respectively.[1-5] Although, the reaction of $Pt(PPh_3)_4$ with Cl_2 does not appear to have been reported, the general concensus among chemists is that *cis*-$PtCl_2(PPh_3)_2$ would result. This is evidenced by the fact that, hitherto, synthetic methods for the synthesis of *trans*-$PtX_2(PPh_3)_2$ (X = Cl, Br, or I) involve either photochemical[6] or thermal[7] isomerization of the cis isomers, or, from the reaction of *trans*-$PtHCl(PPh_3)_2$ with $HgCl_2$[8] instead of the obvious, direct reaction of $Pt(PPh_3)_4$ with the halogens. We now report that, under suitable conditions, the direct oxidative addition of the halogens to $Pt(PPh_3)_4$ leads exclusively to *trans*-$PtX_2(PPh_3)_2$ (X = Cl, Br, or I) and that, under any conditions reported, the first step in these oxidative additions is a trans addition of X_2 to $Pt(PPh_3)_4$.

The fact that previous investigators have reported the isolation of cis isomers is a consequence of isomerization, in the presence of triphenylphosphine, of the initially formed trans isomers to the cis isomers. This trans–cis isomerization has previously been observed to occur rapidly for $PtCl_2(PPh_3)_2$ in chloroform.[8] We have observed that the rate of trans–cis isomerization in benzene for $PtX_2(PPh_3)_2$ (X = Cl, Br, or I) follows the order Cl > Br ≫ I. Thus, in order to demonstrate that the addition of halogens to $Pt(PPh_3)_4$ is a trans addition by isolating trans isomers, the experimental conditions must be such that no free triphenylphosphine is present after the formation of *trans*-$PtX_2(PPh_3)_2$. In this manner, the phosphine-catalyzed trans–cis isomerization reaction can be prevented.

One method available to prevent isomerization of the trans products is to "tie up" the free triphenylphosphine present in the reaction mixture by using more than the stoichiometric amount of halogen required for the oxidative-addition reaction. The excess halogen reacts with PPh_3 to form $[PPh_3X]X$ (and/or other products depending on the amount of X_2 used). Previous investigators, who obtained cis isomers, were reluctant to use an excess of the halogen, presumably for fear of further oxidation of the initially formed $PtX_2(PPh_3)_2$ to $PtX_4(PPh_3)_2$. However, we have observed that the first oxidative addition of X_2 to $Pt(PPh_3)_4$ proceeds faster than the second oxidative addition of X_2 to $PtX_2(PPh_3)_2$; thus, by limiting the reaction time to 3 min or less, the formation of Pt(IV) complexes can be avoided. For I_2 and Br_2, the reaction with $Pt(PPh_3)_4$ for 3 min using 4:1 mole ratio of halogen to Pt(0) complex was found to be sufficient to yield exclusively *trans*-$PtI_2(PPh_3)_2$ and *trans*-$PtBr_2(PPh_3)_2$, respectively. The reactions were carried out by mixing an ethereal solution of the halogen with a benzene solution of $Pt(PPh_3)_4$. The conditions were modified for the reaction of chlorine with $Pt(PPh_3)_4$. Since *trans*-$PtCl_2(PPh_3)_2$ is more rapidly isomerized in the presence of PPh_3 than *trans*-$PtBr_2(PPh_3)_2$ or *trans*-$PtI_2(PPh_3)_2$, it was found necessary to add the $Pt(PPh_3)_4$ solution in a fast dropwise fashion to an excess of a stirred benzene solution of Cl_2 so that at any given time during the addition no free phosphine can be present in the solution. The reaction time was also limited to 1 min to prevent oxidation to $PtCl_4(PPh_3)_2$ because Cl_2 is more reactive with both $Pt(PPh_3)_4$ and $PtCl_2(PPh_3)_2$ than are either Br_2 or I_2. In each instance only the trans isomer was obtained demonstrating that the addition of the halogens to $Pt(PPh_3)_4$ is a trans addition reaction.

The isomers were identified by their elemental compositions, their solubilities in benzene (from which they were recrystallized), their decomposition points, and their infrared spectra in which the 500–600-cm^{-1} region is of particular use. Mastin[7] has reported that there is a very strong absorption at 550 ± 5 cm^{-1} in all *cis*-$PtXY(PPh_3)_2$ and *cis*-$PtX_2(PPh_3)_2$ complexes, but he reports this absorption to be very weak in the trans isomers. We confirm his observation for the cis dihalogen complexes, but we find this absorption to be entirely absent in our spectra of the trans complexes prepared both by the oxidative-addition reactions reported herein and by independent methods.[9]

The reaction of I_2 with $Pt(PPh_3)_4$ was also repeated using the stoichiometric amount of reactants (1:1) for the formation of $PtI_2(PPh_3)_2$. The reaction time was also extended to 15 min. It was found that *trans*-$PtI_2(PPh_3)_2$ was formed in spite of the presence of free triphenylphosphine being present under these conditions. This demonstrates that *trans*-$PtI_2(PPh_3)_2$ isomerizes rather slowly in the presence of PPh_3 and suggests that earlier investigators had obtained the *trans*-$PtI_2(PPh_3)_2$ instead of the reported *cis*-$PtI_2(PPh_3)_2$.[3,4] An error, if made, might have resulted from an analogy to the reaction of Cl_2 and Br_2 with $Pt(PPh_3)_4$ where cis isomers are indeed formed under the conditions of a 1:1 mole ratio of the reactants.

With *trans*-$PtI_2(PPh_3)_2$, cis–trans isomerization appears to occur more readily than trans–cis isomerization. Mastin has reported[7] that the thermal isomerization of the cis isomer occurs in a refluxing chloroform solution containing 2% ethanol. We have found that the isomerization also proceeds in refluxing solution of benzene and even in the solid state at 200°. Thus, *trans*-$PtI_2(PPh_3)_2$ appears to be relatively more thermodynamically stable with respect to *cis*-$PtI_2(PPh_3)_2$ than are *trans*-$PtBr_2(PPh_3)_2$ and *trans*-$PtCl_2(PPh_3)_2$ with respect to their cis isomers.

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Atropisomeric Streptovaricins[1,2]

Sir:

The streptovaricins (and other ansamycin antibiotics)[3] derive an intrinsic helicity from their ansa rings. In connection with extensive studies of the biological activities of the streptovaricins and their derivatives,[2] we have examined the effect of this helicity on the activities displayed. Heating streptovaricin C (**1**) in refluxing toluene overnight (Figure 1) gave a mixture of **1** and atropisostreptovaricin C[4] (**2**, $C_{40}H_{51}NO_{14}$,[5b,c] properties in Table I), in the approximate ratio of 17:1, which were separated by chromatography over silicic acid. Heating a sample of **2** gave a similar mixture of **1** and **2**. Most spectral properties (uv, ir, pmr, mass spectral) of **1** and **2** are identical or nearly so, but the nature of the isomerism of **1** and **2** is established by their rotations of similar magnitude but opposite sign (Table I), by the nearly mirror image relationship of their CD curves,[6] and by the conversion of both **1** and **2** to streptoval C [**3**, $C_{40}H_{49}NO_{14}$,[5] mp 140–143°, $[\alpha]^{24}D$ −92.3° (*c* 0.013, $CHCl_3$)] on treatment with sodium metaperiodate.[7] Significantly, while most cmr chemical shifts for **1** and **2** are nearly identical,[8a] those for C-15 and C-16, which lie *above* the acetate group in **1** but *below* the acetate group in **2**, differ considerably (C-15 at 153.9 ppm from TMS for **1**, 149.3

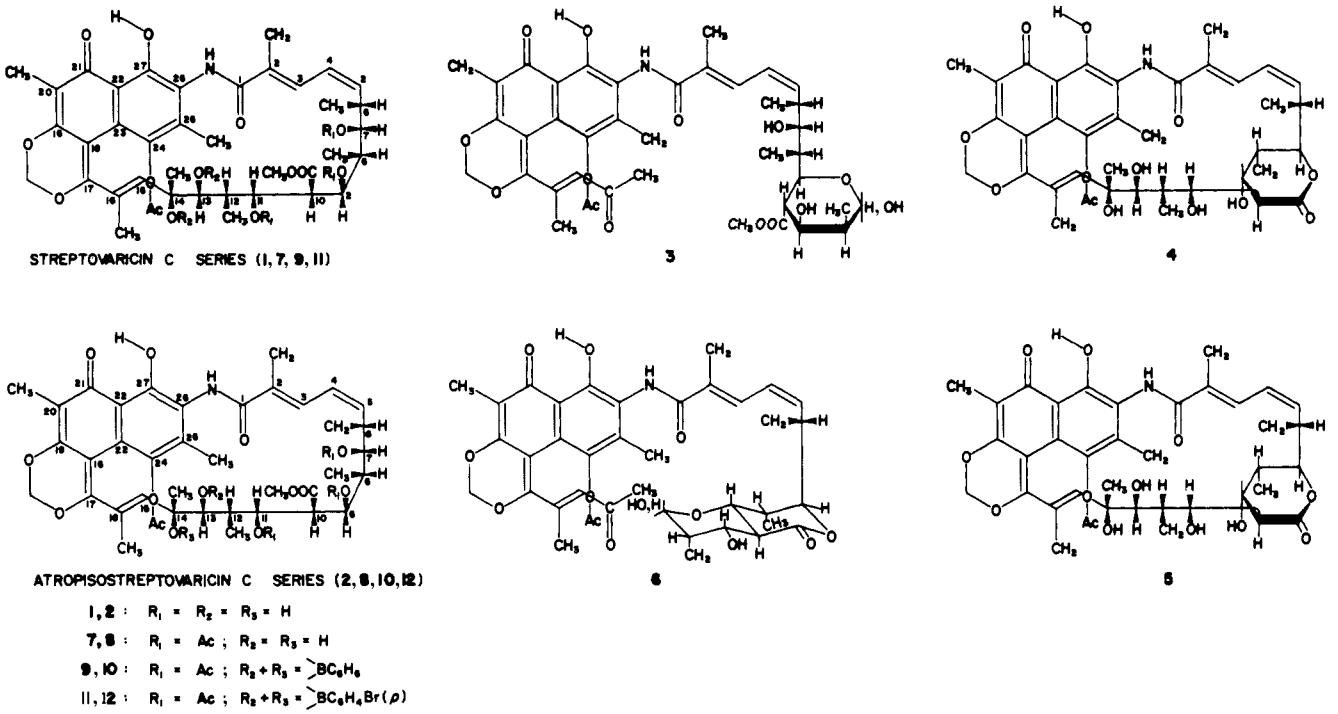

Figure 1. Structures of streptovaricins, their atropisomers and derivatives. In the streptovaricin series (**1, 4, 7, 9, 11**) the ansa chain lies above the aromatic acetate group, while in the atropisostreptovaricin series (**2, 5, 8, 10, 12**) the ansa chain lies below the aromatic acetate. In the streptovals (**3** and **6**) the two atropisomeric forms interconvert at room temperature.

Table I. Properties of Streptovaricin Derivatives (**1, 4, 7, 9, 11**) and their Atropisomers (**2, 5, 8, 10, 12**)

	Streptovaricin or derivative									
	1	**2**	**4**	**5**	**7**	**8**	**9**	**10**	**11**	**12**
Mp, °C	189–191	188–193 (corr)	213–216 (corr)	231–233 (corr)	228–229	177–180	212–215	210–213	215–220	214–217
$[\alpha]D^a$, deg	+602	−551	+630	−452	+448	−558	+279	−871	+231	−517
% inhibition										
RNA pol[b]	78	50	0	0	0		2	23	20	46
RT[c]	31–53	70	68	54	53		44	77	57	75
Zone of inhibition, mm										
B. subtilis UC 564	22	14	0	0	0					
S. aureus UC 80	26	20	0	0	0					
S. lutea UC 130	33	28	0	0	0					
K. pneumoniae UC 57	21	0	0	0	0					
E. coli UC 51	13	0	0	0	0					
S. schottmuelleri UC 126	10	0	0	0	0					
P. vulgaris UC 93	8	0	0	0	0					
M. avium UC 159	15	20	14	0	0					
P. oxalicum	0	0	0	0	0					

[a] $CHCl_3$ solution, *c* 0.1–0.6 (*t*, 22–26°). [b] Concentration: 0.1 μmol/ml, conditions in ref 2. [c] Concentration: 200 μg/ml, conditions in ref 2.

ppm for **2**; C-16 at 130.3 ppm for **1**, 126.1 ppm for **2**; CD_2Cl_2 solutions). The acetate carbonyl carbon also shifts, from 169.0 ppm in **1** to 170.6 ppm in **2**.

Additional examples of the preparation of atropisomeric streptovaricins include the following. (1) Heating streptovaricin C in refluxing pyridine for 2.75 hr (Figure 1) gave a mixture of **1**, **2**, streptovaricin F_C (**4**, $C_{39}H_{47}NO_{13}$),[5] and atropisostreptovaricin F_C (**5**, $C_{39}H_{47}NO_{13}$)[5b,c] in the ratio 6.9:1.6:trace:1. Both **4** and **5** gave streptoval F_C[7](**6**, $C_{39}H_{45}NO_{13}$,[5a] mp 159–163°, $[\alpha]^{24}D$ −162.5° (*c* 0.016, $CHCl_3$)] on periodate oxidation. (2) Streptovaricin F_C (**4**) was heated for 2.5 hr in refluxing pyridine to give nearly exclusively **5**, together with a little recovered **4**. (3) Heating streptovaricin C triacetate (**7**)[2] for 16 hr in refluxing benzene gave a mixture of **7** and atropisostreptovaricin C triacetate (**8**, $C_{46}H_{57}NO_{17}$)[5] in the approximate ratio 9:1. Properties of **4**, **5**, **7**, and **8** are shown in Table I; spectral properties are essentially identical.

In all of the above isomerizations, the natural isomer predominates in the mixture except for the lactone pair **4** and **5**, where the unnatural isomer is favored. Bioactivities of the atropisomeric pairs (Table I) are similar; thus, the absolute helicity of the ansa ring is of surprisingly little import to the bioactivities of the compounds.

In our earlier X-ray investigation,[9] heating streptovaricin C triacetate (**7**) with benzeneboronic acid in refluxing dioxane for 26 hr or with *p*-bromobenzeneboronic acid in refluxing benzene for 18 hr gave two products in each experiment, which can be designated "early" and "late" on the basis of their elution times from silica gel. The "early" products were previously assigned[9] as acyclic, the "late" products as cyclic. Field desorption mass spectrometry[10] now shows that *both* products are cyclic, with molecular ions at *m/e* 981 for the cyclic benzeneboronates (**9** and **10**) and 1059 and 1061 for the cyclic *p*-bromobenzeneboronates (**11** and **12**). The CD curves of "early" and "late" isomeric pairs match those of natural streptovaricins and their atropisomers (Figure 2), respectively. The X-ray investiga-

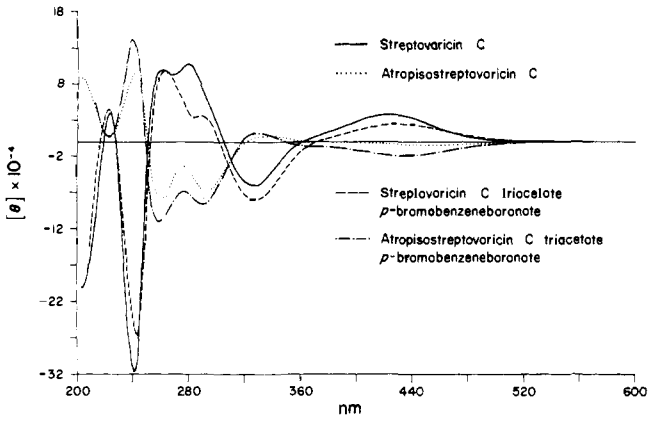

Figure 2. Circular dichroism curves for streptovaricin C (**1**), its atropisomer (**2**), streptovaricin C triacetate *p*-bromobenzeneboronate (**11**), and its atropisomer (**12**).

tion was carried out on the negative-rotating ("late," unnatural) isomer and the actual relative configuration of the natural streptovaricins must be that shown in Figure 1 (**1, 4, 7, 9, 11**).

To assign the absolute configuration of **12,** the two possible enantiomorphs (*i.e.*, **12** and its mirror image) were refined including the anomalous scattering contributions for the bromine and chlorine atoms. The enantiomorph **12** converged with a value of R_2 of 0.101, whereas the opposite enantiomorph converged with R_2 of 0.104, arguing that the absolute configuration is as shown for **12;** thus, that for the natural streptovaricin is that shown, *e.g.*, for **1** (6*R*, 7*R*, 8*R*, 9*R*, 10*S*, 11*S*, 12*R*, 13*S*, 14*R*, helicity P),[11] which agrees[12] with the helicity and absolute configurations at C-8 through C-14 of rifamycin B[13,14] and tolypomycin Y.[15]

To our knowledge these represent the first examples of the conversion of a naturally occurring compound to its atropisomer.

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(6) These arguments assume that the helicity of the molecules accounts for their very high rotations, an assumption in keeping with the much lower rotation of streptoval C (**3**, *vide infra*).
(7) Streptovals C (**3**) and Fc (**6**) have no stable helicity since their atropisomeric forms, like those of streptovarone,[8b] interconvert at room temperature, a conversion demonstrated by the broadening of the methylenedioxy signals in the pmr spectra of streptovarone,[8b] **3** and **6**.
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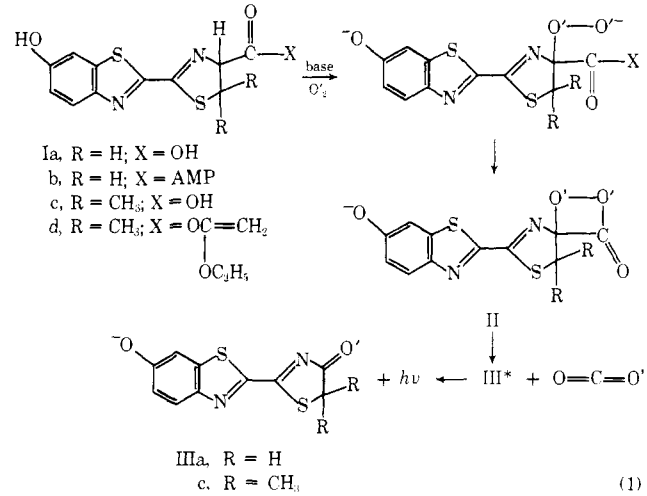
On the Mechanism of Firefly Luciferin Luminescence[1]

Sir:

The bioluminescence and the chemiluminescence of firefly luciferin (Ia)[2] are closely related processes in that both require oxygen,[3,4] both produce carbon dioxide[5,6] and lactam IIIa,[3,7] and both yield yellow-green or red light depending on the conditions.[3,8] On the basis of these facts, the identification of lactam III as the light emitter,[3,7] and analogy to other chemiluminescent reactions, the mechanism of eq 1 was proposed for both the chemi- and bioluminescence of firefly luciferin[3,9-11] (where X = any good leaving group). Since that time, 1,2-dioxetanes have been isolated,[12] and their chemistry has been elucidated;[13] they are, in fact, excellent sources of chemically produced excited states.[14]



(1)

Oxygen-18 studies of both the bio- and chemiluminescence of firefly luciferin (*via* the adenylate Ib) have been reported recently purporting to show that the carbon dioxide formed in the reactions was not labeled in bioluminescence (enzyme + $^{18}O_2$ in H_2O) and labeled to less than 10% in chemiluminescence (*tert*-butoxide + $^{18}O_2$ in DMSO).[15] In both reactions, it was further claimed that one oxygen atom of the carbon dioxide was derived from water.[15] The mechanism of eq 2 was proposed to account for these results.[15] In a related study, bioluminescence in the sea pansy led to <0.1 atom ^{18}O incorporation in the carbon dioxide