Versatile Synthesis of Diethyl Cyclopropanephosphonates

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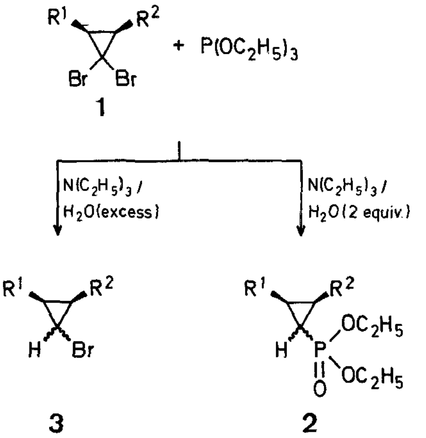
Much attention has been drawn to new methods for the formation of a carbon-phosphorus bond[1]. Earlier we have developed a method for the palladium-catalyzed phosphonation, which is effective for the stereoselective formation of an sp^2 carbon-phosphorus bond to give alkenephosphonates[2,3] and arenephosphonates[3,4]. In this paper, we describe a new reductive phosphonation for the synthesis of diethyl cyclopropanephosphonates **2**.



Treatment of *gem*-dibromocyclopropanes **1** with triethyl phosphite in the presence of triethylamine and water at 90 °C gave a mixture of debrominated diethyl *cis*- and *trans*-cyclopropanephosphonates **2** (Table). The amount of water used is a dominant factor for the success of the reaction. In the absence of water, **1** was recovered almost quantitatively.

On the other hand, the presence of excess water yielded mainly the monobromocyclopropanes **3**. The excess water present hydrolyzes (90 °C, 10–15 h) triethyl phosphite to diethyl phosphite. Hence the formation of monobromocyclopropanes **3** from **1** under these conditions is consistent with the reduction of *gem*-dibromocyclopropanes to monobromocyclopropanes with diethyl phosphite and triethylamine[5].

In spite of these observations, the following findings indicate that diethyl phosphite is assumed to play an important role in the carbon-phosphorus bond formation. The reaction of 1,1-dibromonorcarane with 2 equivalents of triethyl phosphite, diethyl phosphite, and triethylamine, respectively, at 90 °C for 55 h produced the corresponding cyclopropanephosphonate **2b** (39%) and 1-bromonorcarane (9%). Use of ethanol instead of water gave only traces of the phosphonate **2b**.

In the case of *gem*-dibromocyclopropanes having an electron-withdrawing group such as ethoxycarbonyl and cyano, reduction to monobromocyclopropanes proceeded predominantly. 1,1-Dichloro-2-phenylcyclopropane and 1-bromo-2-phenylcyclopropane did not undergo phosphonation under the present reaction conditions.

The phosphonates **2** are not easily accessible compounds, because the dialkyl diazomethanephosphonate commonly used[6] for their synthesis is potentially carcinogenic and explosive. The present method provides a facile synthesis of the diethyl cyclopropanephosphonates **2** under mild reaction conditions.

Diethyl Cyclopropanephosphonates 2; General Procedure:

To a stirred solution of the appropriate *gem*-dibromocyclopropane **1** (5 mmol), triethyl phosphite (20 mmol), and triethylamine (10 mmol), water (10 mmol) is added and the mixture is stirred at 90 °C for 55 h. The reaction proceeds with deposition of a triethylammonium salt, which is filtered off and washed with ether (5 × 5 ml). The combined organic layers are concentrated under reduced pressure. The residue is chromatographed on a silica gel column using ethyl acetate/hexane (3:7) as eluent to give the almost pure product. The phosphonates **2** thus obtained are further purified by distillation or re-chromatography.

Table. Diethyl Cyclopropanephosphonates **2**[a]

Product No.	R^1	R^2	Yield[b] [%]	b.p. [°C]/torr[c]	Molecular formula[d]	I.R. (neat) ν [cm^{-1}]
2a	n-C_6H_{13}	H	70 (24) 32 (48)[e] 28 (32)[f]	98–102°/0.07	$C_{13}H_{27}O_3P$ (262.4)	1240, 1020, 780
2b	$-(CH_2)_4-$		54 (trace)	118–120°/0.21	$C_{11}H_{21}O_3P$ (232.3)	1240, 1020, 780
2c	C_6H_5	H	42 (7)	syrup	$C_{13}H_{19}O_3P$ (254.3)	1240, 1020, 780
2d	$(CH_3)_3SiCH_2$	H	39 (trace)	98–100°/0.15	$C_{11}H_{25}O_3PSi$ (264.4)	1240, 1020, 790

[a] Reactions were carried out by using 4 equivalents of triethyl phosphite and 2 equivalents of triethylamine and water, respectively, unless otherwise stated.

[b] The yields of the bromocyclopropanes **3** are given in parentheses.

[c] Oven temperature (Kugelrohr).

[d] All products gave satisfactory microanalyses: C ±0.36, H ±0.32, P ±0.30.

[e] 4 Equivalents of triethylamine and water were used, respectively.

[f] 2 Equivalents of triethyl phosphite were used.

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