Vinyltriphenylphosphonium Salt-mediated New Synthesis of Functionalized Maleimides†

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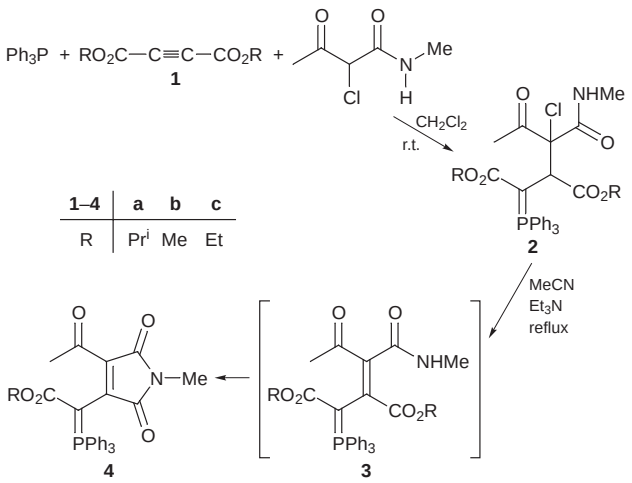
N-Methyl-2-chloroacetoacetamide undergoes a complex reaction with dialkyl acetylenedicarboxylates and triphenylphosphine to produce dialkyl 2-(*N*-methyl-2-chloroacetoacetamide-2-yl)-3-(triphenylphosphoranylidene)-butanedioates, which undergo elimination-cyclization reactions to produce *N*-methyl-4-acetyl-3-(alkoxycarbonyltriphenylphosphoranylidene)-maleimides.

Development of simple synthetic routes for widely used organic compounds from readily available reagents is one of the major tasks in organic synthesis.[1] Maleimide derivatives are among such types of organic compounds with many applications in synthetic[2] and polymer[3] chemistry. Despite their wide applicability, available routes for the synthesis of maleimide derivatives are limited.[4] We here report a facile synthetic route to *N*-methylmaleimide derivatives **4**. Thus, reaction of acetylenic esters **1** with *N*-methyl-2-chloroacetoacetamide in the presence of triphenylphosphine leads to the corresponding phosphorane **2**, which is converted to **4**, presumably *via* the allylidenephosphorane **3** (Scheme 1).



Scheme 1

The ^{1}H NMR spectra of compounds **2a–c** exhibited a doublet ($^3J_{HH}$ 4.8 Hz) for the NCH_3 group at δ *ca.* 2.3, a singlet for the CH_3CO group, along with a characteristic doublet ($^3J_{HP}$ 16–18 Hz) for the CH group. The ester moieties and the PPh_3 group displayed characteristic signals at appropriate chemical shifts. Although compound **2** possesses two stereogenic centers, and two diastereoisomers are expected, only one diastereoisomer is isolated from the reaction mixture. The ^{31}P NMR spectrum of **2a** exhibited only one signal at δ 30.83.

The ^{1}H NMR spectra of compounds **4a–c** displayed signals for acetyl and NCH_3 protons at δ 2.75–2.86, which appear as single sharp lines. The ^{1}H and ^{13}C NMR spectra of **4a–c** are in agreement with the presence of one ester moiety. The ^{31}P NMR spectrum of **4a** exhibited a single peak at δ 19.32.

The mass spectra of maleimides displayed molecular ion peaks at *m/z* 513, 485.5 and 499.6 for **4a**, **4b** and **4c**, respectively. Initial fragmentations involved loss from or complete loss of the side chains and scission of the heterocyclic ring system.

The structural assignments made on the basis of the NMR spectra of compounds **2** and **4** were supported by measurement of their IR spectra. Of special interest are the strong carbonyl absorption bands at 1620–1745 cm^{-1} for all compounds and a fairly broad NH peak at 3317–3441 cm^{-1} for the *N*-methylamido group in compound **2**.

On the basis of the chemistry of trivalent phosphorus nucleophiles[5–7] it is reasonable to assume that maleimide **4** results from initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the reactive 1 : 1 adduct by *N*-methyl-2-chloroacetoacetamide. Then the positively charged ion is attacked by the anion of the CH-acid to form ylide **2**. The maleimide derivative **4** is obtained by refluxing phosphorane **2** in acetonitrile in presence of triethylamine.

In summary, the reaction between triphenylphosphine with electron-deficient acetylenic esters, such as dialkyl acetylenedicarboxylates, in the presence of *N*-methyl-2-chloroacetoacetamide provides a simple entry into the synthesis of polyfunctional maleimides.

Experimental

Triphenylphosphine, *N*-methyl-2-chloroacetoacetamide and **1** were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. ^{1}H, ^{13}C and ^{31}P NMR spectra were measured with Bruker DRX-500 Avance spectrometer at 500, 125.77 and 202.46 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer.

General Procedure for Synthesis of Dialkyl 2-(N-*Methyl*-1-2-*chloroacetoacetamide*-2-*yl*)-3-(*triphenylphosphoranylidene*)*butanedioates* (**2**). —To a magnetically stirred solution of *N*-methyl-2-chloroacetoacetamide (0.30 g, 2 mmol) and triphenylphosphine (0.52 g, 2 mmol) in CH_2Cl_2 (10 ml) was added, dropwise, a mixture of dialkyl acetylenedicarboxylate (2 mmol) in CH_2Cl_2 (4 ml) at −10 °C over 10 min. The mixture was allowed to stand at room temperature for 24 h. The solvent was removed under reduced pressure and to the light brown viscous oil was added 20 ml ethyl acetate. The white precipitate was collected.

2a: mp 175–177 °C (decomp), yield 43%; IR (KBr) (ν_{max}/cm^{-1}): 3441 (NH), 1745, 1724 and 1662 (C=O); δ_H 0.5 and 1.04 [6 H, 2d, $^3J_{HH}$ 6.2 Hz, P=CCO$_2$CH(CH_3)$_2$], 1.40 and 1.47 [6 H, 2d, $^3J_{HH}$ 6.2 Hz, CHCO$_2$CH(CH_3)$_2$], 2.30 (3 H, d, $^3J_{HH}$ 4.8 Hz, NCH_3), 2.55 (3 H, s, CH_3), 4.06 (1 H, d, $^3J_{HP}$ 15.7 Hz, CH), 4.80 (1 H, sept, $^3J_{HH}$ 6.2 Hz, OCH), 5.22 (1 H, sept, $^3J_{HH}$ 6.2 Hz, OCH), 7.4–8.2 (15 H, m, 3 C_6H_5), 10.2 (1 H, br q, $^3J_{HH}$ 4.8 Hz, NH); δ_C 20.12, 20.94, 21.62 and 21.91 (2 CH*Me*$_2$), 26.85 and 28.96 (2 CH_3), 32.26 (d, $^1J_{CP}$ 72.4 Hz, P=C), 36.73 (*C*C=P), 54.97 (d, $^3J_{PC}$ 3.7 Hz, CCl), 69.87 and 71.91 (2 OCH), 116.76 (d, $^1J_{CP}$ 88.9 Hz C_{ipso}), 129.12 (d, $^3J_{CP}$ 12.8 Hz, C_{meta}), 134.58 (d, $^4J_{CP}$ 2.5 Hz, C_{para}), 135.34 (d, $^2J_{CP}$ 10.0 Hz, C_{ortho}), 161.29 (d, $^2J_{CP}$ 5.5 Hz, C=O ester), 162.76 (d, $^3J_{CP}$ 11 Hz, C=O ester), 163.0

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(C=O amide), 196.50 (C=O ketone); δ_P 30.83 (C=PPh_3); *m/z* 609.5 (M^+, 1), 277 (100), 262 (22), 183 (29), 77,(31), 43 (71%) (Found: C, 64.9; H, 6.1; N, 2.2. $C_{33}H_{37}NO_6ClP$ requires C, 65.0; H, 6.1; N, 2.3%).

2b: mp 137–139 °C (decomp), yield 48%; IR (KBr) (ν_{max}/cm^{-1}): 3396 (NH), 1745, 1721 and 1663 (C=O); δ_H 2.39 (3 H, d, $^3J_{HH}$ 4.8 Hz, NCH_3), 2.6 (3 H, s, CH_3CO), 3.61 and 3.92 (6 H, 2 s, 2 OCH_3), 4.28 (1 H, d, $^3J_{HP}$ 18.0 Hz, CH), 7.8–8.3 (15 H, m, 3 C_6H_5), 10.4 (1 H, br q $^3J_{HH}$ 4.8 Hz, NH). δ_C 26.34 and 28.18 (2 CH_3), 32.49 (d, $^1J_{CP}$ 72.5 Hz, P=C), 36.81 (*C*C=P), 52.89 and 53.22 (2 OCH_3), 55.01 (CCl), 116.36 (d, $^1J_{CP}$ 87.9 Hz, C_{ipso}), 129.31 (d, $^3J_{CP}$ 13.6 Hz, C_{meta}), 134.64 (d, $^2J_{CP}$ 10.0 Hz, C_{ortho}), 134.86 (d, $^4J_{CP}$ 2.0 Hz, C_{para}), 161.41 (d, $^2J_{CP}$ 4.5 Hz, C=O ester), 164.30 (d, $^3J_{CP}$ 8.0 Hz, C=O ester), 164.32 (C=O amide), 195.86 (C=O, ketone); *m/z* 553 (M^+, 1), 277 (8), 262 (3), 183 (51), 108 (8), 77 (69), 43 (100%) (Found: C, 63.0; H, 5.2; N, 2.6. $C_{29}H_{29}ClNO_6P$ requires C, 62.9; H, 5.3; N, 2.5%).

2c: mp 152–153 °C (decomp.), yield 47%; IR (KBr) (ν_{max}/cm^{-1}): 3410 (NH), 1751, 1720 and 1668 (C=O); δ_H 0.93 and 1.42 (6 H, t, $^3J_{HH}$ 7.2 Hz, 2 CH_3), 2.40 (3 H, d, $^3J_{HH}$ 4.8 Hz, NCH_3), 2.62 (3 H, s, CH_3), 3.6–4.0 (2 H, ABX_3 system, OCH_2), 4.20 (1 H, d, $^3J_{HP}$ 18.0 Hz, CH), 4.2–4.6 (2 H, ABX_3 system, OCH_2), 7.5–8.2 (15 H, m, 3 C_6H_5), 10.3 (1 H, br q, $^3J_{HH}$ 4.8 Hz, NH); δ_C 12.87 and 13.89 (2 CH_3), 26.84 and 28.79 (2 CH_3), 32.60 (d, $^1J_{CP}$ 71.6 Hz, P=C), 37.1 (P=C*C*), 55.38 (d, $^3J_{CP}$ 3.6 Hz, CCl), 62.43 and 63.61 (2 OCH_2), 116.97 (d, $^1J_{CP}$ 87.9 Hz, C_{ipso}), 129.70 (d, $^3J_{CP}$ 12.8 Hz, C_{meta}), 134.95 (d, $^4J_{CP}$ 2.5 Hz, C_{para}), 135.34 (d, $^2J_{CP}$ 10.0 Hz, C_{ortho}), 161.78 (d, $^2J_{CP}$ 5.4 Hz, C=O ester), 165.0 (d, $^3J_{CP}$ 8.8 Hz, C=O ester), 164.15 (C=O amide), 196.15 (C=O ketone); *m/z* 582 (M^+, 3), 319 (9), 262 (100), 184 (38), 183 (53), 108 (35%) (Found: C, 63.4; H, 5.5; N, 2.5. C $C_{31}H_{33}NO_6ClP$ requires C, 64.0; H, 5.7; N, 2.4 %).

General Procedure for Synthesis of N-*Methyl*-4-*acetyl*-3-*(alkoxycarbonyltriphenylphosphoranylidene)maleimides* (**4**). — Compound **2** was refluxed in acetonitrile (20 ml) in the presence of 3 drops of triethylamine for 24 h. The solvent was removed under reduced pressure and the residue was purified by silica gel (Merck silica gel, 230–400 mesh) column chromatography using hexane–ethyl acetate (1 : 4) as eluent. The solvent was removed in vacuum and the residue was purified by recrystallization from an appropriate solvent.

4a: yellow crystals, mp 183-185 °C (decomp), yield 70%; IR (KBr) (ν_{max}/cm^{-1}): 1723, 1693 and 1672 (C=O); δ_H 0.7 (6 H, d, $^3J_{HH}$, 6.2 Hz, $CHMe_2$) 2.46 (3 H, s, CH_3), 2.75 (3 H, s, NCH_3), 4.75 (1 H, sept, $^3J_{HH}$ 6.2 Hz, OCH), 7.2–8.0 (15 H, m, 3 C_6H_5); δ_C 21.97 ($CHMe_2$), 23.93 and 30.03 (2 CH_3), 68.51 (OCH), 70.67 (d, $^1J_{CP}$ 110.8 Hz, P=C), 111.87 (d, $^3J_{PC}$ 8.1 Hz, P=CC= *C*), 126.75 (d, $^1J_{CP}$ 94.8 Hz, C_{ipso}), 129.14 (d, $^3J_{CP}$ 12.7 Hz, C_{meta}), 132.6 (d, $^4J_{CP}$ 2.3 Hz, C_{para}), 133.7 (d, $^2J_{CP}$ 9.8 Hz, C_{ortho}), 148.11 (d, $^2J_{CP}$ 7.8 Hz, *C*C=P), 166.11 (d, $^2J_{CP}$ 12.2 Hz, C=O ester),169.80 (d, $^3J_{CP}$ 7.2 Hz, C=O amide), 171.06 (C=O amide),192.51 (C=O, ketone); δ_P 19.32 (Ph_3P=C); *m/z* 513 (M^+, 1), 263 (100) 184 (56), 108 (51), 43 (44%) (Found: C, 70.0; H, 5.5; N, 2.6. $C_{30}H_{28}NO_5P$ requires C, 70.2; H, 5.5; N, 2.7%).

4b: yellow crystals, mp 233–235 °C (decomp.), yield 86%; IR (KBr) (ν_{max}/cm^{-1}): 1726, 1693 and 1672 (C=O); δ_H 2.40 (3 H, s, CH_3), 2.86 (3 H, s, NCH_3), 3.25 (3 H, s, OCH_3), 7.3–8.0 (15 H, m, 3 C_6H_5); δ_C 23.50 and 28.95 (2 CH_3), 51.51 (OCH_3), 77.96 (d, $^1J_{CP}$ 110.2 Hz, P=C, 105.16 (d, $3J_{PC}$ 8.2 Hz, C=CC=P), 125.71 (d, $^1J_{CP}$ 95.3 Hz, C_{ipso}), 128.72 (d $^3J_{CP}$ 12.8 Hz, C_{meta}), 132.34 (d, $^4J_{CP}$ 3.6 Hz, C_{para}), 133.10 (d, $^2J_{CP}$ 10.1 Hz, C_{ortho}), 146.07 (d, $^2J_{CP}$ 5.4 Hz, *C*C=P), 166.68 (d, $^2J_{CP}$ 13.6 Hz, C=O ester), 168.52 (d, $^3J_{CP}$ 7.2 Hz, C=O amide), 170.25 (C=O amide), 190.50 (C=O, ketone); *m/z* 485.5 (M^+, 1), 262 (100), 184.3 (12), 183.3 (36), 108 (57%) (Found: C, 69.8; H, 5.1; N, 2.8. $C_{28}H_{24}NO_5P$ requires C, 69.3; H, 5.0; N, 2.9%).

4c: yellow crystals, mp 212–214 °C (decomp.), yield 86%; IR (KBr) (ν_{max}/cm^{-1}): 1720, 1695 and 1673 (C=O); δ_H 0.95 (3 H, t, $^3J_{HH}$ 7.2 Hz, CH_3) 2.45 (3 H, s, CH_3), 2.80 (3 H, s, NCH_3), 3.78 (2 H, q, $^3J_{HH}$ 7.2 Hz, OCH_2), 7.4–8.1 (15 H, m, 3 C_6H_5), δ_C 13.76 (CH_3), 23.54 and 29.20 (2 CH_3), 60.80 (OCH_2), 75.60 (d, $^1J_{CP}$ 108.2 Hz, P=C), 107.07 (d, $^3J_{PC}$ 8.1 Hz, P=CC=*C*), 126.03 (d, $^1J_{CP}$ 94.3 Hz, C_{ipso}), 128.73 (d, $^3J_{CP}$ 13.7 Hz, C_{meta}), 132.32 (d, $^4J_{CP}$ 2.7 Hz, C_{para}), 133.16 (d, $^2J_{CP}$ 9.1 Hz, C_{ortho}), 146.67 (d, $^2J_{CP}$ 5.4 Hz, *C*C=P), 166.32 (d, $^2J_{CP}$ 13.6 Hz, C=O ester), 169.05 (d, $^3J_{CP}$ 8.1 Hz, C=O amide), 170.62 (C=O amide), 191.22 (C=O, ketone); *m/z* 499.6 (M^+, 1), 278.5 (10), 277.5 (27), 262.5 (100), 183.2 (86), 108.2 (62), 77 (14%) (Found: C, 68.8; H, 5.3; N, 2.9. $C_{29}H_{26}NO_5P$ requires C, 69.7; H, 5.3; N, 2.8%).

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