Communications

Direct Observation, Isolation, and Structure of 1:1 Adducts from Carbodiimides and Dialkylphosphorothio(seleno)ic Acids

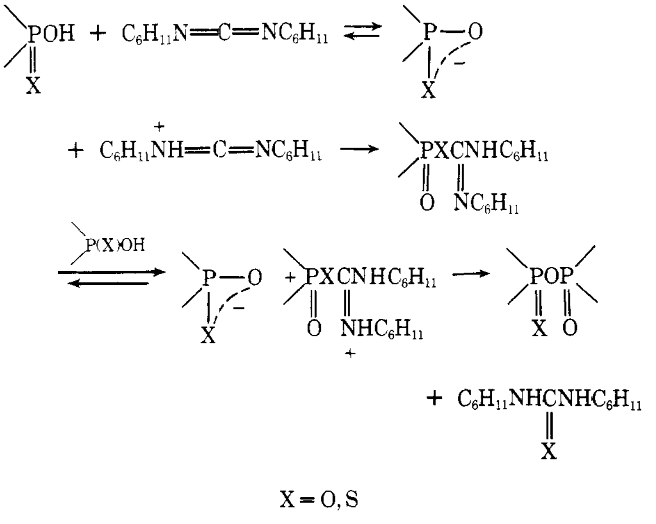
Summary: The reaction between *O,O*-dialkylphosphorothio(seleno)ic acids 1 and carbodiimides (dicyclohexylcarbodiimide, dibenzylcarbodiimide) has been shown to give *N*-phosphorylthio(seleno)ureas **3** and **5**; the low-temperature FT ^{31}P NMR study revealed that they result from the initially formed, unstable *S*(*Se*)-phosphorylisothio(seleno)ureas **2** and **4** via migration of the phosphoryl group from sulfur or selenium to nitrogen.

Sir: The reaction of *O,O*-dialkylphosphoric acids with dicyclohexylcarbodiimide (DCC) has been shown by Khorana and Todd[1] to give pyrophosphates and dicyclohexylurea. Khorana and Todd explained the formation of products by assuming the two-step mechanism involving *O*-phosphorylisourea as an intermediate (see Scheme I). Similar reaction between DCC and monothiophosphonic and monothiophosphinic acids results in the formation of the corresponding monothiopyrophosphate systems and dicyclohexylthiourea.[2] In this case the addition of thio acid to DCC has been assumed to take place by means of the sulfur atom leading to *S*-phosphorylisothiourea, which reacts further with the second molecule of thio acid to give directly the unsymmetrical form of monothio anhydride.

Although this sequence of events is commonly accepted, the postulated 1:1 adducts formed in the first reaction stage have neither been isolated nor observed by means of spectroscopic methods. We now wish to report the first, direct detection by ^{31}P NMR spectroscopy of *S*(*Se*)-phosphorylisothio(seleno)ureas **2** and **4** formed from monothio(seleno)phosphoric acids **1** and carbodiimides (Scheme II), as well as their facile rearrangement to *N*-phosphorylthio(seleno)ureas **3** and **5**, which are new, stable, and isolable intermediates of the reaction under consideration.[3]

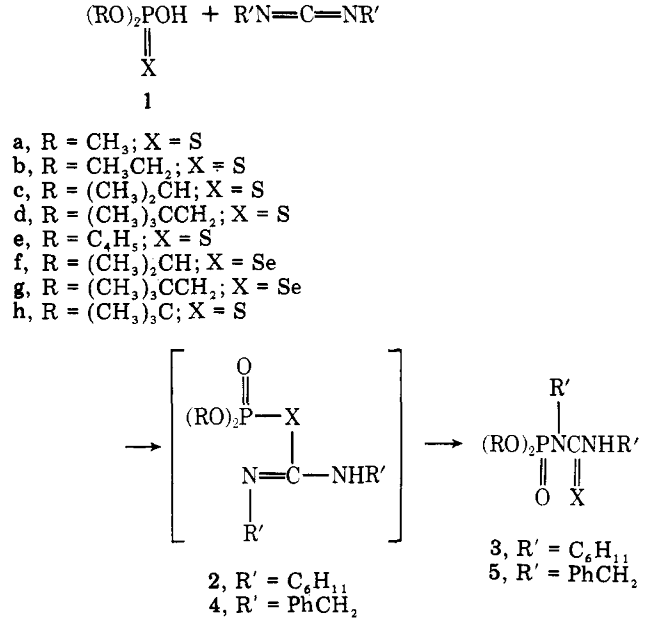
We found that treatment of DCC in ether with an equimolar amount of *O,O*-dialkylphosphorothio(seleno)ic acids (**1**) affords the 1:1 adducts, as evidenced by elemental analysis and mass spectra. Spectroscopic study of the adducts isolated in nearly quantitative yields revealed, however, that they are not the expected *S*-phosphoryldicyclohexylisothioureas (**2**). For instance, the lack of the absorption band at ~1650 cm^{-1} in the infrared spectrum excludes the presence of the >C=N– grouping. Moreover, in the case of the adduct of *O,O*-dineopentyl phosphoroselenoic acid (**1g**) to DCC the ^{31}P–^{77}Se coupling[4] (~400 Hz) characteristic of the direct P–Se bond was not observed in the proton-decoupled ^{31}P NMR spectrum, which rules out the structure **2**. On the other hand, all the spectral data of the adducts are consistent with the isomeric structure of *N*-phosphoryldicyclohexylthio(seleno)urea (**3**).

Scheme I



X = O, S

Scheme II



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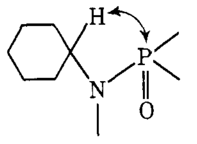
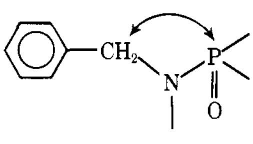
a, R = CH_3; X = S
b, R = CH_3CH_2; X = S
c, R = $(CH_3)_2CH$; X = S
d, R = $(CH_3)_3CCH_2$; X = S
e, R = C_4H_5; X = S
f, R = $(CH_3)_2CH$; X = Se
g, R = $(CH_3)_3CCH_2$; X = Se
h, R = $(CH_3)_3C$; X = S

2, R′ = C_6H_{11}
4, R′ = $PhCH_2$

3, R′ = C_6H_{11}
5, R′ = $PhCH_2$



$^3J_{PH} \simeq 23$ Hz



$^3J_{PH} \simeq 9.5$ Hz

The most important evidence supporting this view is the observation in the ^{31}P NMR spectra of a coupling constant about 23 Hz which can be attributed only to the interaction between phosphorus and the proton at C(1) of the cyclohexyl moiety in **3**.

Since it was not possible to observe the same coupling constant in the ^{1}H NMR spectra of the adducts from DCC due to the complex splitting pattern of the cyclohexyl ring protons, we prepared in a similar manner the adducts from dibenzylcarbodiimide (DBC) and acids **1**. ^{31}P NMR spectra of these adducts showed that the resonance signal of phosphorus is split into a triplet by the methylene protons, whereas the signal of the methylene group in the ^{1}H NMR spectra is split by phosphorus into a doublet with the same coupling constant equal to ~9.5 Hz.

Physical and spectral properties of the adducts **3** and **5** are collected in Table I.[11]

The most reasonable assumption is that thio(seleno)ureas **3** and **5** result from the initially formed, unstable **2** and **4** by the migration of the phosphoryl group from sulfur or selenium to nitrogen.[5] Therefore, in order to prove this hypotesis we monitored the course of the reaction of *O,O*-diisopropylphosphoroselenoic acid (**1f**) with DCC (Figure 1)[11] by the low-temperature ^{31}P NMR. Thus, a solution of DCC in ether was treated with an equimolar amount of **1f** at −80 °C and the resulting mixture was examined at 24.3 MHz using ^{31}P Fourier transform NMR with proton noise decoupling.[6] Two signals of high intensity were observed at $\delta_{^{31}\mathrm{P}}$ −48.5 and −10.3 ppm. The first of them was attributed to the salt of seleno acid **1f** with DCC. It is interesting to point out that the coupling between phosphorus and selenium, $^1J_{^{31}\mathrm{P}-^{77}\mathrm{Se}} = 789$ Hz, was observed, providing additional support of this assignment.[7] The δ −10.3 signal with the characteristic coupling constant $^1J_{^{31}\mathrm{P}-^{77}\mathrm{Se}} = 410$ Hz corresponds undoubtedly to the expected *Se*-diisopropylphosphoryl-*N,N'*-dicyclohexylisoselenourea (**2f**).[8] The spectrum showed also the low intensity signal at +2.2 ppm corresponding to the already characterized *N*-diisopropylphosphoryl-*N,N'*-dicyclohexylselenoura (**3f**) and two doublets centered at −52 and +16.5 ppm due to tetraisopropyl monoselenopyrophosphate. Then we raised the temperature to −50 °C and observed the spectrum every 10 min. It showed gradual decrease of the signals at δ −48.5 and −10.3 ppm and at the same time fast increase of the signal due to **3f**. The signals due to **3f** and selenopyrophosphate in a ratio 4:1 were the only signals in the spectrum at room temperature.

The unstable adducts **2** and **4** were observed similarly using other acids **1** as the reaction components.[9] Their spectral characteristics are given in Table II.[10,11]

The mechanism of the phosphorylation by means of *N*-phosphorylthio(seleno)ureas **3** is under current investigation.

Supplementary Material Available. Tables I and II, including physical and spectral properties of the adducts **2**, **3**, **4**, and **5**, and Figure 1, showing the low-temperature FT ^{31}P NMR study of the reaction between DCC and **1f** (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) H. G. Khorana and A. R. Todd, *J. Chem. Soc.*, 2257 (1953).

(2) M. Mikołajczyk, *Chem. Ber.*, **99**, 2083 (1966).

(3) The only remark concerning the reaction between DCC and dialkyl phosphorothioic acid was found in the paper by McIvor, McCarthy, and Grant, who stated that no reaction took place at room temperature and a mixture of products was obtained on heating: R. A. McIvor, G. D. McCarthy, and G. A. Grant, *Can. J. Chem.*, **34**, 1819 (1956).

(4) The natural abundance of ^{77}Se is 7.58%. For the application of ^{31}P–^{77}Se coupling in structural and stereochemical studies see: I. A. Nuretdinov and E. I. Loginova, *J. Gen. Chem. USSR*, 2380 (1971); Perkin–Elmer NMR Quarterly, **1** (November), 6; W. McFarlane and J. A. Nash, *Chem. Commun.*, 913 (1969); W. J. Stec, A. Okruszek, B. Uznański, and J. Michalski, *Phosphorus*, **2**, 97 (1972); W. J. Stec, *Z. Naturforsch. B*, **31**, 393 (1976).

(5) Similar rearrangement has been observed by Chupp and Leschinsky in the reaction between isocyanides and phosphorus thio acids: J. P. Chupp and K. L. Leschinsky, *J. Org. Chem.*, **40**, 66 (1975).

(6) ^{31}P NMR spectra were obtained with a Jeol-JNM-FX60 Fourier transform NMR spectrometer. Chemical shifts are given in parts per million downfield from external 85% H_3PO_4.

(7) Triethylammonium salt of seleno acid **1f** has $\delta_{^{31}\mathrm{P}}$ −50.4 ppm and $^1J_{^{31}\mathrm{P}-^{77}\mathrm{Se}} = 808$ Hz, whereas the free acid **1f** absorbs at $\delta_{^{31}\mathrm{P}}$ −60.8 ppm with $^1J_{^{31}\mathrm{P}-^{77}\mathrm{Se}} = 910$ Hz.

(8) The proton-undecoupled ^{31}P NMR spectrum revealed that the signals at −48.5 and −10.3 ppm are triplets ($^3J_{\mathrm{POCH}} = 7.3$ Hz), whereas the resonance signal at +2.2 ppm is a double triplet due to an additional coupling $^3J_{\mathrm{PNCH}} = 23$ Hz, discussed earlier.

(9) We were not able to detect under similar conditions the 1:1 adducts of type **2** or **3** from *O*-isopropylmethylphosphonothioic acid and diethylphosphinothioic acid with DCC. The low-temperature FT ^{31}P NMR spectra of the mixtures of *O,O*-diethylphosphoric acid, *O,O*-dineopentylphoric acid, and *O,O*-diphenylphosphoric acid with DCC revealed the formation of corresponding *O*-phosphorylisoureas having $\delta_{^{31}\mathrm{P}}$ +10.1 (10.9), +10.2, and +20.7 (21.6) ppm, respectively. However, in contrast to *S*-phosphorylisothioureas they did not undergo rearrangement to *N*-phosphorylureas, but reacted further to form pyrophosphates. These results and mechanistic differences will be discussed in a full paper.

(10) It is interesting to note that in some instances small, minor peaks (given in Table II in parantheses) are seen in the region characteristic of the adducts **2** and **4** which may be interpreted as evidence of syn–anti isomerism.

(11) See paragraph at the end of paper about supplementary material.

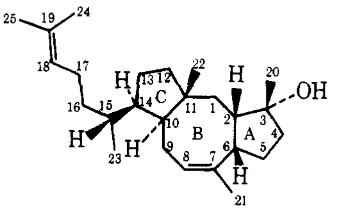
Marian Mikołajczyk,* Piotr Kiełbasiński
Zofia Goszczyńska
Centre of Molecular and Macromolecular Studies
Polish Academy of Sciences
Department of Organic Sulfur Compounds
90-362 Łódź, Boczna 5, Poland

Received July 22, 1977

Sesterterpenes. 1. Stereospecific Construction of the Ceroplastol and Ophiobolin Ring Systems via a Common Bicyclic Intermediate

Summary: The ring systems present in the two major classes of ophiobolane sesterterpenes have been obtained via a common bicyclic intermediate. In each case, the eight-membered ring was constructed by fragmentation of an appropriately functionalized bicyclo[3.3.1]nonane ring system.

Sir: We have been investigating, for some time, the development of protocols for the synthesis of various classes of sesterterpenes. Among those under study are the two major stereochemical subclasses of the ophiobolane system exemplified by ophiobolin F (**1**)[1] and ceroplastol I (**2**).[2] Recent reports from other laboratories have prompted us to report our studies in this area.[3,4]



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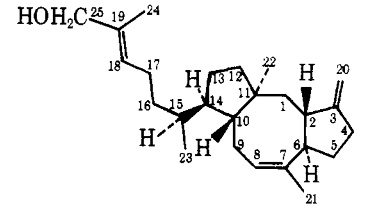

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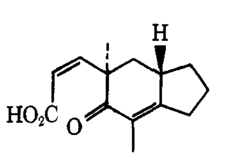
The structures of **1** and **2** present considerable synthetic challenges, since they possess four asymmetric centers about the central eight-membered ring. We were intrigued, however, by the fact that the systems differ in relative stereochemistry at only one center (C-2) about the eight-membered ring, although they possess different absolute stereochemistry. To exploit this observation, we undertook the construction of a bicyclic intermediate, ketone **3**, which we felt might be readily elaborated to intermediates of either stereochemical series. It was hoped that the trienol lactones **4**, which were plausibly derived from **3**, would serve as efficient precursors of bicyclo[3.3.1]nonanones of general structure **5**, and ultimately of



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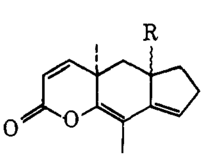
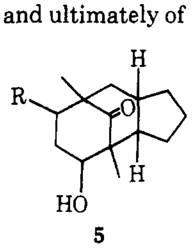


4a, R = α-H
b, R = β-H



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