Supplemental Material

An efficient synthesis of 3-pyrrolin-2-one derivatives in aqueous media

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Typical procedure for the synthesis of 3-pyrrolin-2-ones 3a-i: A mixture of benzaldehyde (0.1 ml, 1 mmol) and aniline (0.1 ml, 1 mmol) in 50% aq EtOH (2 ml) was stirred for 1h. Next, dimethyl acetylenedicarboxylate (0.12 ml, 1 mmol) was added. The mixture was stirred until completion of the reaction as indicated by TLC (15 h). The sticky precipitated solid was filtered, washed with H₂O and recrystallized from EtOH. Compound **3a** was obtained as white crystals.

1,5-Diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3a)

White crystals; mp 187-189°C (Lit.¹⁶ 180-182); Yield: 0.269 g (87%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3209, 1702, 1679, 1597, 1498, 1381, 1232, 1201, 1135. ¹H NMR (400 MHz, CDCl₃) δ : 3.77 (3H, s, OCH₃), 5.76 (1H, s, CH), 7.11–7.49 (10H, m, CH_{arom}), 8.97 (1H, br s, OH) ppm. ¹³C NMR (100 MHz, CDCl₃) δ : 52.11 (CH₃ ester), 61.62 (CH), 112.87 (C), 122.39 (CH), 125.97 (CH), 127.47 (CH), 128.61 (CH), 128.71 (CH), 129.01 (CH), 134.97 (C), 136.17 (C), 156.28 (=COH), 162.80 (CO), 165.33 (CO) ppm. Anal. Calcd. for C₁₈H₁₅NO₄: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.70; H, 4.89; N, 4.56.

1,5-Diphenyl-3-hydroxy-4-ethoxycarbonyl-3-pyrrolin-2-one (3b)

Pale brown crystals, mp 159-161°C (Lit.¹⁶ 163-165); IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3294, 1716, 1684, 1655, 1595, 1498, 1381, 1472, 1389, 1188, 1138, 920. ¹H NMR (400 MHz, CDCl₃) δ : 1.20 (3H, t, CH₃ ester), 4.21 (2H, q, CH₂ ester), 5.76 (1H, s, CH), 7.11–7.51 (10H, m, CH_{arom}), 9.13 (1H, br s, OH) ppm. ¹³C NMR (100 MHz, CDCl₃) δ : 13.95 (CH₃ ester), 61.29 (CH₂ ester), 61.57 (CH), 113.18 (C), 122.30 (CH), 122.75 (C), 125.86 (CH), 127.55 (CH), 128.61 (CH), 128.99 (CH), 135.09 (C), 136.28 (CH), 156.56 (=COH), 162.88 (CO), 165.19 (CO) ppm.

1-Phenyl-5-(2-chlorophenyl)-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3c)

White crystals, mp 200-202°C; IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3300, 1718, 1686, 1656, 1595, 1500, 1454, 1366, 1320, 1257, 1129; ^1H NMR (400 MHz, CDCl_3) δ : 3.76 (3H, s, OCH_3), 6.47 (1H, s, CH), 6.98–7.55 (9H, m, CH_{arom}), 9.11 (1H, br s, OH) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ : 52.17(CH_3 ester), 56.57 (CH), 112.73 (C), 121.75 (CH), 125.97 (CH), 126.88 (CH), 127.55 (CH), 129.10 (CH), 129.74 (CH), 129.84 (CH), 132.60 (C), 134.94 (C), 135.96 (C), 156.92 ($=\text{COH}$), 162.75 (CO), 165.32 (CO) ppm. Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{ClNO}_4$: C, 62.89; H, 4.10; N, 4.07. Found: C, 63.04; H, 4.10; N, 4.15.

1-Phenyl-5-(2-bromophenyl)-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3d)

White crystals, mp 202-204°C; IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3293, 1716, 1686, 1656, 1595, 1500, 1499, 1453, 1366, 1321, 1215, 1133; ^1H NMR (400 MHz, CDCl_3) δ : 3.74 (3H, s, OCH_3), 6.41 (1H, s, CH), 6.93–7.52 (9H, m, CH_{arom}), 9.04 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 52.12(CH_3 ester), 59.43 (CH), 112.80 (C), 122 (CH), 125.51 (C), 126 (CH), 127.11 (CH), 128.16 (CH), 129.08 (CH), 130(CH), 133.16 (CH), 134.16 (C), 135.94 (C), 157.01 ($=\text{COH}$), 162.70 (CO), 165.39 (CO) ppm; Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{BrNO}_4$: C, 55.69; H, 3.63; N, 3.61. Found: C, 55.94; H, 3.44; N, 3.70.

1-Phenyl-5-o-tolyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3e)

White crystals, mp 190-192°C; IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3290, 1716, 1686, 1650, 1595, 1498, 1452, 1364, 1319, 1255, 1198, 1122; ^1H NMR (400 MHz, CDCl_3) δ : 2.58 (3H, s, CH_3), 3.76 (3H, s, OCH_3), 6.07 (1H, s, CH), 6.92–7.44 (9H, m, CH_{arom}), 9.03 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 19.32(CH_3), 52.12(CH_3 ester), 57.13 (CH), 113.44 (C), 122.55 (2CH), 125.08 (C), 126.20 (CH), 126.67 (CH), 128.26 (C), 129.08 (2CH), 130.81 (C), 132.92 (CH), 136.30

(CH), 136.85 (CH), 156.49 (=COH), 163.12 (CO), 165.26 (CO) ppm; Anal. Calcd. for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.71; H, 5.29; N, 4.43.

1-Phenyl-5-m-tolyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3f)

White crystals, mp 160-162°C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3290, 1715, 1682, 1661, 1596, 1494, 1455, 1379, 1324, 1247, 1214, 1007; ^1H NMR (400 MHz, CDCl_3) δ : 2.29 (3H, s, CH_3), 3.77 (3H, s, OCH_3), 5.72 (1H, s, CH), 7.00–7.50 (9H, m, CH_{arom}), 8.98 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 21.41(CH_3), 52.11 (CH_3 ester), 61.61 (CH), 112.97 (C), 122.34 (2CH), 124.89 (CH), 125.92 (CH), 127.71 (CH), 128.49 (CH), 128.99 (2CH), 129.43 (CH), 134.83 (C), 136.26 (C), 138.43 (C), 156.11 (=COH), 162.90 (CO), 165.31 (CO) ppm.

1-Phenyl-5-(2-methoxyphenyl)-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3g)

White crystals, mp 166-168°C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3420, 1722, 1691, 1663, 1597, 1496, 1438, 1380, 1246, 1215, 1187; ^1H NMR (400 MHz, CDCl_3) δ : 3.75 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 5.73 (1H, s, CH), 6.75–7.50 (9H, m, CH_{arom}), 8.99 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 52.14(OCH_3), 52.25(OCH_3), 61.51 (CH), 112.76 (C), 113.08 (CH), 113.81 (CH), 120 (CH), 122.36 (CH), 125.98 (CH), 129.03 (CH), 129.70 (CH), 136.19 (C), 136.55 (C), 156.34 (C), 159.74 (=COH), 162.77 (CO), 165.37 (CO) ppm; Anal. Calcd. for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.01; H, 4.67; N, 4.39.

1-Phenyl-5-(3-methoxyphenyl)-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3h)

White crystals, mp 168-170°C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3420, 1715, 1682, 1661, 1596, 1494, 1435, 1379, 1246, 1214, 1163; ^1H NMR (400 MHz, CDCl_3) δ : 3.75 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 5.73 (1H, s, CH), 6.74–7.50 (9H, m, CH_{arom}), 9.01 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 52.14(OCH_3), 52.25(OCH_3), 61.52 (CH), 112.77 (C), 113.09 (CH), 113.81 (CH), 120.00 (CH), 122.36 (CH), 125.98 (CH), 129.03 (CH), 129.70 (CH), 136.20 (C), 136.55

(C), 156.32 (C), 159.74 (=COH), 162.77 (CO), 165.36 (CO) ppm; Anal. Calcd. for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.16; H, 5.02; N, 4.15.

1-(4-chlorophenyl)-5-phenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one (3i)

($C_{18}H_{14}ClNO_4 \cdot 0.5EtOH$), White crystals, mp 151-153°C (Lit.¹⁶ 144-146 for $C_{18}H_{14}ClNO_4$); IR (KBr) (ν_{max}/cm^{-1}): 3393, 1721, 1693, 1659, 1495, 1375, 1222, 1191, 1132; 1H NMR (400 MHz, $CDCl_3$) δ : 3.75 (3H, s, OCH_3), 5.72 (1H, s, CH), 7.21–7.46 (9H, m, CH_{arom}), 9.27 (1H, br s, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ : 52.13(CH_3 ester), 61.65 (CH), 113.04 (C), 123.34 (CH), 127.43 (CH), 128.78 (CH), 128.83 (CH), 129.12 (CH), 131.24 (C), 134.68 (C), 134.77 (C), 155.56 (=COH), 163.11 (CO), 164.94 (CO) ppm; Anal. Calcd. for $C_{18}H_{14}ClNO_4 + EtOH$: C, 61.62; H, 5.17; N, 3.59. Found: C, 61.69; H, 4.93; N, 3.79.

BRUKER

NAME: Tartlyyat neolen
 EXPNO: 1
 PROCNO: 20120905
 Date_: 8.23
 Time: 18.23
 INSTRUM: spect
 PROBRD: 5 mm PMAH0 3H-
 PULPROG: zgpg30
 TO: 65536
 SOLVENT: CDCl3
 NS: 20
 DS: 0
 SWH: 8012.820 Hz
 F1: 0.122766 Hz
 AQ: 4.0894966 sec
 RG: 1280
 DB: 62.400 Hz
 DR: 6.50 Hz
 TR: 294.6 sec
 D1: 6.00000000 sec
 TD0: 1

--- CHANNEL F1 ---
 NU1: 1H
 P1: 14.00 Hz
 PL1: -2.00 dB
 F1: 11.86359406 MHz
 SFO1: 400.2236020 MHz
 SI: 32768
 SF: 400.2200000 MHz
 M1: 32
 SSB: 0
 GB: 0.30 Hz
 PC: 1.00

3a-¹H-NMR(CDCl₃)

3a- ^{13}C -NMR(CDCl_3)

BRUKER

NAME: Tarbiyat_moslem
EXPNO: 280
PROCNO: 1
Date_: 20120918
Time: 9.40
INSTRUM: spect
PROBHD: 5 mm PASYPO 1H-
PULPROG: zg
TD: 65536
F2: 500.13
SOLVENT: CDCl3
NS: 20
DS: 0
SWH: 8012.820 Hz
FIDRES: 0.122266 Hz
AQ: 4.0894966 sec
RG: 512
DM: 62.400
DC: 6.50
W: 294.4 K
D1: 6.00000000 sec
T0: 1

NAME: 3b
EXPNO: 1
PROCNO: 1
Date_: 20120918
Time: 9.40
INSTRUM: spect
PROBHD: 5 mm PASYPO 1H-
PULPROG: zg
TD: 65536
F2: 500.13
SOLVENT: CDCl3
NS: 20
DS: 0
SWH: 8012.820 Hz
FIDRES: 0.122266 Hz
AQ: 4.0894966 sec
RG: 512
DM: 62.400
DC: 6.50
W: 294.4 K
D1: 6.00000000 sec
T0: 1

NAME: 3b
EXPNO: 1
PROCNO: 1
Date_: 20120918
Time: 9.40
INSTRUM: spect
PROBHD: 5 mm PASYPO 1H-
PULPROG: zg
TD: 65536
F2: 500.13
SOLVENT: CDCl3
NS: 20
DS: 0
SWH: 8012.820 Hz
FIDRES: 0.122266 Hz
AQ: 4.0894966 sec
RG: 512
DM: 62.400
DC: 6.50
W: 294.4 K
D1: 6.00000000 sec
T0: 1

3b- ¹H-NMR(CDCl₃)

9

3c- ^{13}C -NMR(CDCl_3)

Ahmad1 IE37 CDCl3 91/4/3

ppm

0.0000
1.6125

Current Data Parameters
NAME Khordad-91
EXPNO 155
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120623
Time 5.34

INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG zg

TD 32768
SOLVENT CDCl3

NS 115
DS 0

SMH 11990.407 Hz
FIDRES 0.385918 Hz

AQ 1.3664756 sec
RG 256

DM 41.700 usec
DE 6.00 usec

TE 300.0 K
D1 5.00000000 sec

CHNCL F1 1H

P1 11.00 usec
PL1 -1.00 dB

SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768

SF 400.1300163 MHz
WDW EM

SSB 0
LB 0.30 Hz

GB 0
PC 1.00

10 NMR plot parameters
CX 20.00 cm

F1P 16.000 ppm
F1 6402.08 Hz

F2P -4.000 ppm
F2 -1600.52 Hz

PPMCH 1.00000 ppm/cm
HZCH 400.13000 Hz/cm

3d- ¹H-NMR(CDCl₃)

3e- ^{13}C -NMR(CDCl_3)

BRÜKER	
NAME	Tarbutyl acetate
EXPNO	282
PROCNO	1
Date_	20120918
Time	10.03
INSTRUM	400M
PROBHD	5 mm PABBO 1H-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	14
DS	0
SWH	8012.820 Hz
F2HRES	0.122256 Hz
AQ	4.0894966 sec
RG	1440
DM	62.400 mm
DR	6.50 mm
TR	294.4 K
D1	6.00000000 sec
T000	1
===== CHANNEL f1 =====	
NUC1	1H
PC1	14.00 mm
PT1	-2.00 dB
PL1	11.86359406 dB
SR01	400.2236020 MHz
SI	32768
SV	400.2200000 MHz
MIX	SM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

3f- ¹H-NMR(CDCl₃)

— 21.41

[illegible]

3f- ^{13}C -NMR(CDCl_3)

NAME	Yaribipat enol/en
EXPNO	275
PROCNO	1
DATE_	20120905
TIME	12.36
INSTRUM	spect
PROBHD	5 mm PABBO 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
RG	1000
DS	0
SWH	25252.545 Hz
FIDRES	0.385323 Hz
AQ	1.291629 sec
RG	2050
FW	19.800 MHz
DE	1.50 MHz
TE	294.2 K
D1	2.00000000 sec
D11	0.01000000 sec
TD0	1

NAME	Yaribipat enol/en
EXPNO	275
PROCNO	1
DATE_	20120905
TIME	12.36
INSTRUM	spect
PROBHD	5 mm PABBO 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
RG	1000
DS	0
SWH	25252.545 Hz
FIDRES	0.385323 Hz
AQ	1.291629 sec
RG	2050
FW	19.800 MHz
DE	1.50 MHz
TE	294.2 K
D1	2.00000000 sec
D11	0.01000000 sec
TD0	1

NAME	Yaribipat enol/en
EXPNO	275
PROCNO	1
DATE_	20120905
TIME	12.36
INSTRUM	spect
PROBHD	5 mm PABBO 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
RG	1000
DS	0
SWH	25252.545 Hz
FIDRES	0.385323 Hz
AQ	1.291629 sec
RG	2050
FW	19.800 MHz
DE	1.50 MHz
TE	294.2 K
D1	2.00000000 sec
D11	0.01000000 sec
TD0	1

3g- ¹³C-NMR(CDCl₃)

BRÜKER	
NAME	Tarbiyat nozaton
EXPNO	1
PROCNO	1
Date_	20120905
Time	8.53
INSTRUM	5 mm PABBO BH-
PROBHD	5 mm
PULPROG	zgpg30
TD	65536
F2	501.3
SOLVENT	CDCl3
RG	20
DS	0
SWH	8012.820 Hz
F100MHz	0.122266 Hz
AQ	4.0894966 sec
RG	1296
DM	62.400 usec
DE	6.50 usec
TE	294.6 K
D1	6.00000000 sec
TD0	1
----- CHANNEL f1 -----	
NUC1	1H
PC1	14.00 usec
PL1	-2.00 dB
PL10	11.86359406 dB
PRG1	400.2236020 MHz
ST	32768
SI	51
SR	400.2200000 MHz
MIX	9M
SE	0
SH	0.30 Hz
GB	0
PC	1.00

3h- ¹H-NMR(CDCl₃)

3h- ¹³C-NMR(CDCl₃)

3i- $^1\text{H-NMR}(\text{CDCl}_3)$

3i- ^{13}C -NMR(CDCl_3)