Three-component reaction between triphenylphosphine, acetylenic esters and 4-hydroxycoumarin, 4-(phenylamino)coumarin, 4-hydroxyquinolin-2(1*H*)-one or 4-hydroxy-1-methylquinolin-2(1*H*)-one

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Three-component reaction between dialkyl acetylenedicarboxylates and triphenylphosphine in the presence of 4-hydroxycoumarin, 4-(phenylamino)coumarin, 4-hydroxyquinolin-2(1*H*)-one or 4-hydroxy-1-methylquinolin-2(1*H*)-one is described.

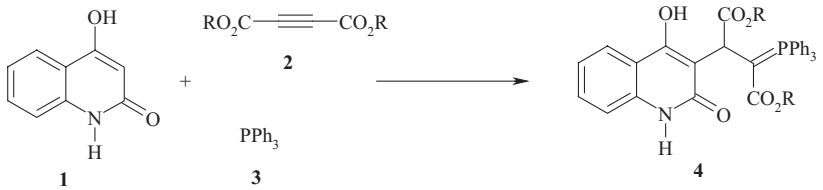
Keywords: acetylenic esters, 4-hydroxycoumarin, 4-(phenylamino)coumarin, 4-hydroxyquinolin-2(1H)-one, triphenylphosphine, phosphorus ylides

The nucleophilic addition of triphenylphosphine to electron-deficient triple bonds leads to a highly reactive zwitterionic intermediate which may be trapped by various electrophiles. The reaction of triphenylphosphine with dimethyl acetylenedicarboxylate (DMAD) in the presence of different organic acidic compounds, in order to trap the diionic intermediate, has been extensively investigated.[1–2,11] In the most of these reactions, the phosphorus ylides were reported as intermediates or the final product. However, there are also many reports of the reaction between triphenylphosphine and acetylenic esters in the presence of an electrophile in which triphenylphosphine acted as catalyst.[3-6] In fact, in these reactions nucleophilic triphenylphosphine connected together the two electrophilic substrates. In continuation of our previous works on the reaction between trivalent phosphorus nucleophiles with acetylenic esters in the presence of organic acidic compounds,[7-11] we report here the results of our study on the reaction between triphenylphosphine and electron-deficient acetylenic esters in the presence of 4-hydroxycoumarin, 4-(phenylamino)coumarin, 4-hydroxyquinolin-2(1*H*)-one or 4-hydroxy-1-methylquinolin-2(1*H*)-one. Thus the reaction between DMAD or diethyl acetylendicarboxylate (DEAD) with 4-hydroxyquinolin-2(1*H*)-one in the presence of triphenylphosphine afforded dialkyl 2-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-3-(triphenylphosphanylidene)succinate **4a, b** in excellent yields (Scheme 1).

The structures of compounds **4a, b** result from their IR, ^{1}H, ^{13}C, and ^{31}P NMR spectra. The mass spectra of the ylides **4** are fairly similar and display molecular ion peaks. The NMR spectra of ylides **4a, b** are consistent with the presence of two conformational isomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group and rotation about the partial double bond in 4-(*E*), 4-(*Z*) geometrical isomers is low on the NMR time scale at ambient temperature (Scheme 2). Conformational isomers in phosphoranes have been previously established and reported in the literature.[12-14]

The ^{1}H NMR spectrum of **4a** shows two sharp lines (δ = 2.82, 3.52 ppm) for the methyl groups of the major isomer, along with a signal for the methine proton at 5.13 ppm, which appears as a doublet ($^{3}J_{PH}$ = 11 Hz). Two single signals are observed at δ = 9.63 and 9.68 ppm which disappear after addition to DMSO solution of **4a** a few drops of D_2O. These signal are related to NH and OH protons. The aromatic protons show multiplets at δ = 6.99-7.58 ppm. The corresponding signals for the minor isomer appear at δ = 3.42, 3.82 ppm for methyl groups and at δ = 4.39 ppm ($^{3}J_{PH}$ = 9 Hz) for the methine proton. The ^{31}P NMR spectrum of compound **4a** displays two signals at 24.49 and 24.85 ppm for the major and minor isomers, respectively. These shifts are similar to those observed for other stable phosphorus ylides.[15,16] The structural assignments made on the basis of the NMR spectra of compound **4a** are supported by its IR spectrum. The ester carbonyl groups exhibit absorption bands at 1736 and 1619 cm^{-1}. The N-H stretching absorption bands appear at 3295–3150 cm^{-1}. On the basis of the well-established chemistry of trivalent phosphorus nucleophiles[2,15] it is reasonable to assume that ylides **4** result from the initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the 1 : 1 adduct by 4-hydroxyquinolin-2(1*H*)-one. Then, the positively charged ion intermediate **5** is attacked by the conjugate anion of 4-hydroxyquinolin-2(1*H*)-one **6** to form the phosphorane **4** (Scheme 3).

Under similar conditions as for the reactions above, triphenylphosphine reacted with DMAD in the presence of 4-(phenylamino)coumarin to produce phosphorane **8** in 90%



2,4	R	%Yield
a	Me	92
b	Et	95

Scheme 1

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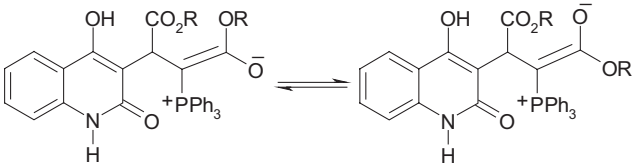
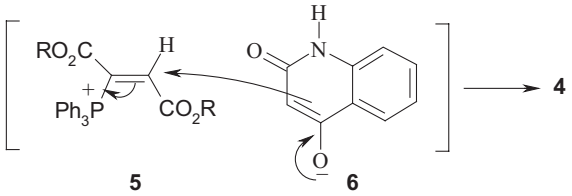


Scheme 2



Scheme 3

yield (Scheme 4). NMR spectra of compound **8** in d_6-DMSO show that for this compound, in contrast to ylides **4a** and **4b**, the rate of conversion of two rotational isomers is too fast in the NMR time scale so that only one set of signals is observed in the ^{1}H and ^{13}C NMR spectra of this compound.

Reaction between triphenylphosphine and acetylenic esters was also carried out in the presence of 4-hydroxycoumarin. When DMAD was used, the only isolated product was methyl 2,5-dioxo-2*H*,5*H*-pyrano[3,2-*c*]chromene-4-carboxylate **10** which obtained in 89% yield (Scheme 5). However, three-component reaction between triphenylphosphine, DEAD and 4-hydroxycoumarin afforded diethyl 2-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)fumarate **11** in 90% yield. The chemical shift of 6.99 ppm of the olefinic proton in the ^{1}H NMR spectrum of compound **11** is consistent with the *E*-geometry of the carbon–carbon double bond.[16] It is reasonable to assume that compound **10** was produced from phosphorane **12** by lactonisation and subsequent elimination of triphenylphosphine (Scheme 6). Compound **11** may be obtained from the intermediate ylide **12** by losing of triphenylphosphine (Scheme 7). The ^{1}H NMR spectrum of compound **10** showed two singlets at 3.87 and 6.79 ppm for methoxy and methine protons, respectively. The ^{13}C NMR spectrum of compound **10** showed 14 distinct signals in accordance with the proposed structure.

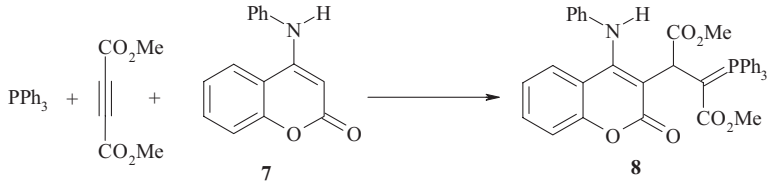
When 4-hydroxy-1-methylquinolin-2(1*H*)-one **14** treated with dimethyl acetylenedicarboxylate in the presence of triphenylphosphine, dimethyl 2-(1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinolin-3-yl)fumarate **15** were formed in 90% yield (Scheme 8).

The ^{1}H NMR spectrum of **15** exhibited three single sharp lines readily recognised as arising from methyl (δ = 3.55 ppm) and methoxy (δ = 3.57 and 3.68 ppm) protons, along with a single signal for the methine proton at 6.89 ppm**.** The aromatic protons appeared as multiplets at δ = 7.26–8.02 ppm. A singlet was observed at δ = 10.72 ppm which arises from OH proton and disappeared after addition of D_2O to DMSO solution of compound **15**.

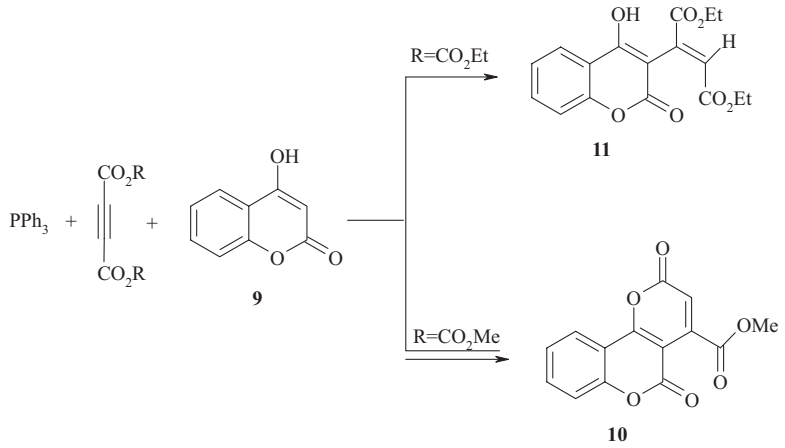
In summary phosphorus ylides may be prepared by a simple, one-pot, three-component reaction of acetylenic esters, triphenylphosphine and 4-(phenylamino)coumarin or 4-hydroxyquinolin-2(1*H*)-one. Similar reaction between triphenylphosphine, DMAD and 4-hydroxy-1-methylquinolin-2(1*H*)-one produces dimethyl 2-(1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinolin-3-yl)fumarate. The present method carries the advantage that not only the reaction is performed under neutral conditions but also the substances can be mixed without any activation or modification.

Experimental

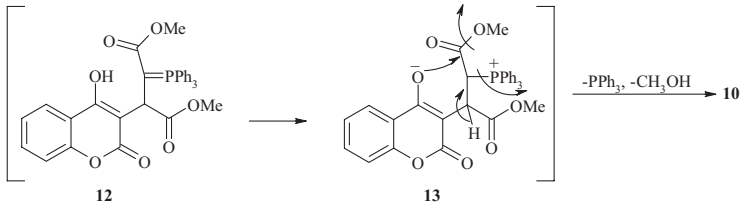
All melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyser. Mass spectra were recorded on a Finnigan-Mat 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on Bruker DRX-300 Avance spectrometer at 300.1, 75.46, and 121.49



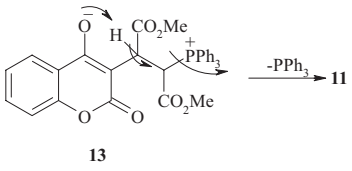
Scheme 4



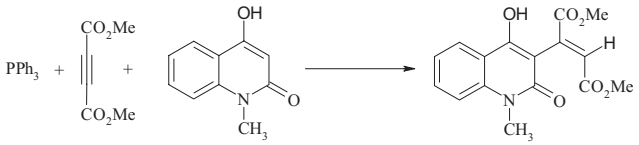
Scheme 5



Scheme 6



Scheme 7



Scheme 8

MHz, respectively. ^{1}H, ^{13}C and ^{31}P NMR spectra were obtained in d_6-DMSO solution using TMS as internal standard or 85% H_3PO_4 as external standard. 4-(phenylamino)coumarin prepared as a previously reported method.[17] The chemicals used in this study were purchased from Fluka and were used without further purification

Dimethyl 2-(4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-3-(triphenylphosphanylidene)succinate (**4a**): Typical procedure for preparation of compounds **4a, b**, **8**, **10**, **11** and **15**: To a magnetically stirred solution of triphenylphosphine (2 mmol) and 4-hydroxyquinolin-2(1*H*)-one (2 mmol) in acetone (10 ml) was added dropwise a mixture of dimethyl acetylenedicarboxylate (2 mmol) in acetone (3 ml) at room temperature over 2 min. The reaction mixture was then stirred for 24 h. Solvent was evaporated and the residue was crystallised from ethyl acetate–hexane mixture. Yield: 92%; Colourless crystals; m.p. 119–120°C. IR (KBr) (ν_{max}, cm^{-1}): 3295, 3125, (NH, OH), 1736, 1708 (C=O). Calcd. for $C_{33}H_{28}NO_6P$: C, 70.08; H, 4.99; N, 2.48%. Found: C, 70.21; H, 4.62; N, 2.45;%. MS (*m/z*,%): 565 (M, 3). Major isomer (80%): ^{1}H NMR (d_6-DMSO): δ 2.82 (s, 3 H, OCH_3), 3.52 (s, 3 H, OCH_3), 5.13 (d, $^3J_{PH}$ = 11 H_Z, 1 H, P =C–CH), 6.99–7.58 (m, 38 H, aromatic*–*for two conformational isomers), 9.63 (s, 1 H, NH), 9.68 (s, 1 H, OH) ^{13}C NMR (d_6-DMSO): δ 42.83 (d, $^1J_{PC}$ = 125 H_Z, C = P), 48.74, 51.48 (2 OCH_3), 55.67 (d, $^2J_{PC}$ = 14.6 H_Z, CH), 125.90 (d, $^1J_{PC}$ = 92 H_Z,C ^{ipso}), 128.79 (d, $^3J_{PC}$ = 12 H_Z, C ^{meta}), 132.32 (d, $^4J_{PC}$ = 2 H_Z,C ^{para})*, 134.07 (d, $^2J_{PC}$ = 10 H_Z, C ^{ortho}), 119.27, 119.54, 123.58, 124.02, 129.29, 129.39, 139.04, 139.56 (aromatic), 166.85 (HO–C =)*, 166.99 (C=O), 168.99 (d, $^2J_{PC}$ = 12 H_Z, C=O)*, 174.70 (d, $^3J_{PC}$ = 11 H_Z, C=O)*. ^{31}P NMR (d_6-DMSO): δ 24.49. Minor isomer (20%): ^{1}H NMR (d_6-DMSO): δ 3.42 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 4.39 (d, $^3J_{PH}$ = 8.7 H_Z,1 H, P =C–CH), 9.57 (s, 1 H, NH), 9.89 (s, 1 H, OH).^{13}C NMR (d_6-DMSO): δ 41.16 (d, $^1J_{PC}$ = 122 H_Z, C = P), 49.96, 52.52 (2 OCH_3), 63.59 (d, $^2J_{PC}$ = 14 H_Z, CH), 125.34 (d, $^1J_{PC}$ = 91 H_Z,C ^{ipso}), 128.43 (d, $^3J_{PC}$ = 11 H_Z, C ^{meta}), 133.18 (d, $^2J_{PC}$ = 10 H_Z, C ^{ortho}), 118.83, 119.37, 123.62, 124.23, 128.22, 128.34, 138.71, 139.01 (aromatic), 167.12 (C=O). ^{31}P NMR ($CDCL_3$): δ 24.85.

Diethyl 2-(4-hydroxy-2-oxo-1,2-dihydro-quinolin-3-yl)-3-(triphenylphosphanylidene)succinate (**4b**): Yield: 95%; Colourless crystals; m.p. 133–134°C. IR (KBr) (ν_{max}, cm^{-1}): 3266, 3050 (NH, OH) 1732, 1705 (C=O). Calcd. for $C_{35}H_{32}NO_6P$: C, 70.82; H, 5.43; N, 2.36%. Found: C, 70.68; H, 5.65; N, 2.15%. MS (*m/z*,%): 593 (M, 1). Major isomer (70%): ^{1}H NMR (d_6-DMSO): δ 0.26 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 1.08 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 3.50 (m, 2 H, OCH_2), 3.99 (m, 2 H, OCH_2), 5.17 (d, $^3J_{PH}$ = 11 H_Z,1 H, P =C–CH), 6.97–7.62 (m, 38 H, aromatic)*, 9..83 (s, 1 H, NH), 9.86 (s, 1 H, OH). ^{13}C NMR (d_6-DMSO): δ 14.15, 14.35 (2 CH_3), 42.32 (d, $^1J_{PC}$ = 126 H_Z, C = P), 57.39, 60.20 (2 OCH_2), 63.48 (d, $^2J_{PC}$ = 15 H_Z, CH), 126.16 (d, $^1J_{PC}$ = 92 H_Z,C ^{ipso}), 128.65 (d, $^3J_{PC}$ = 12 H_Z, C ^{meta}), 132.06 (d, $^4J_{PC}$ = 2.2 H_Z, C ^{para}), 133.75 (d, $^2J_{PC}$ = 10 H_Z, C ^{ortho}), 118.88, 119.29, 123.50, 123.96, 128.11, 129.25, 139.32, 139.63 (aromatic), 166.93 (HO–C=)*, 167.09 (C=O)*, 169.45 (d, $^2J_{PC}$ = 13 H_Z, C=O)*, 174.93 (d, $^3J_{PC}$ = 11 H_Z, C=O)*. ^{31}P NMR ($CDCl_3$): δ 23.41. Minor isomer (30%): ^{1}H NMR (d_6-DMSO) δ 0.45 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 1.35 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 3.81 (m, 2 H, OCH_2), 4.08 (m, 2 H, OCH_2), 4.71 (d, $^3J_{PH}$ = 9 H_Z, 1 H, P =C–CH), 9.22 (s, 1 H, NH), 9.71 (s, 1 H, OH). ^{13}C NMR (d_6-DMSO): δ 14.03, 14.12, (2 CH_3), 43.36 (d, $^1J_{PC}$ = 126 H_Z, C = P), 57.79, 61.34 (2 OCH_2), 63.72 (d, $^2J_{PC}$ = 15 H_Z, CH), 126.72 (d, $^1J_{PC}$ = 92 H_Z, C ^{ipso}), 128.55 (d, $^3J_{PC}$ = 12 H_Z, C ^{meta}), 131.94 (d, $^4J_{PC}$ = 2.2 H_Z, C ^{para}), 133.19 (d, $^2J_{PC}$ = 9.83 H_Z, C ^{ortho}), 119.10, 119.63, 123.11, 124.21, 128.43, 129.81, 138.57, 139.54 (aromatic). ^{31}P NMR (d_6-DMSO): δ 25.12.

Dimethyl 2-(2-oxo-4-phenylamino-2H-chromen-3-yl)-3-(triphenylphosphanylidene)succinate (**8**): Yield: 90%; Colourless crystals; m.p. 136–137°C. IR (KBr) (ν_{max}, cm^{-1}): 3145 (NH), 1734, 1702, (C=O). Calcd. for $C_{39}H_{32}NO_6P$: C, 73.00; H, 5.03; N, 2.18%. Found: C, 72.83; H, 5.21; N, 2.25%. MS (*m/z*,%): 641 (M, 3). ^{1}H NMR (d_6-DMSO): δ 3.06 (s, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 4.23 (d, $^3J_{PH}$ = 18 H_Z, 1 H, P =C–CH), 6.92–7.77 (m, 24 H, aromatic), 9.78 (s, 1 H, NH).^{13}C NMR (d_6-DMSO): δ 42.21 (d, $^1J_{PC}$ = 123 H_Z, C = P), 43.36 (d, $^2J_{PC}$ = 16 H_Z, CH), 49.71, 52.24 (2 OCH_3), 116.84 (d, $^3J_{PC}$ = 5 H_Z, *C*=*C*-NHPh), 126.70 (d, $^1J_{PC}$ = 91 H_Z, C ^{ipso}), 128.92 (d, $^3J_{PC}$ = 12 H_Z, C ^{meta}), 132.32 (d, $^4J_{PC}$ = 3 H_Z, C^{para}), 134.34 (d, $^2J_{PC}$ = 10 H_Z, C ^{ortho}), 117.97, 117.07, 118.18, 120.61, 123.20, 127.50, 129.16, 130.82, 144.23, 148.70 (aromatic), 153.03 (C=C–*NHPh*), 163.76 (C=O), 171.72 (d, $^2J_{PC}$ = 13 H_Z, C=O), 174.20 (d, $^3J_{PC}$ = 7 H_Z, C=O). ^{31}P NMR (d6-DMSO): δ 24.49.

Diethyl 2-(4-hydroxy-2-oxo-2H-chromen-3-yl)fumarate (**11**): Yield: 90%; Colourless crystals; m.p. 130–131°C. IR (KBr) (ν_{max}, cm^{-1}): 3045 (OH), 1721, 1696, (C=O). Calcd. for $C_{17}H_{16}O_7$: C, 61.44; H, 4.85%. Found: C, 61.75; H, 5.01%. MS (*m/z*,%): 332 (M, 10). ^{1}H NMR (DMSO): δ 1.06 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 1.21 (t, $^3J_{HH}$ = 7 H_Z, 3 H, CH_3), 4.06 (q, $^3J_{HH}$ = 7 H_Z, 2 H, OCH_2), 4.21 (q, $^3J_{HH}$ = 7 H_Z, 2 H, OCH_2) 6.99 (s, 1 H, CH), 7.11–7.99 (m, 5 H, aromatic and OH). ^{13}C NMR (d_6-DMSO): δ 13.83, 14.61 (2 CH_3), 60.48, 61.33 (2 OCH_2), 110.99, 116.87, 117.86, 124.99, 129.78, 137.16, 137.52, 137.62, 153.37, 161.45 (aromatic and olefinic carbons), 162.23, 164.81, 165.86 (3 C=O).

Methyl 2,5-dioxo-2H,5H-pyrano[3,2-c]chromen-4-carboxylate (**10**): Yield: 89%; Colourless crystals; m.p. 146–147°C. IR (KBr) (ν_{max}, cm^{-1}): 1728 (C=O). Calcd. for $C_{14}H_8O_6$: C, 61.77; H, 2.96%. Found: C, 61.54; H, 2.72%. MS (*m/z*,%): 272 (M, 3). ^{1}H NMR (d_6-DMSO): 3.87 (s, 3 H, OCH_3), 6.79 (s, 1 H, CH), 7.53–8.02 (m, 4 H, aromatic). ^{13}C NMR (d_6-DMSO): δ 52.97 (OCH_3), 113.51, 117.53, 124.04, 125.73, 128.87, 129.02, 132.12, 132.25, 135.47, 154.04 (aromatic and oleficic carbons), 157.56, 163.75, 164.91 (3C=O).

Dimethyl 2-(1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinolin-3-yl) fumarate (**15**): Yield: 90%; Colourless crystals; m.p. 119–120°C. IR (KBr) (ν_{max}, cm^{-1}): 3305 (OH), 1733, 1712, (C=O). Calcd. for $C_{16}H_{15}NO_6$: C, 60.57; H, 4.77; N, 4.41%. Found: C, 60.35 H, 4.99; N, 4.38%. MS (*m/z*,%): 317 (M, 3). ^{1}H NMR (DMSO): δ 3.55 (s, 3 H, CH_3), 3.57 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 6.89 (s, 1 H, CH), 7.26–8.02 (m, 4 H, aromatic),10.72 (s, 1 H, OH). ^{13}C NMR (d_6-DMSO): δ 29.33 (CH_3), 52.12, 53.02 (2 OCH_3), 106.44, 115.02, 116.36, 122.01, 124.12, 130.31, 131.93, 138.58, 139.59, 157.68 (aromatic and olefinic carbons), 161.35, 164.86, 166.72 (3 C=O).

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