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A Convenient Synthesis of Cyclopropanes from Olefin and Carbon Acid Compounds. Synthesis of Tetraethyl Cyclopropanediyldiphosphonates

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SYNTHETIC COMMUNICATIONS, 24(10), 1425-1431 (1994)

A CONVENIENT SYNTHESIS OF CYCLOPROPANES FROM OLEFIN AND CARBON ACID COMPOUNDS. SYNTHESIS OF TETRAETHYL CYCLOPROPANEDIYLDIPHOSPHONATES

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Abstract: Cyclopropanes were obtained from electron deficient olefins and acid carbon compounds by oxidation by iodine in the presence of KF on alumina. The reaction allows the synthesis of cyclopropanediyldiphosphonates.

During the study of oxidative coupling of acid carbon compound on KF-alumina with iodine[1] we found traces of cyclopropane compounds. We optimized the condition of formation of cyclopropanes and we obtained a new method for cyclopropanation of electron deficient olefins with acid carbon compounds catalysed by KF on alumina with iodine as oxidant (Scheme 1).

This reaction is close to the already known reaction of halomalonates with electron deficient olefins catalysed by bases[2] or copper salts[3], and close to the addition of

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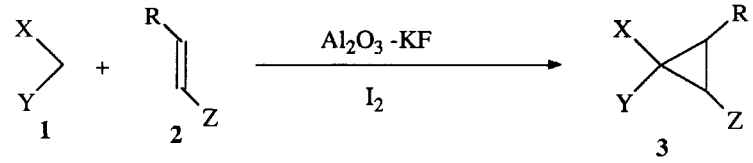
Scheme 1



X, Y = CN, $COOC_2H_5$
R = H, C_6H_5, C_4H_3S Z = COC_6H_5, CN, $COOC_2H_5$, NO_2

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acid carbon compounds on haloacrylate in the presence of a base[4]. The main advantage of our reaction is the use of more available reactants. We observed the same limitations as those precedently reported, particularly the steric hindrance of the olefin. Mechanistic studies did not give clear results and many concurrencial mechanisms (radical-anion radical-carbon) seem to take place.The results are reported in table I.

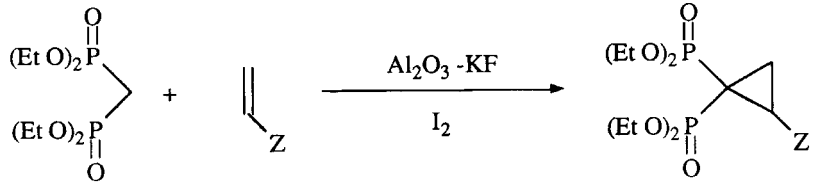
D. Hutchinson[4] suggested that modifications of geometry and complexation properties occurring when transforming methylene diphosphonic acid into cyclopropanediyldiphosphonic acid can be interesting for the biological (antiviral) properties of this pyrophosphate analog. Synthesis of unfonctionalised cyclopropranediyldiphosphonate has already been described with a poor yield[4-5]. Tetraethyl cyclopropanediyldiphosphonate was obtained in one step from 1,2-dibromoethane (5 mmol) and tetraethyl methylenediphosphonate on KF-alumina in a poor yield (6%) instead of 5 steps in literature (5%)[1]. Recently Chengye et al.[6] obtained functionalised cyclopropanediyl diphosphonates from bromomethylenediphosphonate and thallium ethoxide, compounds which are not easily available. Bromomethylene diphosphonate is synthesised in two rather laborious steps[7]. A more easy method giving heavy metal free phosphonate seems necessary for studying the biological properties of the cyclopropanediyl-diphosphonates.

Table 1: Synthesis of Cyclopropanes from Olefins and Carbon Acid Compounds

X	Y	R	Z	Yield (%)[a]
CN	$COOC_2H_5$	H	$COOC_2H_5$	62
CN	$COOC_2H_5$	H	CN	57
CN	$COOC_2H_5$	C_6H_5	COC_6H_5	87
$COOC_2H_5$	$COOC_2H_5$	H	$COOC_2H_5$	60
$COOC_2H_5$	$COOC_2H_5$	H	CN	61
$COOC_2H_5$	$COOC_2H_5$	C_6H_5	COC_6H_5	85
$COOC_2H_5$	$COOC_2H_5$	C_6H_5	NO_2	76

a) A mixture of isomers is obtained.

Scheme 2



Z = CN (55 %) Z= $COOCH_3$ (54%) Z=SOC_6H_5 (42%)

Our cyclopropanation method applied to electron deficient olefins and tetraethyl methylenediphosphonate (Scheme 2) gave cyclopropanes with terminal olefins, the substituted olefin like chalcone and ω-nitrostyren gave no cyclopropanation products. This can be explained by steric hindrance of the methanediphosphonate group. Yields of this new reaction are moderate in the case of tetraethyl methanediphosphonate but the easily available reactants and the absence of heavy metal (important for biological applications) make this new procedure attractive.

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Biological properties of new cyclopropanediyldiphosphonic acids are under investigation[6].

Experimental

Infrared spectra were recorded on Perkin Elmer 684 IR spectrophotometer in KBr with absorptions in cm^{-1}. Proton (^{1}H NMR) and carbon (^{13}C NMR) NMR spectra in ppm downfield from internal Me_4Si were recorded on a Brucker AC 250 instrument from a solution of the product in d_6-DMSO or $CDCl_3$. Phosphorous NMR spectra (^{31}P NMR) in ppm downfield from internal Me_4Si were recorded on a Brucker WP 90 instrument. Mass spectra were recorded on a Nermag R10.10H spectrometer.

General Procedure

Synthesis of cyclopropanes

In a typical experimental procedure, the carbon acid compound (5 mmol), iodine (5 mmol, 1.27 g) and the olefin (5 mmol) are stirred in dry THF (15 ml). KF on alumina (16 g) is added and the mixture is stirred at room temperature for 15 h. The pale yellow mixture is extracted with acetonitrile (3x25 ml) and after evaporation of the solvent, the residue is chromatographied.

Spectral and analytical data of cyclopropanes are identical to those described in the literature[2,3]. (see table 1).

Tetraethyl cyclopropanediyl diphosphonate

1,2-Dibromoethane (5 mmol) and tetraethyl methylenediphosphonate were adsorbed on potassium fluoride on alumina (16 g), after standing 4 h at room temperature, the solid was extracted with acetonitrile. After evaporation of the solvent the residue is chromatographied ($MeOH/CHCl_2$ = 5/95) : yield 6%, spectral and analytical data are in agreement with those described by Hutchinson[1].

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Functionalised tetraethyl cyclopropanediyldiphosphonates

In a typical experimental procedure, tetraethyl methylenediphosphonate (5 mmol), iodine (5 mmol, 1.27 g) and methyl acrylate (**2**) (5 mmol) are stirred in dry THF (15 ml). KF on alumina (16 g) is added and the mixture is stirred at room temperature for 15 h. The pale yellow mixture is extracted with acetonitrile (3x25 ml) and after evaporation of the solvent, the residue is chromatographied, (for (**3**) $MeOH/CHCl_2$ = 5/95) :

Tetraethyl 1,1-cyanocyclopropanediyl-diphosphonate

Obtained from acrylonitrile (45%) ; $C_{12}H_{23}NO_6P_2$; ^1H NMR ($CDCl_3$) δ : 1.4 (t, J = 7 Hz, 12 H, P-O-C-CH_3), 1.4-2.8 (m, 3 H, CH_2-CH-CN), 4.2 (dq, $J^1 = J^2$ = 7 Hz, 8H, P-O-CH_2) ; ^{13}C NMR ($CDCl_3$) δ : 8.8 (t, J = 6 Hz, P-C-$\underline{C}H_2$), 10.9 (t, J = 172 Hz, P-$\underline{C}$-P), 16.5 (P-O-C-$\underline{C}H_3$), 28 (t, J = 4 Hz, $\underline{C}$-CN), 63.5 (P-O-C), 16.5 (CN) ; ^{31}P NMR ($CDCl_3$) δ : 17.8 (d, J = 18 Hz), 18.4 (d, J = 18 Hz) ; MS m/z (%) : 339 (M^+, 36), 311 (24), 210 (49), 202 (55), 174 (14), 147 (47), 66 (100).

Methyl 2,2-bis(diethylphosphono)-cyclopropanecarboxylate

Obtained from methyl acrylate (44%) ; $C_{13}H_{26}OP_2$; ^1H NMR (CCl_4) δ : 1.35 (t, J = 7 Hz, 12 H, P-O-C-CH_3), 2.05 (s, 3 H, C-O-CH_3), 1.9-2.4 (m, 2 H, CH_2-C-CO), 2.75 (m, 1 H, CH-CO), 4.1 (dq, J^1=J^2 = 7 Hz, 8 H, P-O-CH_2) ; NMR ^{13}C ($CDCl_3$) δ : 10 (t, J = 180 Hz, P-$\underline{C}$-P), 14.3 (t, J = 4 Hz, P-C-$\underline{C}H_2$), 16.5 (P-O-C-$\underline{C}H_3$), 26.4 (t, J = 4 Hz, $\underline{C}$-$COOCH_3$), 52.5 (COO-$\underline{C}H_3$), 63.5 (P-O-C), 168.5 (CO) ; ^{31}P NMR ($CDCl_3$) δ :19.7 (d, J = 22.3 Hz), 23.3 (d, J = 22.3 Hz) ; IR (film) : 1740 (C=O), 1250 (P=O), 1025, (P-O-C), 970 ; MS m/z (%) : 372 (M^+, 18), 312 (12), 242 (35), 234 (38).

Tetraethyl 1,1-phenylsulfinylcyclopropanediyl-diphosphonate

Obtained from phenyl vinylsulfoxide (32%) ; $C_{17}H_{28}O_7P_2S$; ^1H NMR

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(CDCl3) δ : 1.1 (dt, J^1= 7, J^2 = 14 Hz, 2H, P-C-CH_2), 1.2 (m, 1 H, CH-SO), 1.3 (t, J = 7 Hz, 12 H, P-O-C-CH_3), 4.1 (dq, J^1=J^2 = 7 Hz, 8 H, P-O-CH_2), 7.4 (m, 5 H, Ar) ; ^{13}C NMR (CDCl3) δ : 8.8 (P-C-$\underline{C}H_2$), 10.9 (t, J = 170 Hz, P-$\underline{C}$-P), 14.5 (t, J = 4 Hz, $\underline{C}$H-SO), 16.5 (P-O-C-$\underline{C}H_3$), 63.5 (P-O-C), 124, 129, 131, 144 (Ar) ; ^{31}P NMR (CDCl3) δ : 19.8 (d, J = 31 Hz), 20.4 (d, J = 31).

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