65% yield.

In conclusion, the transition metal complexing-selective N-blocking method presented in this communication offers, when combined with conventional N-protecting and de-N-protecting techniques, an excellent and predictive way of preparing a variety of intermediates for chemical modification.

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Received March 17, 1978