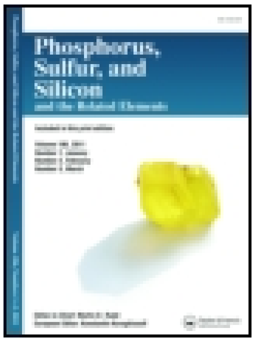

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An unexpected reaction of diethyl phosphite with electron-deficient dialkyl dicyanofumarates

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ABSTRACT
Diethyl phosphite reacts with both dimethyl dicyanofumarate and dicyanomaleate in boiling 1,2-dichloroethane to yield, after chromatographic workup, a 1:1-mixture of the corresponding meso- and dl-dicyanosuccinates. The analogous transformation was observed in the cases of diethyl and diisopropyl dicyanofumarates. A reaction pathway via initial formation of a P–C bond followed by its hydrolytic cleavage is proposed.

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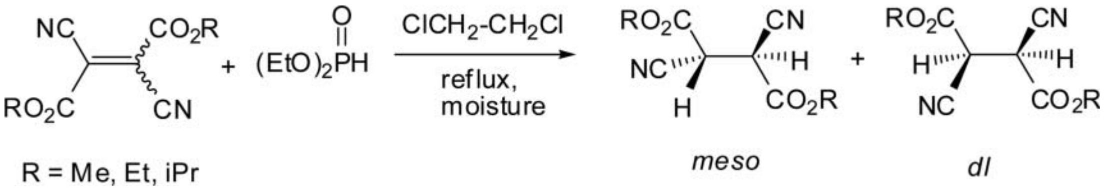
Addition reactions; reaction mechanisms; electron deficient alkenes; dialkyl phosphites; Michael addition

GRAPHICAL ABSTRACT

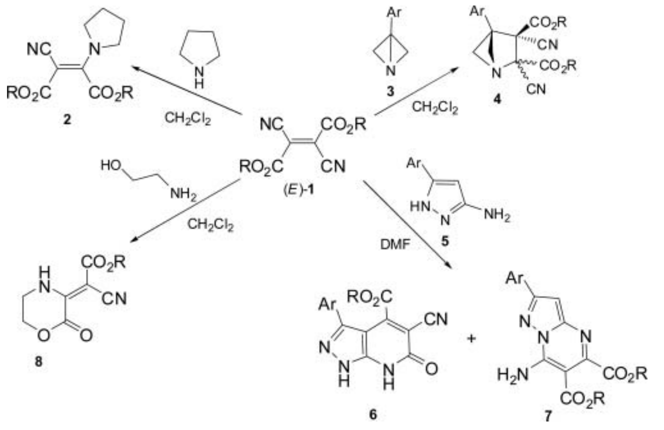


Introduction

The electron-deficient dialkyl dicyanofumarates (*E*)-**1** and dicyanomaleates (*Z*)-**1** are well known as a pair of isomeric olefins, which can be used as prone dienophiles,[1] dipolarophiles,[2] and Michael acceptors.[3] In the latter case, the reactions with N-nucleophiles such as primary and secondary amines occur *via* an addition/elimination mechanism leading to enamines of type **2**[3b] (Scheme 1). On the other hand, similar reactions with strained 1-aza[1.1.0]bicyclobutanes **3** led to 1-azabicyclo[2.1.1]hexanes **4**.[3a] In the case of 3-amino-5-aryl-1*H*-pyrazoles **5**, two competitive additions onto (*E*)-**1** *via* the nucleophilic C(4) and NH_2, respectively, leading to **6** and **7** were observed.[4] Reactions of (*E*)-**1** with β-amino alcohols were shown to occur *via* initial N-nucleophilic attack, followed by cyclization, to give morpholin-2-one derivatives **8** as final products.[5] In addition, reactions of (*E*)-**1** with other N-nucleophiles such as hydrazine hydrate[5] and carbohydrazides were also studied.[6]

Dialkyl and diarylphosphites constitute an important class of P-nucleophiles. For example, the nucleophilic additions to the C=N group of Schiff bases (Kabachnik-Fields reaction)[7] is widely applied for the synthesis of α-aminoalkylphosphonates. Their reactions with activated and non-activated olefins are also known. Whereas the addition onto nitroalkenes follows the typical Michael addition course,[8] the hydro-phosphorylation of terminal olefins in the presence of Mn(III) occurs *via* radical intermediates.[9] Interestingly, treatment of *gem*-dibromoalkenes with diethylphosphite and triethylamine affords a mixture of (*E*/*Z*)-monobromoalkenes.[10]

The aim of the present study was to examine the reactivity of diethyl phosphite with dialkyl dicyanofumarates (*E*)-**1** as activated alkenes and the potential use of this reaction for the synthesis of hitherto unknown, polyfunctionalized alkylphosphonates.



Scheme 1

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Results and discussion

The reaction of diethyl phosphite with dimethyl dicyanofumarate ((*E*)-**1a**) in boiling 1,2-dichloroethane was complete after 7 h and the ^{1}H NMR spectrum of the crude mixture, preliminarily purified by filtration through a short silica gel layer, showed the presence of two singlets of equal intensity at 4.27 and 4.21 ppm as well as two equally intense singlets at 3.93 and 3.92 ppm. The integration of these signals revealed a ratio of 1:3 corresponding to two CH and two MeO groups. Unexpectedly, the spectrum did not show signals, which could be attributed to EtO groups expected for the 1:1 adduct. On the other hand, the ^{31}P NMR spectrum of the crude mixture showed two signals located at 7.4 and −13.2 ppm. Whereas the first signal is typical for diethyl phosphite, the second one may be correlated with diethyl phosphate. In the ^{1}H NMR spectrum of the crude mixture, measured without preliminary filtration through silica layer, two signals at 4.27 and 4.21 ppm were accompanied by another two singlets of a major product located at 4.60 and 4.58 ppm, respectively.

After chromatographic workup, a non-separable 1:1 mixture of two products was obtained as colorless oil. The ^{1}H NMR spectrum displayed the same signals of CH and MeO groups observed in the reaction mixture (after filtration through SiO_2). In addition, the ^{13}C NMR data evidenced two sets of signals located at 36.88/36.96, 54.76/54.82, 112.22/112.40, and 162.75/162.87 ppm. Based on these data and by comparison with reported data,[11] the products were identified as *meso*- and *dl*-dimethyl succinates **9a** (Scheme 2). The optimized yield of the products was 55%.

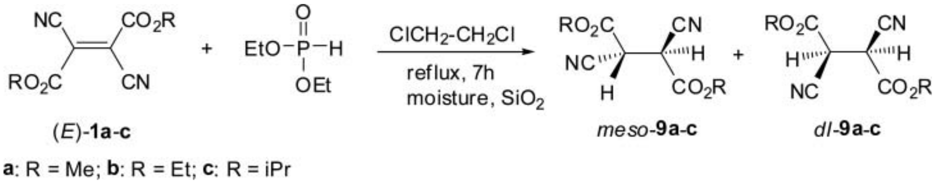
The analogous reaction of diethyl phosphite with dimethyl dicyanomaleate ((*Z*)-**1a**) gave the same mixture of products in comparable yield. Similarly, the experiments performed with diethyl and diisopropyl dicyanofumarates ((*E*)-**1b** and (*E*)-**1c**), respectively, yielded, after chromatographic purification, 1:1-mixtures of the corresponding *meso*- and *dl*-succinates **9b** and **9c,** respectively, in good yields.

In order to check the scope of this unexpected hydrogenation of electron-deficient ethylenes of type **1**, additional experiments with fumarodinitrile, dimethyl fumarate, as well as tetracyanoethylene and diethyl phosphite were performed under the same conditions. In the first two cases, starting materials were recovered, whereas in the third case decomposition was observed.

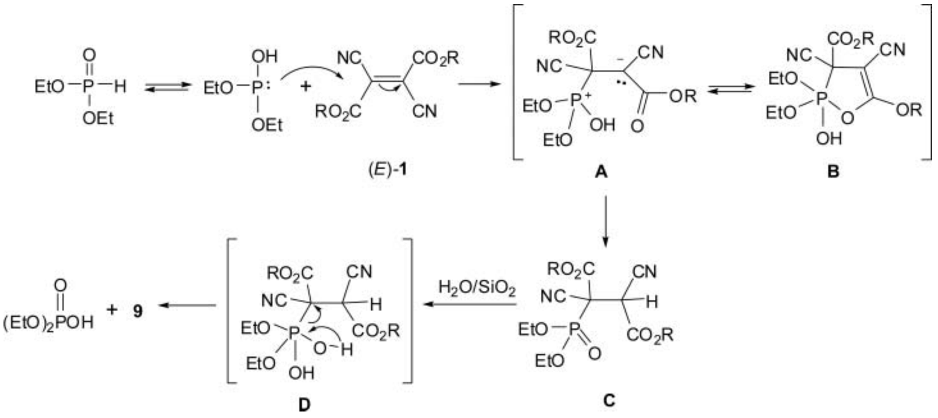
The conversion of (*E*)-**1b** into the corresponding succinates **9b** was reported previously to occur upon hydrogenation over PtO_2 in ethanol.[12] On the other hand, a mixture of isomers **9a** was obtained by treatment of (*E*)-**1a** with dimethoxycarbene and subsequent hydrolytic cleavage.[11]

The mechanistic explanation of the reaction shown in Scheme 3 is based on the assumption that the nucleophilic attack of the diethyl phosphite *via* the P-atom[7a,13a] leads to the zwitterionic intermediate **A**, which may exist in equilibrium with the oxaphosphol derivative **B** (Scheme 3). The intramolecular proton transfer in **A** affords intermediate **C**, which reacts with water yielding adduct **D**, which undergoes a dissociation to give the succinates **9** and diethyl phosphate.

The role of water and silica gel in the final formation of dimethyl dicyanosuccinate (**9a**) was confirmed *via* additional test experiments in which the reaction of (*E*)-**1a** with diethyl phosphite was performed in dry (experiment A) and wet (experiment B) 1,2-dichloroethane. The experiment in wet 1,2-dichloroethane was also performed in the presence of a suspended small portion of silica gel (experiment C). Thus, in the ^{1}H NMR spectrum of the crude mixture of experiments B and C, the isomers of **9** were formed as sole products. The presence of diethyl phosphate formed as the second product of the



Scheme 2



Scheme 3

hydrolytic cleavage of C was evidenced by the presence of two signals registered at δ 1.34 (t, $J_{H,H} = 7$ Hz, CH_3), and 4.10–4.15 (m, CH_2), respectively.[13b] On the other hand, in experiment A, the isomers of **9** were formed side by side with an unstable intermediate product with two, mentioned above, characteristic singlets located at 4.60 and 4.58 ppm, respectively. Very likely, they corresponded to a mixture of the water sensitive *dl*- and *meso*-isomers of the intermediate compound **C**, i.e. the initially formed Michael adduct (Scheme 3).

Conclusions

The presented study showed that the electron-deficient dicyanofumarates and dicyanomaleates react with diethyl phosphite in the absence of any catalyst in boiling 1,2-dichloroethane to give after chromatographic work-up the corresponding succinates as a 1:1 mixture of diastereoisomers. The control experiments with other electron-deficient ethylenes demonstrated that both CN and CO_2R groups are required for a successful reaction. To the best of our knowledge, this is first case of a hydrogenation of an ethylene derivative upon treatment with a dialkyl phosphite and subsequent hydrolytic cleavage of the in situ formed Michael adduct. The importance of the presence of both electron-withdrawing groups is reflected by the smooth bond cleavage in the proposed intermediate **D**.

Experimental

Melting points were determined in a capillary using a Melt-Temp. II (Aldrich) apparatus and are uncorrected. The IR spectra were recorded on a NEXUS FT-IR spectrophotometer as film or KBr pellets; absorptions in cm^{-1}. The ^1H, ^{13}C, and ^{31}P NMR spectra were measured on a Bruker Avance III instrument (600, 150, and 243 MHz, resp.) using solvent signals as reference. Chemical shifts (δ) are given in ppm and coupling constants J in Hz. All crude mixtures were separated by preparative TLC.

Starting materials

Dialkyl dicyanofumarates **1a**–**c** were obtained from the corresponding alkyl cyanoacetates by reaction with $SOCl_2$.[14] The $SOCl_2$ used for this reaction was freshly purified by distillation over quinoline and linseed oil.[15] Diethyl phosphite and 1,2-dichloroethane were used as commercially available materials.

Reactions of Diethyl Phosphite with Dialkyl Dicyanofumarates

A solution of the corresponding dialkyl dicyanofumarates **1a**–**c** (1 mmol) and diethyl phosphite (1.5 mmol) in 1,2-dichloroethane (2 mL) was heated to reflux. The progress of the reaction was monitored by ^1H NMR spectroscopy and in all cases complete conversion of **1** was evidenced after 6 h. After this time, the solvent was evaporated. The obtained mixtures were purified by preparative TLC (SiO_2), using a mixture of petroleum ether and ethyl acetate (7:3 for **9a**, 6:4 for **9b**, and 8:2 for **9c**) as the eluent. Product **9c** was additionally crystallized from hexane containing a small amount of dichloromethane.

Dimethyl 2,3-Dicyanobutanedioate (ca. 1:1 Mixture of meso-9a and dl-9a)[11]

Colorless thick oil; yield: 55 % (108 mg). ^1H NMR ($CDCl_3$): $\delta =$ 3.92 (s, 6H, CH_3); 3.93 (s, 6H, CH_3); 4.21 (s, 2H, CH); 4.27 (s, 2H, CH). ^{13}C NMR ($CDCl_3$): $\delta =$ 36.8 (CH_3), 36.9 (CH_3); 54.7 ($CHCN$), 54.8 ($CHCN$); 112.2 (CN), 112.4 (CN), 162.7 ($C{=}O$), 162.9 ($C{=}O$). IR (film): 3020*m*, 2963*vs*, 2919*vs*, 2259*s* ($\nu_{C\equiv N}$), 1770*vs* ($\nu_{C=O}$), 1743*vs* ($\nu_{C=O}$), 1653*m*, 1440*vs*, 1270*vs*, 1184*s*, 1098*s*, 1009*s*, 985*s*, 932*m*, 874*m*, 840*m*, 798*m*, 776*m*.

Diethy l 2,3-Dicyanobutanedioate (ca. 1:1 Mixture of meso-9b and dl-9b)[16]

Colorless thick oil; yield: 72 % (161 mg). ^1H NMR ($CDCl_3$): $\delta =$ 1.38 (t, $J_{H,H} = 7.1$ Hz, 6H, CH_3); 1.39 (t, $J_{H,H} = 7.1$ Hz, 6H, CH_3); 4.23 (*s*, 2H, CH), 4.28 (*s*, 2H, CH); 4.36–4.41 (*m*, 8H, CH_2). ^{13}C NMR ($CDCl_3$): $\delta =$ 13.7 (CH_3); 13.8 (CH_3); 37.1 ($CHCN$); 37.2 ($CHCN$); 64.4 (CH_2CH_3); 64.5 (CH_2CH_3); 112.4 (CN); 112.6 (CN); 162.2 ($C{=}O$), 162.4 ($C{=}O$). IR (film): 2988*s*, 2916*s*, 2259*m* ($\nu_{C\equiv N}$), 1750*vs* ($\nu_{C=O}$), 1647*m*, 1471*m*, 1447*m*, 1371*s*, 1301*s*, 1258*s*, 1224*s*, 1097*s*, 1098*s*, 1019*s*, 931*m*, 854*s*, 840*m*, 786*m*.

Diisopropyl 2,3-Dicyanobutanedioate (ca. 1:1 Mixture of meso-9c and dl-9c)

Colorless crystals, yield: 66 % (166 mg), mp: 54–56°C (hexane/CH_2Cl_2). ^1H NMR ($CDCl_3$): $\delta =$ 1.37 (dd, $J_{H,H} = 6.3$, 1.7 Hz, 12H, CH_3); 1.38 (dd, $J_{H,H} = 6.3$, 0.5 Hz, 12H, CH_3); 4.17 (s, 2H, $CHCN$); 4.22 (s, 2H, $CHCN$); 5.14–5.21 (m, 4H, $CH_{i\text{-}Pr}$). ^{13}C NMR ($CDCl_3$): $\delta =$ 21.3 (CH_3); 21.4 (CH_3); 37.3 ($CHCN$); 37.4 ($CHCN$); 73.1 ($CH_{i\text{-}Pr}$); 73.2 ($CH_{i\text{-}Pr}$); 112.6 (CN); 112.8 (CN); 161.7 ($C{=}O$); 161.9 ($C{=}O$). IR (KBr): 2987*m*, 291ms, 2935*m*, 2263*w* ($\nu_{C\equiv N}$), 1743*vs* ($\nu_{C=O}$), 1467*m*, 1377*m*, 1321*m*, 1296*s*, 1283*s*, 1258*s*, 1227*s*, 1202*m*, 1102*s*, 9352*m*, 838*m*, 825*m*. EI-MS: 251 [100, $(M{-}1)^+$], 252 [14, $(M)^+$]. Anal. calcd. for $C_{12}H_{16}N_2O_4$ (252.27): C 57.13, H 6.39, N 11.10; found: C 57.15, H 6.15, N 11.10 %.

Reaction of Diethyl Phosphite with Dimethyl Dicyanofumarate—Test Experiments

A solution of dimethyl dicyanofumarate (**1a**) (97 mg, 0.5 mmol) and diethyl phosphite (104 mg, 0.75 mmol) in: (A) dry 1,2-dichloroethane (1 mL); (B) “wet” 1,2-dichloroethane, or (C) “wet” 1,2-dichloroethane with a small portion (ca. 100 mg) of silica gel, was placed in a 5 mL flask and heated in an oil bath at 85°C for 6 h. After this time, the solvent was evaporated and the residues were obtained as viscous oils. In the case of experiment C, the solution was firstly filtered through silica gel and the separated silica gel was washed with a portion of dichloromethane (10 mL) containing a few drops of methanol. The obtained crude mixtures were dissolved in $CDCl_3$ and immediately analyzed by ^1H NMR spectroscopy.

References

1. Sustmann, R.; Trappanchai, S.; Bandmann, H. *J. Am. Chem. Soc.* **1996**, 118, 12555-12561. (b) Ikeda, I.; Ikeda, H.; Takahashi, Y.; Yamada, M.; Mizuno, K.; Tero-Kubota, S.; Yamauchi, S. *J. Am. Chem. Soc.* **2008**, 130, 2466-2472.
2. Huisgen, R.; Mitra, A.; Moran, J.R. *Chem. Ber.* **1987**, 120, 159-170. (b) Mlostoń, G.; Huisgen, R.; Giera, H. *Tetrahedron* **2002**, 58, 4185-4193. (c) Woznicka, M.; Rutkowska, M.; Mlostoń, G.; Majchrzak, A.; Heimgartner, H. *Pol. J. Chem.* **2006**, 80, 1683-1693.
3. Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **2006**, 89, 442-449. (b) Mlostoń, G.; Celeda, M.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2009**, 92, 1520-1537.
4. Ali, K.A.; Ragab, E.A.; Mlostoń, G.; Celeda, M.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2013**, 96, 633-642.
5. Mlostoń, G.; Pieczonka, A.M.; Ali, K.A.; Linden, A.; Heimgartner, H. *Arkivoc* **2012**, 181-192.
6. Mlostoń, G.; Pieczonka, A.M.; Wróblewska, A.; Linden, A.; Heimgartner, H. *Heterocycles* **2012**, 86, 343-356.
7. Ma, J.A. *Chem. Soc. Rev.* **2006**, 35, 630-636. (b) Zefirov, N.S.; Matveeva, E.D. *Arkivoc* **2008**, 1-17.
8. Zhu, Y.; Malerich, J.P.; Rawal, V.H. *Angew. Chem. Int. Ed.* **2010**, 49, 153-156.
9. Tayama, O.; Nakano, A.; Iwahama, T.; Sakaguchi, S.; Ischii, Y. *J. Org. Chem.* **2004**, 69, 5494-5496.
10. Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. *J. Org. Chem.* **1981**, 46, 3745-3747.
11. Sliwinska, A.; Warkentin, J. *Org. Lett.* **2007**, 9, 2605-2607.
12. Duncia, J.V.; Santella III, J.B.; Higley, C.A.; Pitts, W.J.; Wityak, J.; Frietze, W.E.; Rankin, F.W.; Sun, J.-H.; Earl, R.A.; Tabaka, A.C.; Teleha, C.A.; Blom, K.F.; Favata, M.F.; Manos, E.J.; Daulerio, A.J.; Stradley, D. A.; Horichu, K.; Copelad, R.A.; Scherle, P.A.; Trzaskos, J.M.; Magolda, R.L.; Trainor, G.L.; Wexler, R.R.; Hobbs, F.W.; Olson, R.E. *Bioorg. Med. Chem. Lett.* **1998**, 8, 2839-2844. (b) Felton, D.G. I.; Orr, S.F. D. *J. Chem. Soc.* **1955**, 2170-2176.
13. Mastryukova, T.A.; Aladzheva, I.M.; Leont'eva, I.V.; Petrovski, P. V.; Fedin, E.I.; Kabachnik, M.I. *Pure Appl. Chem.* **1980**, 52, 945-957. (b) Kuiper, J.M.; Hulst, R.; Engberts, J.F. N. *Synthesis* **2003**, 695-698.
14. Ireland, C.J.; Pizey, J.S. *J. Chem. Soc., Chem. Commun.* **1972**, 4-5.
15. Beckert, R.; Fanghänel, E.; Habicher, W.D.; Knölker, H.-J.; Metz, P.; Schwetlick, K. *Organikum*, 23rd ed.; Wiley-VCH Verlag GmbH: Weinheim, **2009**; pp. 769.
16. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1992**, 22, 3169-3179.