Supplementary Material for Organic & Biomolecular Chemistry

Electronic Supplementary Information

Simple and Facile Synthesis of Tetralone-Spiro-Glutarimides and Spiro-Bisglutarimides from the Baylis-Hillman Acetates

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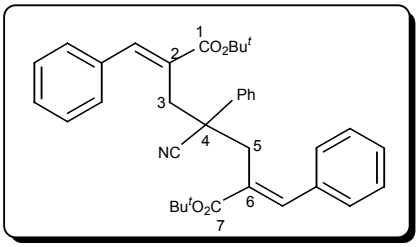
EXPERIMENTAL SECTION

General Methods: Melting points were recorded on a Superfit (India) capillary melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO-FT-IR model 5300 spectrometer using solid samples as KBr plates. ^{1}H NMR (400 MHz) and ^{13}C NMR (50 / 100 MHz) spectra were recorded in deuterochloroform ($CDCl_3$) or deuterodimethyl sulfoxide (DMSO-d_6) or in deuterochloroform ($CDCl_3$) containing deuterodimethyl sulfoxide (DMSO-d_6) on a Bruker-AVANCE-400 and Bruker-AC-200 spectrometer using tetramethylsilane (TMS, $\delta = 0$) as an internal standard. Elemental analyses were recorded on a Thermo-Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on Shimadzu-LCMS-2010 A mass spectrometer. The X-ray diffraction measurements were carried out at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å).

Di-*tert*-butyl 2,6-di[(*E*)-benzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2a):

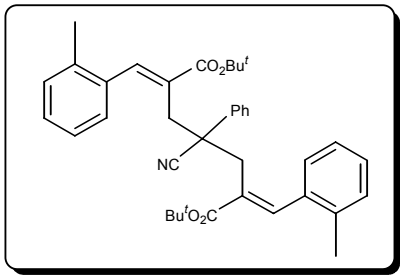


To a stirred suspension of oil free excess NaH (10 mmol, 0.24 g) in anhydrous toluene were added benzyl cyanide (2 mmol, 0.234 g) and *tert*-butyl 3-acetoxy-2-methylene-3-phenylpropanoate (**1a**) (5 mmol, 1.38 g) at room temperature and heated under reflux for 1 h in N_2 atmosphere. Then the reaction mixture was allowed to come to room temperature and cooled to 0 ^{o}C. Excess NaH was carefully quenched with very slow addition of water at 0 ^{o}C. Reaction mixture was extracted with ether (3 X 30 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The residue, thus obtained, was purified by column chromatography (5% ethyl acetate in hexanes) followed by crystallization (from 3% ethyl acetate in hexanes at 0 ^{o}C)$^{\#}$ to afford the di-*tert*-butyl 2,6-di[(*E*)-benzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (**2a**), as a colorless solid in 73% (0.80 g) yield**;** mp: 118-120 ^{o}C; IR (KBr): ν 2235,

1711, 1635 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 18H), 3.09 & 3.34 (ABq, 4H, J = 13.6 Hz), 6.98-7.38 (m, 15H), 7.62 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 28.00, 35.95, 48.28, 81.34, 120.39, 126.53, 127.50, 128.04, 128.16, 128.42, 128.84, 130.27, 135.60, 137.54, 142.01, 166.94; LCMS (*m/z*): 548 $(M-H)^-$; Anal. Calcd. for $C_{36}H_{39}NO_4$: C, 78.66; H, 7.15; N, 2.55; Found: C, 78.67; H, 7.11; N, 2.64.

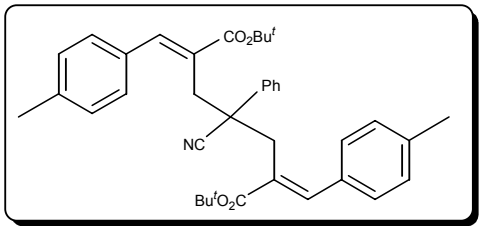
[#]The crude product contains 8% (*Z*)-isomer, as indicated by the ^1H NMR spectral analysis. However crystallization provides pure (*E*)-isomer. In the case of **2c-i,** crude compounds show the presence of 5-14% (*Z*)-isomer . However, crystallization (3% ethyl acetate in hexanes for **2b-g** and 8% ethyl acetate in hexanes for **2h** & **2i**), provides the pure (*E*)-isomer. In the case of **2b,** ^1H NMR of the crude product did not show the presence of any (*Z*)-isomer.

Di-*tert*-butyl 2,6-di[(*E*)-2-methylbenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2b):



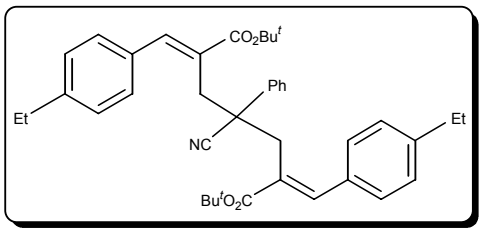
Yield: 81%; mp: 127-129 ^oC; IR (KBr): ν 2237, 1718, 1628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.50 (s, 18H), 1.92 (s, 6H), 2.98 & 3.14 (ABq, 4H, J = 13.6 Hz), 6.82-6.92 (m, 6H), 6.98-7.22 (m, 7H), 7.62 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.73, 27.97, 35.42, 47.84, 81.34, 120.10, 125.49, 126.09, 127.14, 127.99, 130.12, 130.29, 134.88, 137.11, 137.28, 141.67, 166.70; LCMS (*m/z*): 578 $(M+H)^+$; Anal. Calcd. for $C_{38}H_{43}NO_4$: C, 79.00; H, 7.50; N, 2.42; Found: C, 79.05; H, 7.49; N, 2.41.

Di-*tert*-butyl 2,6-di[(*E*)-4-methylbenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2c):



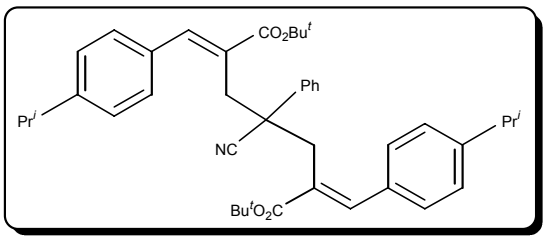
Yield: 80%; mp: 124-126 ^{o}C; IR (KBr): ν 2235, 1709, 1635 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 18H), 2.35 (s, 6H), 3.12 & 3.38 (ABq, 4H, J = 13.6 Hz), 6.96-7.13 (m, 11H), 7.16-7.21 (m, 2H), 7.60 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.33, 27.97, 36.03, 48.45, 81.12, 120.47, 126.60, 127.48, 128.11, 129.03, 129.10, 129.47, 132.64, 137.81, 138.08, 142.06, 167.14; LCMS (*m/z*): 576 $(M-H)^-$; Anal. Calcd. for $C_{38}H_{43}NO_4$: C, 79.00; H, 7.50; N, 2.42; Found: C, 78.91; H, 7.51; N, 2.46.

Di-*tert*-butyl 2,6-di[(*E*)-4-ethylbenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2d):



Yield: 78%**;** mp: 80-82 ^{o}C; IR(KBr): ν 2361, 1703, 1633 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, 6H, J = 7.6 Hz), 1.44 (s, 18H), 2.64 (q, 4H, J = 7.6 Hz), 3.13 & 3.39 (ABq, 4H, J = 13.6 Hz), 6.98-7.22 (m, 13H), 7.60 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 15.43, 28.02, 28.68, 36.10, 48.45, 81.17, 120.49, 126.63, 127.45, 127.91, 128.08, 129.08, 129.49, 132.91, 137.79, 142.13, 144.38, 167.16; LCMS (*m/z*): 604 $(M-H)^-$; Anal. Calcd. for $C_{40}H_{47}NO_4$: C, 79.30; H, 7.82; N, 2.31; Found: C, 79.20; H, 7.82; N, 2.38.

Di-*tert*-butyl 2,6-di[(*E*)-4-isopropylbenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2e):



Yield: 72%; mp: 110-111 ^{o}C; IR (KBr): ν 2239, 1711, 1628 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (d, 12H, J = 6.8 Hz), 1.45 (s, 18H), 2.89 (sept, 2H, J = 6.8 Hz), 3.14 & 3.39 (ABq, 4H, J = 13.6 Hz), 6.97-7.07 (m, 7H), 7.08-7.19 (m, 6H), 7.60 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 23.90, 28.02, 33.94, 36.12, 48.45, 81.17, 120.47, 126.46, 126.60, 127.40, 128.04, 129.05, 129.47, 133.03, 137.74, 142.13, 148.97, 167.16; LCMS (*m/z*): 632 $(M-H)^-$; Anal. Calcd. for $C_{42}H_{51}NO_4$: C, 79.58; H, 8.11; N, 2.21; Found: C, 79.63; H, 8.13; N, 2.32; **Crystal data** for **2e**: empirical formula, $C_{42}H_{51}NO_4$; formula weight, 633.84;

crystal color, habit: colorless, rectangular; crystal dimensions, 0.41 X 0.28 X 0.16 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 11.799(2) Å, b = 14.900(3) Å, c = 21.767(4) Å; α = 90.00; β = 98.298(3); γ = 90.00; V = 3786.6(11) $Å^3$; space group, *P 21/n* (International Table No. 14); Z = 4; D_{calcd} = 1.112 g / cm^3; F_{000} = 1368; λ(Mo-K_α) = 0.71073 Å; R ($I \geq 2\sigma_1$) = 0.0580; wR^2 = 0.1491. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **2e** CCDC # 656194).

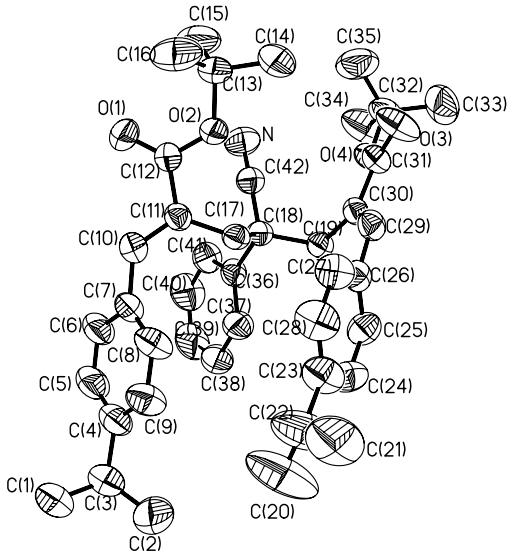
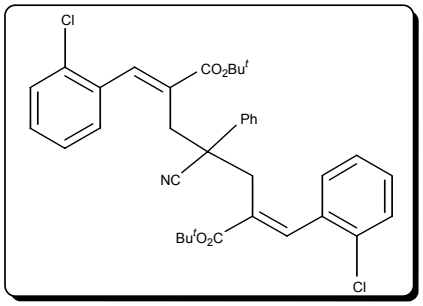


Figure 1 ORTEP diagram (50% probability) of compound **2e**
(Hydrogen atoms are omitted for clarity)

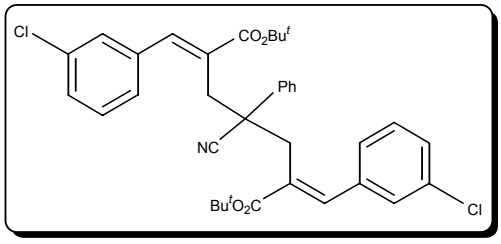
Di-*tert*-butyl 2,6-di[(*E*)-2-chlorobenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2f):



Yield: 70%; mp: 140-142 °C; IR (KBr): ν 2239, 1707, 1635 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.47 (s, 18H), 2.99 & 3.24 (ABq, 4H, J = 13.6 Hz), 6.95-7.10 (m, 7H), 7.12-7.32 (m, 6H), 7.63 (s, 2H); ^{13}C NMR

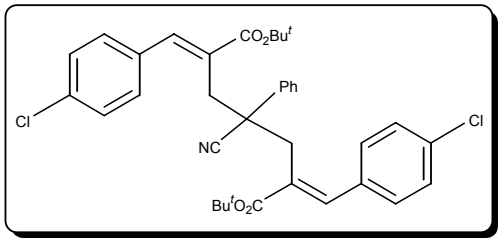
(50 MHz, $CDCl_3$): δ 28.00, 35.95, 47.67, 81.66, 120.10, 126.29, 126.51, 127.50, 128.25, 129.25, 129.71, 131.67, 134.15, 134.32, 136.86, 139.22, 166.34; LCMS (*m/z*): 640 $(M+Na)^+$, 642 $[(M+2)+Na]^+$, 644 $[(M+4)+Na]^+$; Anal. Calcd. for $C_{36}H_{37}Cl_2NO_4$: C, 69.90; H, 6.03; N, 2.26; Found: C, 69.75; H, 6.07; N, 2.34.

Di-*tert*-butyl 2,6-di[(*E*)-3-chlorobenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2g):



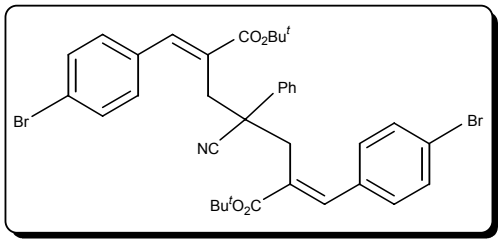
Yield: 65%; mp: 151-152 °C; IR (KBr): ν 2235, 1709, 1635 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.46 (s, 18H), 3.10 & 3.30 (ABq, 4H, J = 13.6 Hz), 6.92-7.25 (m, 13H), 7.54 (s, 2H); ^{13}C NMR (50MHz, $CDCl_3$): δ 27.97, 36.10, 48.20, 81.68, 120.13, 126.48, 126.70, 127.70, 128.06, 128.11, 128.62, 129.64, 131.41, 134.34, 136.94, 137.35, 140.33, 166.43; LCMS (*m/z*): 618 $(M+H)^+$, 620 $[(M+2)+H]^+$, 622 $[(M+4)+H]^+$; Anal. Calcd. for $C_{36}H_{37}Cl_2NO_4$: C, 69.90; H, 6.03; N, 2.26; Found: C, 69.72; H, 6.03; N, 2.22.

Di-*tert*-butyl 2,6-di[(*E*)-4-chlorobenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2h):



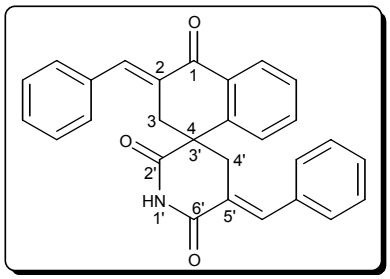
Yield: 66%; mp: 184-186 °C; IR (KBr): ν 2235, 1714, 1633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 18H), 3.09 & 3.13 (ABq, 4H, J = 13.6 Hz), 6.99 (d, 4H, J = 8.4 Hz), 7.04-7.18 (m, 5H), 7.23 (d, 4H, J = 8.4 Hz), 7.56 (s, 2H);^{13}C NMR (50 MHz, $CDCl_3$): δ 28.00, 36.20, 48.40, 81.61, 120.22, 126.60, 127.74, 128.28, 128.67, 130.17, 130.87, 133.98, 137.33, 140.67, 166.65; LCMS (*m/z*): 640 $(M+Na)^+$, 642 $[(M+2)+Na]^+$, 644 $[(M+4)+Na]^+$; Anal. Calcd. for $C_{36}H_{37}Cl_2NO_4$: C, 69.90; H, 6.03; N, 2.26; Found: C, 69.96; H, 5.99; N, 2.16.

Di-*tert*-butyl 2,6-di[(*E*)-4-bromobenzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (2i):



Yield: 63%; mp: 187-189 ^{o}C; IR (KBr): ν 2235, 1712, 1633 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 18H), 3.08 & 3.31 (ABq, 4H, J = 13.6 Hz), 6.92 (d, 4H, J = 8.4 Hz), 7.02-7.18 (m, 5H), 7.36 (d, 4H, J = 8.4 Hz), 7.53 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 27.97, 36.17, 48.33, 81.61, 120.18, 122.26, 126.58, 127.74, 128.28, 130.39, 130.92, 131.60, 134.41, 137.23, 140.67, 166.60; LCMS (*m/z*): 727 $(M+Na)^+$, 729 $[(M+2)+Na]^+$, 731 $[(M+4)+Na]^+$; Anal. Calcd. for $C_{36}H_{37}Br_2NO_4$: C, 61.12; H, 5.27; N, 1.98; Found; C, 61.29; H, 5.25; N, 1.98.

2,5′-Di[(*E*)-benzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3a):



To a stirred solution of di-*tert*-butyl 2,6-di[(*E*)-benzylidene]-4-cyano-4-phenyl-1,7-heptanedioate (**2a**) (0.5 mmol, 0.275 g) in 1,2-dichloroethane (DCE, 3 mL) were added conc. H_2SO_4 (2.5 mmol, 0.245 g, 0.13 mL) and tirfluoroacetic anhydride (TFAA, 2.5 mmol, 0.525 g, 0.35 mL) at room temperature. The reaction mixture was heated under reflux for 6 h and then allowed to cool to room temperature. Reaction mixture was poured into aqueous K_2CO_3 solution and extracted with EtOAc (3 X 25 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained was purified by column chromatography (30% ethyl acetate in hexanes) to provide, 2,5′-di[(*E*)-benzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (**3a**), as a colorless

solid in 80% (0.168 g) yield**;** mp: 184-186 ^{o}C; IR (KBr): ν 3300-2800 (multiple bands), 1711, 1693, 1651, 1624 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.08 (s, 2H), 3.38 & 3.48 (ABq, 2H, J = 14.8 Hz), 6.88 (d, 2H, J = 6.6 Hz), 7.13-7.41 (m, 9H), 7.43-7.51 (m, 1H), 7.53-7.62 (m, 1H), 7.72 (s, 1H), 7.85 (s, 1H), 8.20 (d, 1H, J = 7.2 Hz), 8.68 (s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.23, 36.15, 48.25, 124.07, 126.64, 128.64, 128.67, 129.10, 129.17, 129.42, 129.55, 129.74, 129.87, 132.58, 133.63, 133.90, 134.60, 140.29, 142.49, 166.30, 174.45, 185.72; LCMS (*m/z*): 420 $(M+H)^+$; Anal. Calcd. for $C_{28}H_{21}NO_3$: C, 80.17; H, 5.05; N, 3.34; Found: C, 80.27; H, 5.00; N, 3.35; **Crystal data** for **3a**: empirical formula, $C_{28}H_{21}NO_3$; formula weight, 419.46; crystal color, habit: colorless, block; crystal dimensions, 0.44 X 0.28 X 0.22 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 9.0369(18) Å, b = 25.751(5) Å, c = 9.2740(18) Å; α = 90.00; β = 96.108(3); γ = 90.00; V = 2145.9(7) Å^3; space group, *P21/n* (International Table No. 14); Z = 4; D_{calcd} = 1.298 g / cm^3; F_{000} = 880; λ(Mo-K_α) = 0.71073 Å; R ($I \geq 2\sigma_1$) = 0.0427; wR^2 = 0.1031. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **3a** CCDC # 656195).

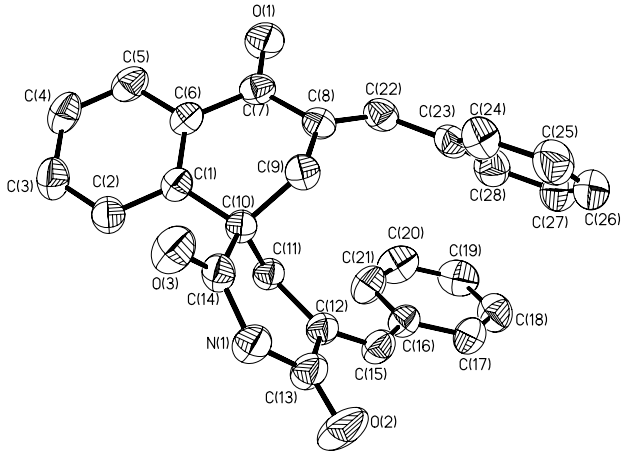
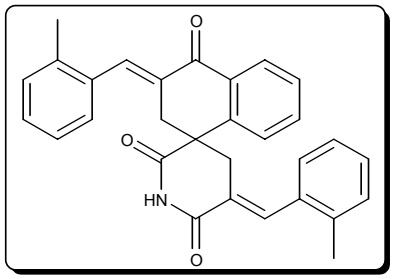


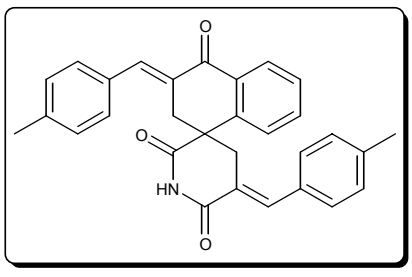
Figure 2 ORTEP diagram (50% probability) of compound **3a**
(Hydrogen atoms are omitted for clarity)

2,5′-Di[(*E*)-2-methylbenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3b):



Yield: 75%; mp: 232-234 ^{o}C; IR (KBr): ν 3300-2800 (multiple bands), 1718, 1684, 1650, 1624 cm^{-1}; ^{1}H NMR (400 MHz, 50 % DMSO-d_6 in $CDCl_3$): δ 1.92 (s, 3H), 2.05 (s, 3H), 2.87 & 3.36 (ABq, 2H, J = 15.0 Hz)*, 3.00-3.12 (m, 2H), 6.73 (d, 1H, J = 7.5 Hz), 7.00-7.36 (m, 8H), 7.44-7.52 (m, 1H), 7.55-7.65 (m, 1H) 7.71 (s, 1H), 7.81 (s, 1H), 8.10 (d, 1H, J = 7.6 Hz), 11.21 (br s, 1H) ; ^{13}C NMR (100 MHz, 50% DMSO-d_6 in $CDCl_3$): δ 18.16, 18.34, 33.90, 33.98, 46.01, 124.21, 124.30, 125.17, 126.75, 126.88, 126.99, 127.06, 127.61, 127.69, 128.83, 128.96, 129.31, 131.24, 131.57, 132.24, 135.96, 136.31, 136.39, 137.92, 141.62, 165.04, 173.07, 184.00; LCMS (*m/z*): 448 $(M+H)^{+}$; Anal. Calcd. for $C_{30}H_{25}NO_3$: C, 80.51; H, 5.63; N, 3.13; Found: C, 80.55; H, 5.61; N, 3.16; *[*One of the doublets (second part) of the AB quartet arising from one of the methylenes (two protons) partly merges with moisture peak in DMSO-d_6 at δ 3.27. When we recorded in the presence of Eu(fod)$_3$ as a shift reagent, a multiplet at δ 2.84-3.15 for two methylenes (four protons) was observed].*

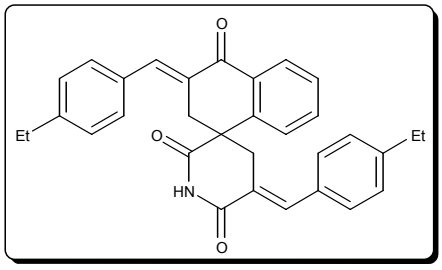
2,5′-Di[(*E*)-4-methylbenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3c):



Yield: 77%; mp: 227-229 ^{o}C; IR (KBr): ν 3200-2950 (multiple bands), 1718, 1674, 1655, 1618 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H), 2.39 (s, 3H), 3. 08 (s, 2H), 3.39 & 3.48 (ABq, 2H, J = 14.9 Hz),

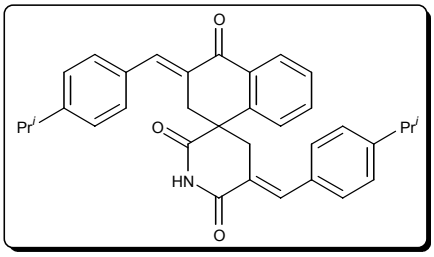
6.81 (d, 2H, *J* = 7.6 Hz), 7.04-7.34 (m, 7H), 7.44-7.51 (m, 1H), 7.53-7.61 (m, 1H), 7.70 (s, 1H), 7.85 (s, 1H), 8.20 (d, 1H, *J* = 7.6 Hz), 8.41 (s, 1H, D_2O exachangeable); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.47, 21.53, 35.34, 36.23, 48.25, 123.16, 126.59, 128.61, 129.08, 129.38, 129.41, 129.58, 130.00, 130.88, 131.83, 132.67, 133.82, 139.52, 139.98, 140.50, 142.51, 142.66, 166.56, 174.61, 185.89; LCMS (*m/z*): 448 $(M+H)^+$; Anal. Calcd. for $C_{30}H_{25}NO_3$: C, 80.51; H, 5.63; N, 3.13; Found: C, 80.66; H, 5.62; N, 3.16.

2,5′-Di[(*E*)-4-ethylbenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3d):



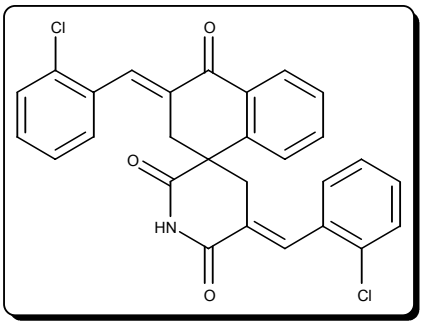
Yield: 78%; mp: 150-152 °C; IR (KBr): ν 3200-2800 (multiple bands), 1714, 1684, 1650, 1630 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.10-1.38 (m, 6H), 2.55-2.81 (m, 4H), 3.10 (s, 2H), 3.41 & 3.49 (ABq, 2H, *J* = 14.6 Hz), 6.83 (d, 2H, *J* = 7.6 Hz), 7.05-7.34 (m, 7H), 7.42-7.51 (m, 1H), 7.52-7.61 (m, 1H), 7.71 (s, 1H), 7.85 (s, 1H), 8.21 (d, 1H, *J* = 7.6 Hz), 8.66 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.30, 15.38, 28.77, 28.83, 35.29, 36.19, 48.29, 123.07, 126.59, 128.18, 128.22, 128.61, 129.01, 129.05, 129.68, 130.08, 131.07, 132.03, 132.65, 133.82, 140.49, 142.50, 142.65, 145.75, 146.23, 166.53, 174.59, 185.93; LCMS (*m/z*): 476 $(M+H)^+$; Anal. Calcd. for $C_{32}H_{29}NO_3$: C, 80.82, H, 6.15, N, 2.95; Found: C, 80.84; H, 6.19; N, 2.91.

2,5′-Di[(*E*)-4-isopropylbenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3e):



Yield: 75%; mp: 179-180 ^{o}C; IR (KBr): ν 3250-2900 (multiple bands), 1718, 1693, 1652, 1628 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22-1.32 (m, 12H), 2.82-3.00 (m, 2H), 3.12 (s, 2H), 3.33-3.59 (m, 2H), 6.84 (d, 2H, J = 6.5 Hz), 7.03-7.34 (m, 7H), 7.41-7.51 (m, 1H), 7.52-7.62 (m, 1H), 7.70 (s, 1H), 7.84 (s, 1H), 8.21 (d, 1H, J = 6.7 Hz), 8.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.81, 34.05, 34.09, 35.26, 36.15, 48.32, 123.01, 126.62, 126.75, 126.81, 128.61, 128.99, 129.03, 129.75, 130.11, 131.19, 132.15, 133.82, 140.45, 142.54, 142.59, 150.29, 150.80, 166.62, 174.64, 185.98; LCMS (*m/z*); 504 $(M+H)^+$; Anal. Calcd. for $C_{34}H_{33}NO_3$: C, 81.08; H, 6.60; N, 2.78; Found: C, 81.18; H, 6.61; N, 2.81.

2,5′-Di[(*E*)-2-chlorobenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3f):



Yield: 82%; mp: 187-189 ^{o}C; IR (KBr): ν 3200-3050 (multiple bands), 1720, 1680, 1612 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.83 & 3.53 (ABq, 2H, J = 14.4 Hz), 3.05 & 3.09 (2s, 2H), 6.64 (d, 1H, J = 5.8 Hz), 7.08-7.64 (m, 10H), 7.89 (s, 1H), 7.97 (s, 1H), 8.21 (d, 1H, J = 6.3 Hz), 8.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.70, 36.12, 47.92, 125.79, 126.12, 126.75, 128.83, 129.31, 129.52, 129.93, 129.98, 130.12, 130.28, 130.67, 131.79, 132.09, 132.23, 133.34, 134.05, 134.59, 134.85, 137.15, 139.69, 142.22, 165.83, 173.97, 185.35; LCMS (*m/z*): 488 $(M+H)^+$, 490 $[(M+2)+H]^+$, 492 $[(M+4)+H]^+$; Anal. Calcd. for $C_{28}H_{19}Cl_2NO_3$: C, 68.86; H, 3.92; N, 2.87; Found: C, 68.80; H, 3.90; N, 2.98; **Crystal data** for **3f**: empirical formula, $C_{28}H_{19}Cl_2NO_3$; formula weight, 488.34; crystal color, habit: colorless, plate; crystal dimensions, 0.41 X 0.22 X 0.18 mm^3; crystal system, triclinic; lattice type, primitive; lattice parameters, a = 9.0278(7) Å, b = 10.5146(9) Å, c = 13.4184(11) Å; α = 79.220(1); β = 75.225(1); γ = 72.025(1); V = 1163.34(16) Å^3; space group, *P-1* (International Table No. 2); Z = 2; D_{calcd} = 1.394 g / cm^3; F_{000} = 504;

λ(Mo-K_α) = 0.71073 Å; R $(I \geq 2\sigma_1)$ = 0.0412; wR^2 = 0.1006. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **3f** CCDC # 656196).

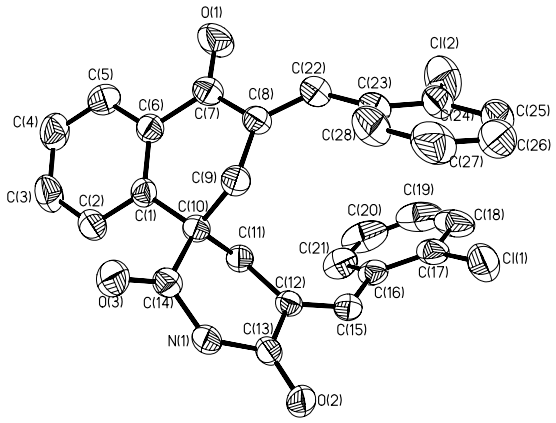
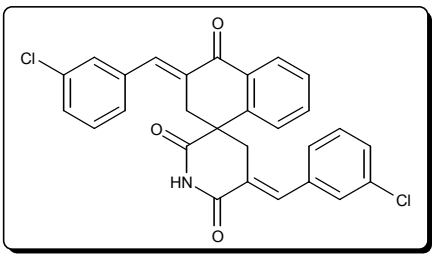


Figure 3 ORTEP diagram (50% probability) of compound **3f**
(Hydrogen atoms are omitted for clarity)

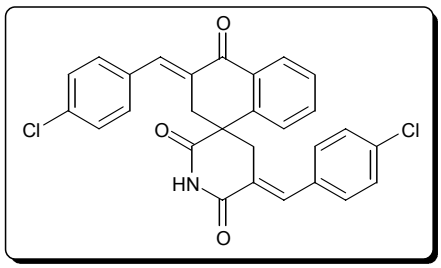
2,5′-Di[(*E*)-3-chlorobenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3g):



Yield: 67%; mp: 229-231 ^{o}C; IR (KBr): ν 3300-2950 (multiple bands), 1714, 1697, 1666, 1628 cm^{-1}; ^{1}H NMR (400 MHz, 66.6% DMSO-d_6 in $CDCl_3$): δ 3.08 & 3.42 (ABq, 2H, J = 15.4 Hz), 3.17-3.29 (m, 2H),* 7.00-7.70 (m, 13H), 8.06 (d, 1H, J = 7.6 Hz), 11.36 (s, 1H); ^{13}C NMR (100 MHz, 66.6% DMSO-d_6 in $CDCl_3$): δ 32.98, 33.39, 45.08, 124.72, 125.69, 125.81, 126.28, 126.34, 126.48, 126.93, 127.01, 127.09, 127.47, 128.40, 128.42, 130.32, 130.75, 131.69, 131.72, 131.92, 134.14, 134.28, 134.75, 135.85, 140.89, 164.01, 172.16, 183.15; LCMS (*m/z*): 486 $(M-H)^-$, 488 $[(M+2)-H]^-$, 490 $[(M+4)-H]^-$; Anal. Calcd. for $C_{28}H_{19}Cl_2NO_3$: C, 68.86; H, 3.92; N, 2.87; Found: C, 68.73; H, 3.93; N, 2.83; *[*One of the methylenes*

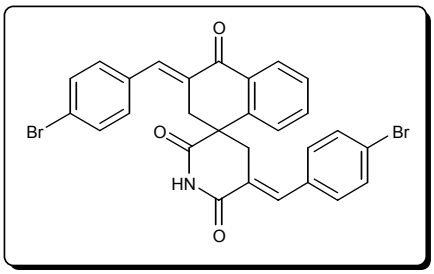
(two protons) appears as multiplet at δ 3.17-3.29 which partly merges with moisture peak in DMSO-d_6 at δ 3.32].

2,5′-Di[(*E*)-4-chlorobenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3h):



Yield: 77%; mp: 236-238 ^{o}C; IR (KBr): ν 3300-3000 (multiple bands), 1712, 1685, 1652, 1626 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.04 (s, 2H), 3.33 & 3.47 (ABq, 2H, J = 14.8 Hz), 6.82 (d, 2H, J = 7.3 Hz), 7.08-7.40 (m, 7H), 7.41-7.54 (m, 1H), 7.55-7.63 (m, 1H), 7.66 (s, 1H), 7.80 (s, 1H), 8.21 (d, 1H, J = 7.2 Hz), 8.35 (s, 1H); ^{13}C NMR (100 MHz, 50% DMSO-d_6 in $CDCl_3$): δ 34.00, 34.45, 46.35, 124.84, 125.57, 127.20, 127.27, 127.54, 129.55, 129.76, 129.98, 131.23, 131.31, 131.90, 132.60, 133.36, 133.50, 136.25, 137.64, 141.61, 165.06, 173.21, 184.11; LCMS (*m/z*): 488 $(M+H)^+$, 490 $[(M+2)+H]^+$, 492 $[(M+4)+H]^+$; Anal. Calcd. for $C_{28}H_{19}Cl_2NO_3$: C, 68.86; H, 3.92; N, 2.87; Found: C, 68.66; H, 3.95; N, 2.86.

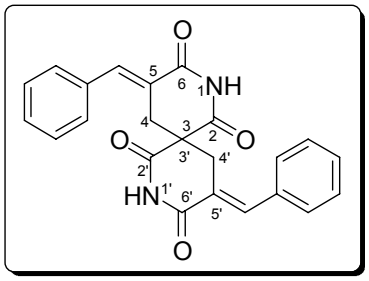
2,5′-Di[(*E*)-4-bromobenzylidene]-[1,2,3,4-tetrahydronaphthalen-1-one]-4-spiro-3′-[piperidine-2′,6′-dione] (3i):



Yield: 71%; mp: 233-235 ^{o}C; IR (KBr): ν 3300-3050 (multiple bands), 1707, 1684, 1650, 1620 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (s, 2H), 3.33 & 3.46 (ABq, 2H, J = 15.0 Hz), 6.74 (d, 2H, J = 8.4 Hz), 7.05 (d, 2H, J = 8.4 Hz), 7.24-7.54 (m, 6H), 7.56-7.73 (m, 1H), 7.64 (s, 1H), 7.78 (s, 1H), 8.22 (d, 1H, J =

7.8 Hz), 8.28 (s, 1H); ^{13}C NMR (100 MHz, 50% DMSO-d_6 in $CDCl_3$): δ 33.98, 34.41, 46.32, 121.78, 121.92, 124.91, 125.56, 127.19, 127.24, 129.75, 129.84, 130.18, 130.46, 131.29, 131.63, 132.30, 132.59, 136.24, 137.63, 141.60, 165.03, 173.18, 184.10; LCMS (*m/z*): 574 $(M-H)^-$, 576 $[(M+2)-H]^-$, 578 $[(M+4)-H]^-$; Anal. Calcd. for $C_{28}H_{19}Br_2NO_3$: C, 58.26; H, 3.32; N, 2.43; Found: C, 58.38; H, 3.33; N, 2.44.

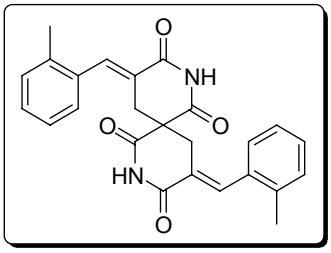
3,3′-Spiro-bis[5-{(*E*)-benzylidene}piperidine-2,6-dione] (4a):



To a stirred solution of *tert*-butyl 3-acetoxy-2-methylene-3-phenylpropanoate (**1a**) (2 mmol, 0.552 g) in acetonitrile (3 mL) were added malononitrile (1 mmol, 0.066 g, 0.06 mL) and triethyl amine (1 mmol, 0.131 mL). After stirring at room temperature for 1 h, solvent acetonitrile and Et_3N were evaporated under the reduced pressure. The resulting residue was diluted with dichloromethane (5 mL) and cooled to 0 ^oC. To this solution at 0 ^oC conc. H_2SO_4 (2 mmol, 0.192 g, 0.10 mL) and trifluoroacetic anhydride (TFAA, 2 mmol, 0.42 g, 0.28 mL) were added. Then the reaction mixture was allowed to warm to room temperature. After stirring for 24 h at room temperature the reaction mixture was poured into aqueous K_2CO_3 solution. The solid separated was filtered and well washed with water followed by ethyl acetate. Thus the obtained solid was dried under *vaccuo,* to provide pure 3,3′-spiro-bis[5-{(*E*)-benzylidene}piperidine-2,6-dione] (**4a**), as a colorless solid in 75% (0.289 g) yield; mp: 255 ^oC (dec.); IR (KBr): ν 3200-2830 (multiple bands), 1711, 1680, 1610 cm^{-1}; ^{1}H NMR (400 MHz, 50% DMSO-d_6 in $CDCl_3$): δ 2.86 & 3.34 (ABq, 4H, J = 15.2 Hz), 7.19-7.41 (m, 10H), 7.72 (s, 2H), 11.08 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 31.02, 50.84 125.59, 128.88, 129.34, 129.87, 134.34, 138.90, 165.97, 170.54; LCMS (*m/z*): 387 $(M+H)^+$; Anal. Calcd. for $C_{23}H_{18}N_2O_4$: C, 71.49; H, 4.70; N, 7.25; Found: C, 71.33; H, 4.71; N, 7.17.

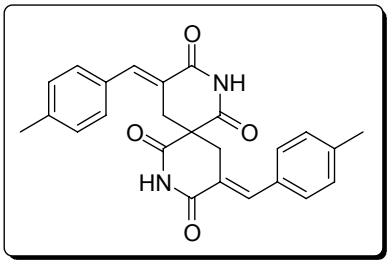
Similar procedure was followed for the compound **4c** as the solid separates out after the reaction mixture was poured into aqueous K_2CO_3 solution. In the case of other compounds **4b**, **4d** & **4e**, after pouring into aqueous K_2CO_3 solution, the compound was extracted with ethyl acetate (3 X 50 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude, thus obtained was purified by column chromatography, using 100% ethyl acetate to furnish pure product (**4b** or **4d** or **4e**) as a colorless solid.

3,3′-Spiro-bis[5-{(*E*)-2-methylbenzylidene}piperidine-2,6-dione] (4b):



Yield: 56%; mp: 190-192 ^oC: IR (KBr): ν 3200-2830 (multiple bands), 1711, 1680, 1622 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 2.15 (s, 6H), 2.80 & 3.10 (ABq, 4H, J = 15.4 Hz), 6.92-7.41 (m, 8H), 7.69 (s, 2H), 11.29 (br s, 2H)*; ^{13}C NMR (100 MHz, DMSO-d_6): δ 19.58, 30.95, 51.05, 125.89, 126.38, 128.61, 129.16, 130.38, 133.66, 137.21, 138.26, 166.16, 170.94; LCMS (*m/z*): 415 $(M+H)^+$; Anal. Calcd. for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76; Found: C, 72.23; H, 5.34; N, 6.74; *[*For observation of -NH-proton we recorded the ^1H NMR spectrum with more sample*].

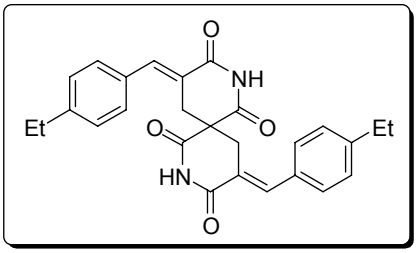
3,3′-Spiro-bis[5-{(*E*)-4-methylbenzylidene}piperidine-2,6-dione] (4c):



Yield: 64%; mp: 245 ^oC (dec.); IR (KBr): ν 3200-2800 (multiple bands), 1711, 1684, 1618 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 2.33 (s, 6H), 3.08 & 3.32* (ABq, 4H, J = 15.8 Hz), 7.19-7.41 (m, 8H), 7.68 (s,

2H), 11.20 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.13, 31.12, 50.82, 124.60, 129.53, 130.01, 131.51, 139.11, 139.34, 166.08, 170.59; LCMS (*m/z*): 415 $(M+H)^+$; Anal. Calcd. for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76; Found: C, 72.63; H, 5.37; N, 6.84; *[*One of the doublet of AB quartet for CH_2 protons (four protons) is merged with moisture in DMSO-d_6. To prove this, our attempts using Eu(fod)$_3$ as a shift reagent, were unsuccessful. However, when we recorded in pyridine-d_5 as a deuterated solvent clear appearence of AB quartet at δ 3.32 & 3.97 (4H, J =15.6 Hz) was observed*].

3,3′-Spiro-bis[5-{(*E*)-4-ethylbenzylidene}piperidine-2,6-dione] (4d):



Yield: 59%; mp: 218-220 ^{o}C; IR (KBr): ν 3200-2850 (multiple bands), 1724, 1699 1630 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, 6H, *J* = 7.6 Hz), 2.70 (q, 4H, *J* = 7.6 Hz), 2.94 & 3.53 (ABq, 4H, *J* = 15.6 Hz), 7.17-7.30 (m, 8H), 7.93 (s, 2H), 8.23 (s, 2H, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.46, 28.20, 31.18, 50.85, 124.65, 128.36, 130.14, 131.80, 139.08, 145.52, 166.12, 170.61; LCMS (*m/z*): 443 $(M+H)^+$; Anal. Calcd. for $C_{27}H_{26}N_2O_4$: C, 73.28; H, 5.92; N, 6.33; Found: C, 73.07; H, 5.92; N, 6.23; **Crystal data** for **4d**: empirical formula, $C_{27}H_{26}N_2O_4$; formula weight, 442.50; crystal color, habit: colorless, rectangular; crystal dimensions, 0.40 X 0.32 X 0.26 mm^3; crystal system, triclinic; lattice type, primitive; lattice parameters, *a* = 10.0689(7) Å, *b* = 10.7855(8) Å, *c* = 12.4469(9) Å; α = 101.142(1); β = 108.914(1); γ = 105.628(1); *V* = 1171.60(15) Å^3; space group, *P-1* (International Table No. 2); *Z* = 2; D_{calcd} = 1.254 g / cm^3; F_{000} = 468; λ(Mo K_α) = 0.71073 Å; *R* ($I \geq 2\sigma_I$) = 0.0617; wR^2 = 0.1824. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **4d** CCDC # 656197).

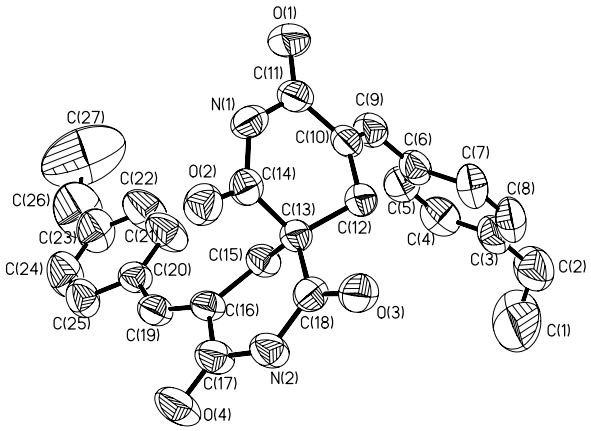
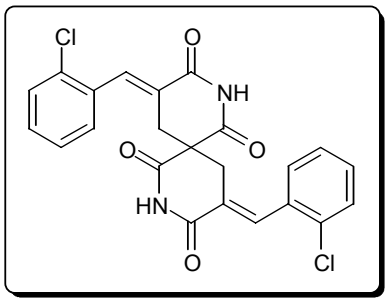


Figure 4 ORTEP diagram (50% probability) of compound **4d**
(Hydrogen atoms are omitted for clarity)

3,3′-Spiro-bis[5-{(*E*)-2-chlorobenzylidene}piperidine-2,6-dione] (4e):



Yield: 55%; mp: 240-241 ^{o}C; IR (KBr): ν 3200-2800 (multiple bands), 1716, 1687, 1639 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.90 & 3.17 (ABq, 4H, J = 15.6 Hz), 7.34 (d, 2H, J = 7.6 Hz), 7.38-7.48 (m, 4H), 7.56 (d, 2H, J = 7.6 Hz), 7.68 (s, 2H), 11.42 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.87, 50.84, 127.42, 127.90, 129.88, 130.58, 130.99, 132.64, 133.55, 135.51, 165.60, 170.42; LCMS (*m/z*): 455 $(M+H)^+$; 457 $[(M+2)+H]^+$, 459 $[(M+4)+H]^+$; Anal. Calcd. for $C_{23}H_{16}Cl_2N_2O_4$: C, 60.67; H, 3.54; N, 6.15; Found: C, 60.55; H, 3.51; N, 6.11.