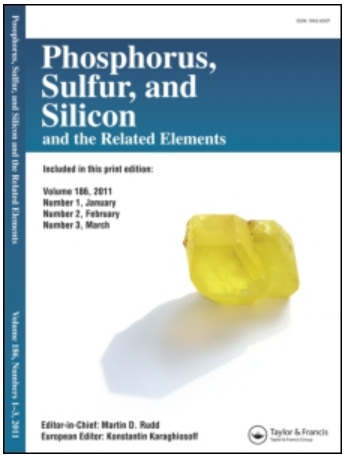

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis of Diastereomeric Phosphorus Ylides: A Facile Route to Dialkyl-(*E*)-2-{1-[2-oxodihydro-3(*2H*)-furanyliden]ethyl }-2-butenedioate

Sakineh Asghari[a]; Robabeh Baharfar[a]; Safiyeh Safiri[a]
[a] Department of Chemistry, University of Mazandaran, Babolsar, Iran

To cite this Article Asghari, Sakineh , Baharfar, Robabeh and Safiri, Safiyeh(2005) 'Synthesis of Diastereomeric Phosphorus Ylides: A Facile Route to Dialkyl-(*E*)-2-**{**1-[2-oxodihydro-3(*2H*)-furanyliden]ethyl }-2-butenedioate', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 12, 2805 — 2812
To link to this Article: DOI: 10.1080/104265090968307
URL: http://dx.doi.org/10.1080/104265090968307

Phosphorus, Sulfur, and Silicon, 180:2805–2812, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090968307

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Synthesis of Diastereomeric Phosphorus Ylides: A Facile Route to Dialkyl-(*E*)-2-{1-[2-oxodihydro-3(*2H*)-furanyliden]ethyl}-2-butenedioate

Sakineh Asghari
Robabeh Baharfar
Safiyeh Safiri
Department of Chemistry, University of Mazandaran, Babolsar, Iran

*2-acetylbutyrolactone undergoes a smooth reaction with triphenylphosphine and dialkyl acetylenedicarboxylates to produce dialkyl 2-(3-acetyl-2-oxotetrahydro-3-furanyl)-3-(1,1,1-triphenyl-1^5-phosphanilidene) succinate. These compounds undergo an intramolecular Wittig reaction to produce highly strained spiro compounds in boiling benzene, which spontaneously undergo ring-opening reactions to produce dialkyl (*E*)-2-{1-[2-oxodihydro-3(2H)-furaniliden]ethyl}-2-butenedioates.*

Keywords 2-Acetylbutyrolactone; acetylenic esters; intramolecular Wittig reaction

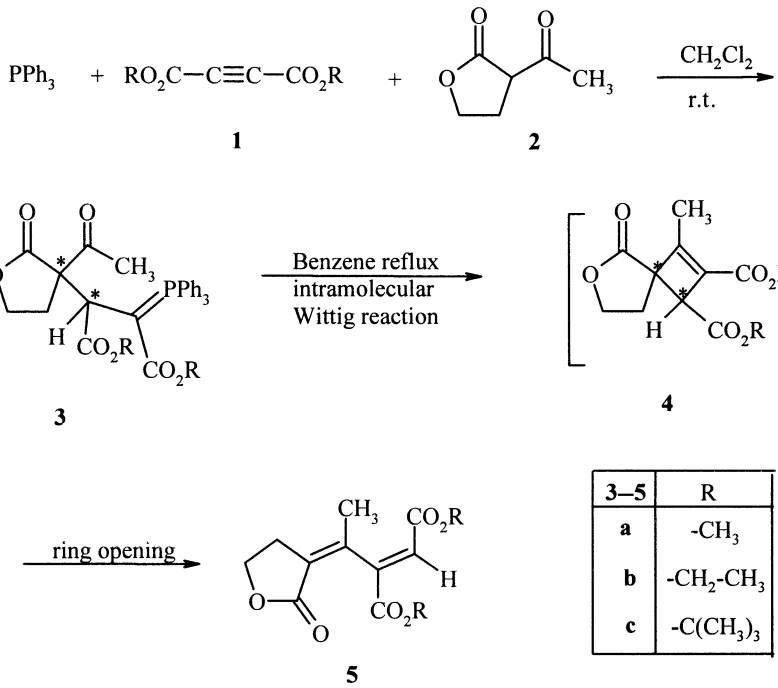
INTRODUCTION

Organophosphorus compounds, i.e., those bearing a carbon atom directly bound to a phosphorus atom, are synthetic targets of interest, not least because of their value for a variety of industrial, biological, and chemical synthetic uses.[1–2] Phosphorus ylides are reactive systems, which take part in many reactions of value in the synthesis of organic products.[2–8]

As part of our current studies on the development of phosphorus ylides and highly functionalized 1,3-dienes, we now report a facile synthesis of stabilized diastereomeric ylides **3a–c**, which are converted to highly strained spiro compounds **4a–c** via an intramolecular Wittig reaction. Because compounds **4a–c** are very unstable, therefore spontaneously undergo ring-opening reactions to produce functionalized 1,3-dienes **5a–c** (Scheme 1).

Thus, the reaction of 2-acetylbutyrolactone **2** with dialkyl acetylenedicarboxylates **1** in the presence of triphenylphosphine leads to the corresponding 1,3-diene **5** in fairly good yields.

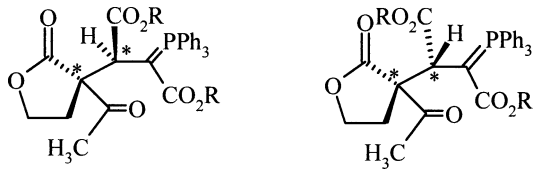
Received January 18, 2005; in final form March 10, 2005.
Address correspondence to Sakineh Asghari, University of Mazandaran, Department of Chemistry, PO Box 453, Babolsar, Iran. E-mail: s.asghari@umz.ac.ir



SCHEME 1

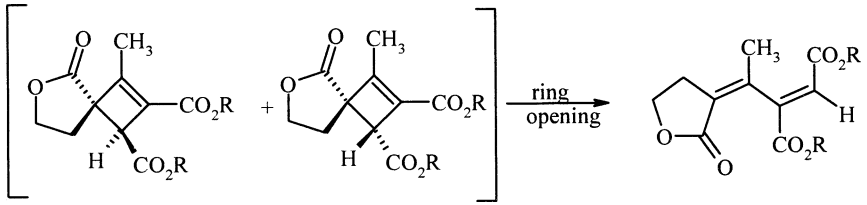
RESULT AND DISCUSSION

On the basis of the chemistry of trivalent phosphorus nucleophiles,[9,10] it is reasonable to assume that phosphorus ylide **3** results from the initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the reactive 1:1 adduct by 2-acetylbutyrolactone then the positively charged ion is attacked by the enolate anion of 2-acetyl butyrolactone to form the stable ylides **3a–c**. Compounds **3a–c** possess two stereogenic centers, and two diastereomers are expected (I and II). We isolated two diastereomers from the reaction mixture (Scheme 2).



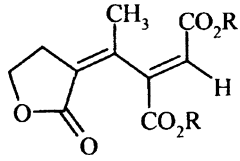
SCHEME 2 Diastereomeric isomers (**I** and **II**).

Both diastereomers were refluxed separately in benzene. They underwent an intramolecular Wittig reaction to produce unstable spiro compounds **4a–c**. These compounds spontaneously produced via a ring opening reaction of highly functionalized 1,3-dienes **5a–c**. It should be pointed out that both diastereomeric ylides were converted to 1,3-dienes with the same geometry. This result indicates that the ring opening reactions did not take place as a concerted reaction (Scheme 3).



SCHEME 3

The stereochemistry of the dienes **5a–c** was investigated using NOE experiment.[11] The irradiation of the methyl protons in compound **5a** leads to an enhancement (by about 2.5%) of the intensity of CH_2 signal in the butyrolactone moiety with no enhancement of the intensity of the olefinic proton signal. Irradiation of the CH_2 protons also caused an enhancement of the intensities of the CH_3 group (by about 4.5%). On the basis of these results, the following geometry for the compound **5** can be suggested (Scheme 4).



SCHEME 4

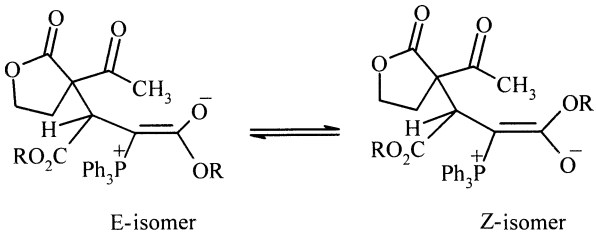
The structures of **3a–c** (I and II) were deduced from their ^1H, ^{13}C NMR, IR, and mass spectra.

The ^1H NMR spectra of the stable ylides **3a–I** (first diastereomer) exhibited a singlet at about $\delta = 1.75$ for CH_3 group, a doublet ($^3J_{PH} = 19.5$ Hz) at about $\delta = 3.5$ for $CHCO_2R$ and two singlets at about 2.86 and 3.73 for two OCH_3 groups. The^{13}C NMR spectrum of **3a–I** displayed a doublet ($^1J_{PC}$ 122.3 Hz) at about $\delta = 39.71$ for the P=C group and a doublet ($^2J_{PC}$ 13.7 Hz) at about 48.3 for $CHCO_2R$ moieties. The mass spectrum of **3a** displayed a molecular ion peak at m/z 532. Fragmentations involve the loss of one of the side chain (OCH_3, CH_3OH, CO_2CH_3 , PPh_3, -Ph). The structural assignment made on the basis of the ^1H and ^{13}C

NMR spectra for compound **3a–I** was supported by a measurement of their IR spectra. Of special interest are the strong carbonyl absorption bands at 1760, 1730, and 1720 cm^{-1}. The ^{1}H, ^{13}C NMR, IR, and mass spectra of **3a–II** (second diastereomer) are similar to that of **3a–I** with little differences between them (see Experimental section).

For compound **3a** only one rotamer was observed for each diastereomer.

Compounds **3b** and **3c** show four multiplets for two OCH_2 groups and four singlets for two $OCMe_3$ groups with an unequal intensity ratio, respectively. As the temperature was increased, these collapsed to two multiplets for two ethoxy groups in **3b** and two singlets for two tert-butoxy groups in **3c**. This observation is attributed to the temperature dependent equilibrium between the geometric (rotational) isomers, *E* and *Z*, i.e., the result of restricted rotation (Scheme 5).



SCHEME 5

Selected ^{1}H and ^{13}C NMR chemical shifts and coupling constants in the diastereomeric ylides **3a–c** are shown in Table I. Partial assignments of IR and mass spectra are given in the Experimental sections.

The structures of **5a–c** were deduced from ^{1}H, ^{13}C NMR, IR, and mass spectra. The ^{1}H NMR spectrum of the 1,3-butadiene derivative **5a** exhibited a triplet ($^{5}J_{HH}$ 1.6 Hz) at about 2.05 for the CH_3 group, as a result of long-range proton–proton coupling, two singlets at about 3.7 and 3.77 for two OCH_3 groups and a singlet at about 6.8 for the olefinic proton. The ^{13}C NMR spectrum of **5a** displayed a singlet at about 22.25 for CH_3, two singlets at about 51.94 and 52.9 for two OCH_3 groups, four signals in the olefinic region. The mass spectrum of **5a** displayed a molecular ion peak at *m/z* 254. Fragmentations involve the loss of one of the side chain (OCH_3, $HOCH_3$, CO_2Me). The structure of **5a** was supported by measurements of its IR spectrum. Of special interest are the strong carbonyl absorption bands at 1753, 1716, and 1670 cm^{-1}. The ^{1}H and ^{13}C NMR spectra of **5b** and **5c** are similar to those of **5a**, except for the ester groups, which exhibited characteristic resonance with appropriate chemical shifts. The mass spectra of **5b** and

TABLE I Selected ^{1}H and ^{13}C NMR Chemical Shift (δ in ppm) and Coupling constant (J in Hz) for Ylides of 3a–c

Ylides **3**	^{1}H/^{13}C NMR: δ (ppm) ($CDCl_3$, TMS)
3a–I	δ_H: 2.86 and 3.73 ($2OCH_3$), 3.51 (1H, d, $^3J_{PH}$ 19.5 HZ, CH) δ_C: 39.71 (d, $^1J_{PC}$ 122.29 Hz, P═C), 48.26 (d, $^2J_{PC}$ 13.7 Hz, CH), 48.77 and 52.16 ($2OCH_3$), 201.65 (C═O, ketone)
3a–II	δ_H: 2.92 and 3.73 ($2OCH_3$), 3.55 (1H, d, $^3J_{PH}$ 18.4 Hz, CH) δ_C: 37.86 (d, $^1J_{PC}$ 118.1 Hz, P═C), 47.89 (d, $^2J_{PC}$ 13.5 Hz, CH), 48.82 and 52.16 ($2OCH_3$), 201.37 (C═O, ketone)
3b–I	
(*Z*-isomer)	δ_H: 0.35 and 1.29(6H, 2t, $^3J_{HH}$ 7.1 Hz, $2CH_3$), 3.49 (1H, d, $^3J_{PH}$ 19.7 Hz, CH), 4.17–4.37 (4H, m, $2OCH_2$), δ_C: 13.77 and 14.25 ($2CH_3$), 39.15 (d, $^1J_{PC}$ 122.3 Hz, P═C), 48.31 (d, $^2J_{PC}$ 13.7 Hz, CH), 57.76 and 61.17 ($2OCH_2$), 201.76 (C═O, ketone)
(*E*-isomer)	δ_H: 1.11 and 1.35(6H, 2t, $^3J_{HH}$ 7.1 Hz, $2CH_3$), 3.45 (1H, d, $^3J_{PH}$ 19.8 Hz, CH), 4.17–4.37 (4H, m, $2OCH_2$), δ_C: 14.33 and 14.98 ($2CH_3$), 39.2 (d, $^1J_{PC}$ 122.1 Hz, P═C), 47.59 (d, $^2J_{PC}$ 14.46 Hz, CH), 58.24 and 61.10 ($2OCH_2$), 201.2 (C═O, ketone)
3b–II	
(*Z*-isomer)	δ_H: 0.34 and 1.26 (6H, t, $^3J_{HH}$ 7.07 Hz, $2CH_3$), 3.53 (1H, d, $^3J_{PH}$ 18.05 Hz, CH), 3.85–4.22 (4H, m, $2OCH_2$) δ_C: 13.70 and 14.22 ($2CH_3$), 37.45 (d, $^1J_{PC}$ 122.6 Hz, CH), 47.90 (d, $^2J_{PC}$ 12.41 Hz, CH), 57.69 and 61.29 ($2OCH_2$), 201.56 (C═O, ketone)
(*E*-isomer)	δ_H: 1.22 and 1.26(6H, 2t, $^3J_{HH}$ 7.1 Hz, $2CH_3$), 3.55 (1H, d, $^3J_{PH}$ 17.8 Hz, CH), 4.02–4.22 (4H, m, $2OCH_2$) δ_C: 14.13 and 15.29 ($2CH_3$), 37.36 (d, $^1J_{PC}$ 122.6 Hz, CH), 46.99 (d, $^2J_{PC}$ 12.41 Hz, CH), 62.47 and 63.38 ($2OCH_2$), 202.74 (C═O, ketone)
3c–I	
(Z-isomer)	δ_H: 0.86 and 1.51(2s, $2CMe_3$), 3.35(d, $^3J_{PH}$ 19.9 Hz, CH) δ_C: 28.23 and 28.32 ($2CMe_3$), 38.62 (d, $^1J_{PC}$ 122.7 Hz, P═C), 49.26 (d, $^2J_{PC}$ 14.0 Hz, CH), 77.24 and 81.22 ($2OCMe_3$), 202.06 (C═O, ketone)
(*E*-isomer)	δ_H: 1.36 and 1.50(s, $2CMe_3$), 3.33 (d, $^3J_{PH}$ 21.7 Hz, CH) δ_C: 28.48 and 28.54 ($2OCMe_3$), 40.26 (d, $^1J_{PC}$ 131.7 Hz, P═C), 48.65 (d, $^2J_{PC}$ 14.22 Hz, CH), 67.66 and 78.02 ($2OCMe_3$), 201.56 (C═O, ketone)
3c–II	δ_H: 0.82 and 1.46(2s, $2CMe_3$), 3.36(d, $^3J_{PH}$ 17.7 Hz, CH) δ_C: 28.18 and 28.28($2CMe_3$), 37.01(d, $^1J_{PC}$ 122.7 Hz, P═C), 48.67(d, $^3J_{PC}$ 13.99 Hz, CH), 77.24 and 81.39 ($2OCMe_3$), 201.90 (C═O, ketone)

5c exhibited molecular ion peaks at about m/z 282 and 338 for ethyl and tert-butyl derivatives, respectively.

^{1}H and ^{13}C NMR chemical shifts and coupling constants in the compounds **5a–c** are shown in Table II. Partial assignments of IR and mass spectra are given in the Experimental sections.

In conclusion, we have found that the reaction of 2-acetylbutyrolactone with dialkyl acetylenedicarboxylate in the presence of

TABLE II ^{1}H and ^{13}C NMR Chemical Shift (δ in ppm) and coupling constant (J in Hz) for 5a–c

Compound	^{1}H/^{13}C NMR: δ (ppm) ($CDCl_3$, TMS)
5a	δ_H: 2.05 (3H, t, $^5J_{HH}$ 1.6 Hz, CH_3), 3.70 and 3.77(6H, 2s, $2OCH_3$), 6.80 (1H, s, CH); δ_C: 22.25 (CH_3), 51.94 and 52.9 ($2OCH_3$), 122.83, 126.11, 143.62 and 147.12 (olefinic carbons), 164.79 and 165.08 (2C=O, ester), 169.44 (C=O, lactone)
5b	δ_H: 1.26 (3H, t, $^3J_{HH}$ 7.1 Hz, CH_3), 1.28 (3H, t, $^3J_{HH}$ 7.1 Hz, CH_3), 2.05 (3H, t, $^5J_{HH}$ 1.7 Hz, CH_3), 2.99 (2H, m, CH_2), 4.14 (2H, q, $^3J_{HH}$ 7.1 Hz, OCH_2), 4.23 (2H, q, $^3J_{HH}$ 7.1 Hz, OCH_2), 4.36 (2H, t, $^3J_{HH}$ 7.1 Hz, OCH_2), 6.78 (1H, s, CH) δ_C: 14.06 ($2CH_3$), 22.32 (CH_3), 26.82 (CH_2), 60.82, 61.84 and 65.04 ($3OCH_2$), 122.60, 126.29, 143.84 and 147.09 (olefinic carbons), 164.29 and 164.65 (2C=O, ester), 169.38 (C=O, lactone)
5c	δ_H: 1.39 (9H, s, CMe_3), 1.43 (9H, s, CMe_3), 1.99 (3H, s, CH_3), 2.94 (2H, t, $^3J_{HH}$ 7.2 Hz, CH_2), 4.32 (2H, t,$^3J_{HH}$ 7.2 Hz, OCH_2), 6.58 (1H, s, CH) δ_C: 22.57 (CH_3), 26.87 (CH_2), 27.89 and 27.98 (2CMe_3), 64.88 (OCH_2), 81.29 and 82.25 (2O*C*Me_3), 121.96, 127.55, 144.51 and 146.99 (olefinic carbons), 163.62 and 164.14 (2C=O, ester), 169.24 (C=O, lactone)

triphenylphosphine leads to a facile synthesis of diastereomeric phosphorus ylides (I and II), which are converted to highly functionalized 1,3-dienes.

EXPERIMENTAL

Dialkyl acetylenedicarboxylates, triphenylphosphine, and 2-acetylbutyrolactone were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured on an Electerothermal 9100 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a BRUKER DRX-500 AVANCE spectrometer at 500 and 125.8 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.

Preparation of Dimethyl 2-(3-Acetyl-2-oxotetrahydro-3-furanyl)-3-(1,1,1-triphenyl-1^5-phosphanilidene)-succinate(3a, $C_{30}H_{29}O_7P$): General Procedure

To a magnetically stirred solution of 2-acetylbutyrolactone (0.215 mL, 2 mmol) and triphenylphosphine (0.52 g, 2 mmol) in CH_2Cl_2, 10 mL was added, dropwise to a mixture of dimethyl acetylenedicarboxylate

(0.245 mL, 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 the residue was purified by silica gel (Merck silica gel, 230–400 mesh) column chromatography using hexane:ethyl acetate (3:2) as an eluent. Two diastereomeric ylides were isolated. The solvent was removed under reduced pressure; ylides **3a–I** and **3a–II** were obtained as white powders.

First diastereomer **3a–I**, white powder, m.p. 170–171°C, yield 45%, IR (KBr) (υ_{max}, cm^{-1}): 1760, 1730 (C=O), 1631, 1485 (C=C), 1103 (C—O); MS, *m/z* (%): 532 (1), 405 (31), 347 (19), 277 (100), 262 (48), 77 (16).

Second diastereomer **3a–II**, white powder, m.p. 127.5–129.5°C, yield 35%, IR (KBr)(υ_{max}, cm^{-1}): 1766, 1730, 1720 (C=O), 1627, 1485 (C=C), 1103 (C—O); MS, *m/z* (%): 532 (M^+)(5), 405 (47), 347 (28), 277 (100), 262 (53), 77 (13).

Diethyl 2-(3-Acetyl-2-oxotetrahydro-3-furanyl)-3-(1,1,1-triphenyl-1^5-phosphanil-idene)-succinate(3b, $C_{32}H_{33}O_7P$)

First diastereomer **3b–I**, white powder, m.p. 171–172°C, yield 45%, IR (KBr)(υ_{max}, cm^{-1}): 1759, 1732, 1703 (C=O), 1630, 1482 (C=C), 1102 (C—O); MS, *m/z* (%): 560(M^+)(1), 433 (31), 361 (17), 333 (10), 278 (79), 262 (100), 183 (43), 43 (13).

Second diastereomer **3b–II**, white powder, m.p. 141–142°C, yield 30%, IR (KBr)(υ_{max}, cm^{-1}): 1754, 1718 (C=O), 1627, 1426 (C=C), 1109 (C—O); MS, *m/z* (%): 560 (M^+)(7), 433 (73), 361 (17), 333 (17), 277 (100), 262 (47), 183 (28), 43 (77).

Di-tert-butyl 2-(3-Acetyl-2-oxotetrahydro-3-furanyl)-3-(1,1,1-triphenyl-1^5-phosph-anilidene)-succinate(3c, $C_{36}H_{41}O_7P$)

First diastereomer **3C–I**, white powder, m.p. 150–152°C, yield 40%, IR(KBr)(υ_{max}, cm^{-1}): 1759, 1722 (C=O), 1629, 1477 (C=C), 1101 (C—O); MS, *m/z* (%): 616 (M^+)(4), 277 (100), 262 (69), 227 (24), 209 (24), 183 (48), 57 (100).

Second diastereomer **3C–II**, white powder, m.p. 142–144°C, yield 30%; IR (KBr)(υ_{max}, cm^{-1}) 1758, 1726, 1708 (C=O), 1628, 1481 (C=C), 1122 (C—O); MS, *m/z* (%): 616 (M^+)(2), 278 (38), 277 (100), 262 (47), 183 (62), 77 (28), 57 (35), 43 (28).

Preparation of Dimethyl (E)-2-{1-[2-Oxodihydro-3(2H)-furaniliden]ethyl}-2-butenedioate (5a, $C_{12}H_{14}O_6$)

Compound **3a** (**I** or **II**) was refluxed in benzene for 24 h. The solvent was removed under reduced pressure and the viscous residue was purified

by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using of ethyl acetate: hexane (3:2). The solvent was removed under reduced pressure and the product was obtained from recrystallisation from ether.

5a

White powder, m.p. 82–84°C, yield 75%, IR(KBr)(υ_{max}, cm^{-1}): 1753, 1716, and 1670 (C=O), 1623 and 1483 (C=C), 1105 (C–O), MS, *m/z* (%): 254 (M^+)(3), 223 (29), 195 (100), 163 (24).

Diethyl (E)-2-1-[2-Oxodihydro-3(2H)furaniliden]ethyl-2-butenedioate (5b, $C_{14}H_{18}O_6$)

White powder, m.p. 70.2–73°C, yield 70%, IR(KBr)(υ_{max}, cm^{-1}): 1750, 1722, 1667 (C=O), 1639, 1482 (C=C), 1177 (C–O); MS, *m/z* (%): 282 (M^+)(1), 237 (35), 209 (100), 181 (27), 163 (16).

Di-Tert-butyl (E)-2-1-[2-Oxodihydro-3(2H)furaniliden]ethyl-2-butenedioate (5c, $C_{18}H_{26}O_6$)

White powder, m.p. 74–76°C, yield 70%, IR(KBr)(υ_{max}, cm^{-1}): 1742, 1718, 1679 (C=O), 1626, 1476 (C=C), 1108 (C–O); MS, *m/z* (%): 338 (M^+)(4), 283 (16), 227 (41), 209 (32), 181 (100), 164 (21), 57 (41).

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