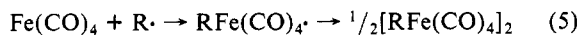
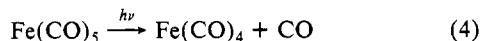
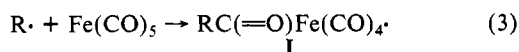
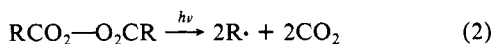


several organic substances.<sup>9</sup> An intense spectrum of I ( $R = C_9H_{19}$ ,  $g = 2.0496$ ) is obtained by photolysis at  $-40^\circ C$  in the presence of decanoyl peroxide. The 11.0-G quartet is obtained by using  $Fe(^{13}CO)_5$ .  $^{57}Fe(CO)_5$  ( $I(^{57}Fe) = 1/2$ ) gives a doublet of 6.5 G confirming the mononuclearity of I. Some of the reactions that take place are shown below. The addition of an alkyl radical



to coordinated CO (eq 3) is unprecedented but may well occur in many homogeneously catalyzed carbonylation reactions.

The low-temperature photolysis of alkyl and acyl chlorides and bromides in pentane (generally at  $-130^\circ C$ ) in the presence of  $Fe(CO)_5$  also leads, after brief warm-up, to clean spectra of I. Initially, the predominant species are thermally unstable  $(CO)_4FeX$  radicals<sup>10</sup> which disappear on warming. We suppose that the oxidative addition of the CX bond to the photochemically generated  $Fe(CO)_4$  fragments is followed by loss of the halogen atom from the diamagnetic  $R(X)Fe(CO)_4$  intermediates. The resulting  $RFe(CO)_4$  radicals dimerize at the low temperatures used. On warming, the dimers dissociate, and the  $RFe(CO)_4$  radicals are converted to I by facile alkyl migration.

Another source of I is the low-temperature photolysis in pentane of  $Fe(CO)_5$  in the presence of aldehydes. In this case, radicals I result most likely by loss of a hydrogen atom from the initially formed  $(CO)_4Fe(H)COR$  diamagnetic intermediates.<sup>11</sup> Benzaldehyde gives a particularly robust benzoyliron radical (Figure 1A). If 0.5  $\mu L$  of  $(CH_3O)_3P$  is added by microsyringe to the ESR tube at  $-80^\circ C$ , the spectrum of I is replaced, after a quick shake, by a triplet (17.5 G,  $\Delta H = 2$  G,  $g = 2.0351$ ) for 2 equiv  $^{31}P$  atoms (Figure 1B). If the phosphite is added to a solution of I prepared with  $Fe(^{13}CO)_5$ , the 11 G quartet (Figure 1C) is replaced by the same triplet (17.5 G) split into two doublets (14.6, 5.8 G; Figure 1D). The spectrum of I obtained with benzaldehyde- $\alpha$ - $^{13}C$  is identical with that of unlabeled I. This spectrum is replaced, however, by a triplet of doublets (17.6, 5.9 G) on addition of the phosphite. Finally, the same procedure with benzaldehyde- $\alpha$ - $^{13}C$  and  $Fe(^{13}CO)_5$  gives a triplet of doublets of triplets (17.5, 14.5, 5.8 G). There is thus no doubt that two phosphorus ligands have entered the coordination sphere of I in the equatorial positions of a TBP. The distortion after substitution and/or electronic effects make now visible the two axial  $^{13}C$  atoms (5.8 G), which were invisible in the unsubstituted TBP, while the single equatorial  $^{13}C$  atom (14.5 G) remains approximately unchanged.

We have carried out EHMO calculations<sup>12</sup> for the hypothetical (formyl) $Fe(CO)_4$  and  $HFe(CO)_4$  radicals in TBP and square-pyramidal (SP) structures as models for I and  $RFe(CO)_4$  radicals, respectively. We have grouped the squares of the atomic orbital coefficients ( $\times 100$ ) of the SOMO as shown in Table I to visualize the MO containing the unpaired electron. In the radicals of TBP geometry the unpaired electron resides mostly in the Fe atomic orbitals in the equatorial plane ( $\sim 50\%$ ) and in the atomic orbitals of the equatorial CO ligands ( $\sim 40\%$ ).<sup>13</sup> There is very little unpaired-electron population outside of the equatorial plane. This

orbital, smeared over seven equatorial atoms, gives little incentive to the TBP radicals to dimerize as was observed for I. The large s-orbital population for the equatorial C atoms (1.7% and 1.6%) is also consistent with the 11-G splitting for three equivalent  $^{13}C$  atoms in I. For the SP radicals, on the other hand, the unpaired electron is substantially localized (20% and 30%) in  $Fe d_{z^2}$  and  $p_z$  orbitals, which form a lobe directed along the z axis ready to form an Fe-Fe bond.<sup>14</sup> Our hypothesis that  $RFe(CO)_4$  radicals were not observed because of dimerization is then justified assuming that they have SP geometry.

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(14) For the d-orbital splitting scheme for 17-electron SP species, see: Elian, M.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 1058.

## Monensin 26-Pyromellitate Forms Lithium Channels in Monolayer Lipid Membranes

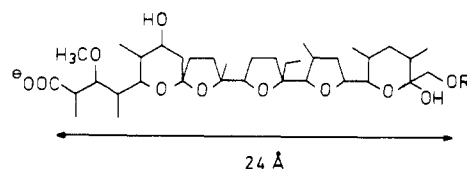
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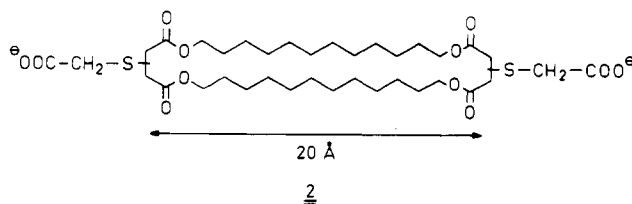
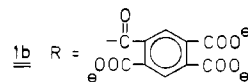
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We recently reported preparations of extremely thin ( $\sim 20$  Å) monolayered vesicle membranes made from  $\alpha,\omega$ -bifunctional amphiphiles ("bolaamphiphiles").<sup>1,2</sup> In this communication we describe an  $\alpha,\omega$ -bifunctional amphiphile with a polar chain in a hydrophobic skeleton of equal length. It functions as a channel for lithium ions in the 20-Å monolayer membrane but not in a 40-Å bilayer lipid membrane. The 20-Å channel former is easily accessible from commercial monensin.

Monensin **1a** is a well-known ionophore with a hydrophobic and a hydrophilic side. It predominantly exists in a cyclic con-



**1a**  $R = H$



(1) Fuhrhop, J.-H.; David, H. H.; Ellermann, K.; Mathieu, J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 1982.

(2) Fuhrhop, J.-H.; Mathieu, J. *J. Chem. Soc., Chem. Commun.* **1983**, 144.

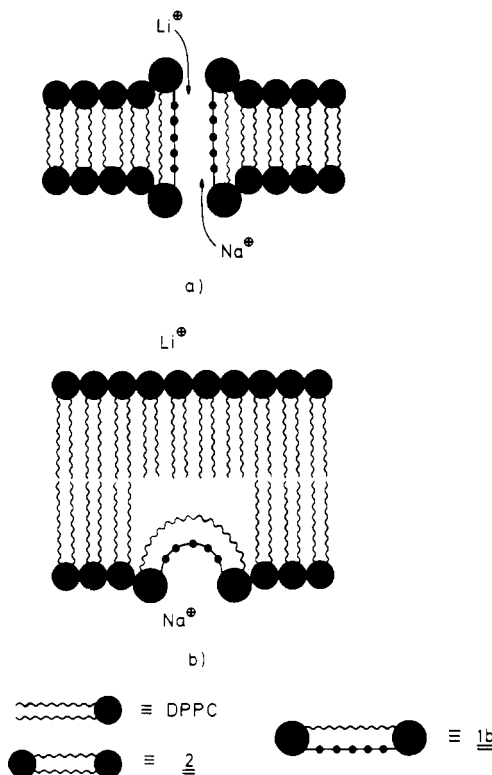
(9) Typical procedure: An ESR quartz tube is filled under nitrogen with 0.4 mL of olefin-free pentane, 1  $\mu L$  of  $Fe(CO)_5$ , and 2–5  $\mu L$  of an organic compound. The low-temperature irradiation is carried out in a standard quartz Dewar for variable-temperature ESR surrounded by the coils of a low-pressure Hg discharge tube (mostly 2500-Å UV) in the shape of a tight spiral. The cooling is provided by a flow of cold nitrogen. After irradiation, the tube is plunged into liquid nitrogen and is transferred to the ESR cavity kept at the desired low temperature.

(10) Krusic, P. J., unpublished results.

(11) If the photolysis is carried out below  $-100^\circ C$ ,  $HFe_2(CO)_8$  radicals (Krusic, P. J. *J. Am. Chem. Soc.* **1981**, *103*, 2131) are also observed.

(12) Extended Hückel Calculations, Quantum Chemistry Program Exchange, No. 358, Indiana University.

(13) The d orbital splitting scheme for a TBP is well-known. See, e.g.: Rossi, A. R.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 365.



**Figure 1.** (a) Model of a monolayered membrane with an  $\alpha,\omega$ -double-charged channel former **1b**. The channel is presumably formed by several molecules of **1b**. (b) **1b** is too short to cross a bilayer membrane.

formation and forms complexes with alkali ions.<sup>3</sup> We prepared the monopyromellitic ester **1b** with pyromellitic dianhydride in pyridine.<sup>4</sup> In this derivative the negative charges at both ends of the molecule should favor a stretched conformation. **1b** is soluble in water at pH 7 and precipitates below pH 4.

Monolayer membrane vesicles were prepared by sonication of the symmetric bolaamphiphile **2**.<sup>5</sup> Lithium ions were entrapped within the inner aqueous volume, when **2** was sonicated in the presence of 0.03 M lithium chloride in the solution. Gel filtration on Sephacryl S 1000 with 0.03 M NaCl removed the external lithium ions. The chromatographed vesicles were tested for lithium ions by atomic emission spectroscopy.<sup>6</sup> The monolayered vesicles reproducibly entrapped the expected amounts of lithium ions. Addition of the monensin derivative **1b** to the aqueous solution after sonication did not change this figure. This experiment proves, that **1b** does not act as an ionophore for lithium ions.

If, however, the amphiphile **2** was cosonicated with 1.0, 0.1, or 0.01 mol % of **1b** no lithium was entrapped (Table I). 0.01 mol % corresponds to 1 molecule of **1b** per  $10^4$  molecules of **2** or in the order of 1–10 molecules of **1b** per vesicle.<sup>7</sup> This would indicate that less than 10 molecules of **1b** are sufficient to make a monolayer vesicle membrane penetrable to lithium ions. At 0.001 mol % of **1b** no lithium was released from the vesicles (Table I). From these experiments we conclude the formation of discrete channels (Figure 1a).

The same experiments were performed with dipalmitoyl-phosphatidylcholine (DPPC) bilayer membrane vesicles and 1 mol % of **1b**. No leakage of lithium occurred (Table I). The bolaamphiphile **1b** is too short to cross the bilayer lipid membrane (Figure 1b).

**Table I.** Lithium Concentration<sup>a</sup> of Gel Filtrated<sup>b</sup> Vesicles Containing the Channel Former **1b**

[ <b>1b</b> ], mol %	$C_{Li^+}$ vesicle <b>2</b> , <sup>c</sup> ppb	$C_{Li^+}$ vesicle DPPC, <sup>c</sup> ppb
0	29	25
0.001	28	
0.01	0	
0.1	0	
1.0	0	23

<sup>a</sup> ppb values from atomic emission spectra (AES) are given. <sup>b</sup> 1 mL of the vesicle dispersion ( $1.0 \times 10^{-3}$  M) was applied to a Sephacryl S 1000 column ( $1 \times 25$  cm, 0.03 mol NaCl). Vesicles eluted in the 4–6-mL fraction, which was used for AES. <sup>c</sup> Cosonication of **1b** with **2** or DPPC at 50 °C.

It was also observed that compound **1b** itself forms vesicles on sonication. These vesicles entrapped the water-soluble dye pyranine (8-hydroxy-1,3,6-pyrenetrisulfonate),<sup>8</sup> but no lithium.

In summary we have presented the first ion channel, which is selective for thin membranes ( $\leq 20$  Å), and proof for the thinness of the thinnest membrane reported so far. The number of channels per vesicle can be varied from, presumably, one to several thousand. Several applications of the perforated vesicle membranes can be imagined, if efficient stopcocks can be developed to close and reopen the holes. This possibility is investigated currently. Head groups different from pyromellitic acid, e.g., positively charged ammonium groups, will also be investigated.

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**Registry No.** **1b**, 91003-04-2; lithium, 7439-93-2.

(8) Kano, K.; Fendler, J. H. *Biochim. Biophys. Acta* **1978**, 509, 289.

### Kalihinol-A, a Highly Functionalized Diisocyano Diterpenoid Antibiotic from a Sponge

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The isocyano function occurs naturally in compounds isolated from terrestrial microorganisms and from marine sponges. A majority of the sponge metabolites have been sesquiterpenes. Isocyanoterpenes have generally been monofunctionalized and have often been accompanied by corresponding isothiocyano and formamido derivatives. We report here the structure of a new richly functionalized tricyclic diterpene, which bears isocyano, hydroxyl, tetrahydropyranyl, and chlorine functions. Compound **1**, which we have named kalihinol-A,<sup>3</sup> exhibits in vitro activity against *Bacillus subtilis*, *Staphylococcus aureus*, and *Candida albicans*.

(1) On sabbatical leave from the University of West Florida, Pensacola, FL, Fall 1983.

(2) UNESCO Fellow from the University of Calcutta, Spring 1983.

(3) Kalihini is a residential neighborhood in Honolulu and the first author's early home. The numbering follows that of biflorin.<sup>10</sup>

(4) Kupchan, S. M.; Britton, R. W.; Ziegler, M. F.; Sigel, C. W. *J. Org. Chem.* **1973**, 38, 178–179.

(3) Anteunis, M. J. O.; Rodius, N. A. *Bioorg. Chem.* **1978**, 7, 47.

(4) Apell, H.-H.; Bamberg, E.; Alpes, H.; Läuger, P. *J. Membr. Biol.* **1977**, 31, 171.

(5) Mathieu, J., Dissertation Freie Universität Berlin, in preparation.

(6) Stengelin, S.; Beress, L.; Lauffer, L.; Hucho, F. In "Toxins as Tools in Neurochemistry"; Hucho, F., Ouchinnikov, Y.A., Eds.; W. de Gruyter: Berlin, New York, 1983; p 101.

(7) An average number of  $1.2 \times 10^5$  molecules in the monolayer vesicle membrane was assumed. The average diameter from electron microscopy was 1000 Å.