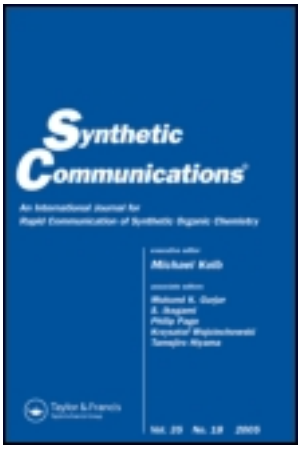

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Synthesis and Characterization of Benzenesulfonyl Hydrazones and Benzenesulfonamides

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Abstract: In the search for structural cyclic imide analogues of therapeutic interest, the syntheses and characterization of benzenesulfonyl hydrazones and benzenesulfonamides are described. The benzenesulfonyl chlorides (2) and (3) were obtained through the Diels–Alder reaction between N-p-chloro-sulfonylfenylmaleimide (1) and furan or 2-methylfuran. The reactions of (2) and (3) with hydrazine and amines afforded the hydrazides and sulfonamides, respectively. The sulfonylhydrazones were obtained through a condensation between the sulfonylhydrazides with different benzaldehydes.

Keywords: Benzenesulfonyl chlorides, Diels–Alder reaction, sulfonamides, sulfonylhydrazones

INTRODUCTION

Sulfonylhydrazones and sulfonamides have been shown to be active in several pharmacological tests, demonstrating antibacterial, antitumor, diuretic, antiviral, and antinociceptive activity.[1–5]

This study aims to synthesize and characterize benzenesulfonamides (4–8) and benzenesulfonylhydrazones (11–20). The sulfonylchloride (1) was obtained as previously described.[6] The chlorides (2) and (3) were prepared through a Diels–Alder reaction of (1) with furan or 2-methylfuran. The sulfonamides (4–8) and the sulfonylhydrazides (9) and (10) were obtained from (2) or (3) with pyrrolidine or morpholine and hydrazine hydrate. The hydrazides

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(9) and (10) were characterized by the condesation with benzaldehydes to yield the sulfonylhydrazones (11–20) (Scheme 1).

The structures were confirmed through ^{1}H NMR and ^{13}C NMR spectroscopic analysis and CNH elemental analysis.

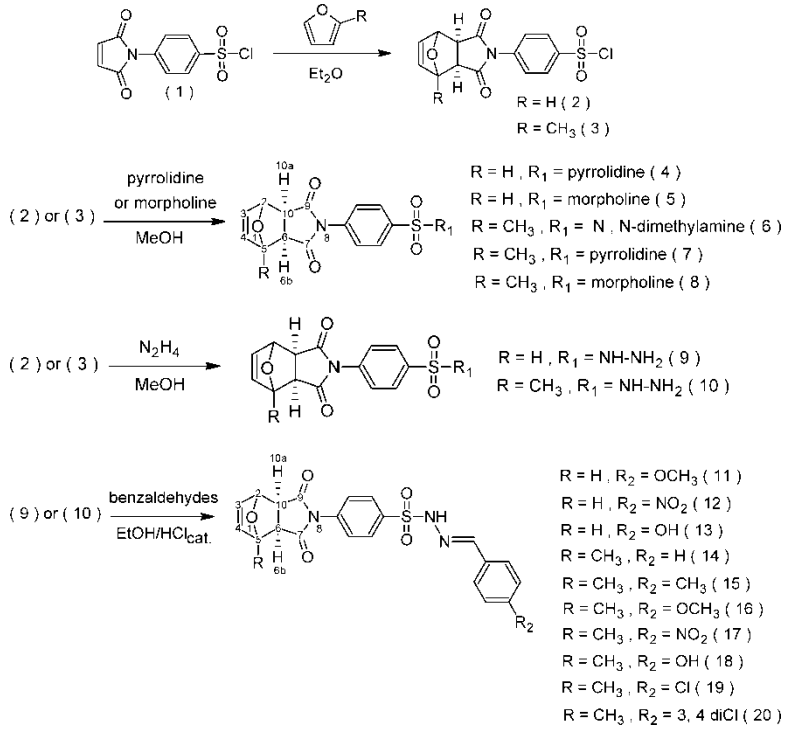
Under the experimental conditions only the exo-isomers were isolated.

The formation of exo-isomers was detected, initially, by thin-layer chromatography (TLC) and later confirmed through ^{1}H NMR, ^{13}C NMR, and elementary CHN analysis.

The ^{1}H NMR spectrum, in two dimensions spectroscopy (COSY), of the exo-isomers shows a sharp singlet for the $H_{6a,10a}$ hydrogens with no coupling with $H_{2,5}$ hydrogens because the dihedral angle between them is approximately 90°.[7] This is in contrast with the four-line pattern observed for the exo-protons of the endo-isomers.[8,9]

EXPERIMENTAL

All compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR, and microanalysis. The purity of these compounds was determined by TLC. Infrared



Scheme 1.

spectra were obtained with a Perkin Elmer 16PC spectrophotometer (Perkin Elmer, Wellesley, MA, USA). ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AC-200F spectrometer (Rheinstetten, Germany) (at 200 MHz and 50 MHz, respectively). $CDCl_3$ and DMSO were used as solvents with tetramethylsilane (TMS) as the internal standard; chemical shifts (δ) are reported in parts per million. For the CHN analysis, a Perkin Elmer 2400 CHN elemental analyser (Boston, MA, USA) was used. In the TLC, aluminium sheets with 60 F-254 silica gel (0.2 mm thick) were utilized.

General Experimental Procedure

4-(2,5-Dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzenesulfonyl Chloride (1)

Chloride **1** was obtained as described in the literature.[6] Yield: 84%. Mp 138.5–139.4 °C (lit.[6] mp 138–139°C). IR (KBr)ν_{Max}: 1780, 1718 (C═O), 1374, 1186 ($-SO_2$), 838 (arom.).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl] benzenesulfonyl Chloride (2)

Chloride **2** was obtained as described in the literature.[6] Yield: 88%. Mp 136.5–137.4 °C (lit.[10] Mp 137–139°C). IR (KBr)ν_{Max}: 1782, 1720 (C═O), 1363, 1166 ($-SO_2$), 870 (arom.).

4-[(2*R*,6*S*)-1-Methyl-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]benzenesulfonyl Chloride (3)

Chloride **3** was obtained as described in the literature.[10] Yield: 79%. Mp 113.9–115.3 °C (lit.[10] mp 115–117°C). IR (KBr)ν_{Max}: 1779, 1704 (C═O), 1373, 1181 ($-SO_2$), 839 (arom.).

(2*R*,6*S*)-4-[4-(Pyrrolidin-1-ylsulfonyl)phenyl]-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (4)

Pyrrolidine (0.63 mL, 8.82 mmol) was added dropwise to a mixture of 4-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}] dec-8-en-4-yl)benzenesulfonyl chloride (2) (1.50 g, 4.42 mmol) in methanol (10 mL) in an ice bath. The formed solid was filtered off with suction. The product was crystallized from ethanol–ethyl acetate (2:1). Yield: 47%. Mp 144.1–144.5°C. Anal. calcd. for $C_{18}H_{18}N_2O_5$ S: C, 57.74; H, 4.85; N, 7.48; S, 8.56. Found: C, 56.20; H, 4.90; N, 7.34; S, 8.46. ^{1}H NMR δ ppm, DMSO-d^6: ArH (2d: 7.97 and 7.50, $J = 7.4$ Hz); -CH═CH- (s: 6.62); -CH-O-CH- (s: 5.27); -CH_2-N-CH_2- and H_{6a} and H_{10a} (m: 3.13); -$(CH_2)_2$- (m: 1.70). ^{13}C NMR δ ppm, DMSO-d^6: CH_2-CH_2-CH_2-N

(24.80); CH_2-N-CH_2- (47.69); (CH-C═O)$_2$ (47.91); CH-O-CH- (80.96); C Ar (127.44; 128.19); -CH═CH- and -HC-SO_2 Ar (135.76); -CH-N-Ar (136.73); C═O (175.44). Using this procedure, the following sulfonamides were prepared.

(2*R*,6*S*)-4-[4-(Morpholin-4-ylsulfonyl)phenyl]-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (5)

Yield: 26%. Mp 139.5–140.2°C. Anal. calcd. for $C_{18}H_{18}N_2O_6S$: C, 55.38; H, 4.65; N, 7.18; S, 8.21. Found: C, 55.16; H, 4. 67; N, 7.08; S, 8.07. ^{1}H NMR δ ppm, DMSO-d^6: ArH (2d: 7.91 and 7.55, $J = 6.9$ Hz); -CH═CH- (s: 6.62); -CH-O-CH- (s: 5.28); -CH_2-O-CH_2- (s broad: 3.64); (-CH-C═O)$_2$; H_{6a} and H_{10a} (s: 3.14); -CH_2-N-CH_2- (s, broad: 2.90). ^{13}C NMR δ ppm, DMSO-d^6: CH_2-N-CH_2- (46.57); (CH-C═O)$_2$ (48.81); CH_2-O-CH_2- (65.64); CH-O-CH- (81.19); C Ar (129.05; 129.39); -CH═CH- (134.79); -HC-SO_2 Ar (136.79); -CH-N-Ar (137.68); C═O (176.02).

N,*N*-Dimethyl-4-[(2*R*,6*S*)-1-methyl-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]benzenesulfonamide (6)

Yield: 40%. Mp 124.8–125.7 °C. Anal. calcd. for $C_{17}H_{18}N_2O_5S$: C, 56.34; H, 5.01; N, 7.73; S, 8.85. Found: C, 55.93; H, 5.05; N, 7.67; S, 8.77. ^{1}H NMR δ ppm, DMSO-d^6: ArH (2d: 7.92 and 7.53, $J = 7.1$ Hz); -CH═CH- (2d: 6.63 and 6.44, $J = 5.7$ Hz); -CH-O- (s: 5.16); H_{6a} and H_{10a} (d: 3.27–2.97, $J = 6.4$ Hz); CH_3-N-CH_3 (s: 2.57); -CH_3- (s: 1.65). ^{13}C NMR δ ppm, DMSO-d^6: CH_3 (15.57); CH_3-N-CH_3 (34.36); CH-10 (49.64); CH-6 (50.82); CH-O (80.59); C-O (88.01); C Ar (126.19; 127.44); -CH-CH═CH- (134.94); -C-CH═CH (135.87); -HC-SO_2 Ar (137.07); -CH-N-Ar (140.47); C═O-7 (173.96); C═O-9 (175.29).

(2*R*,6*S*)-1-Methyl-4-[4-(pyrrolidin-1-ylsulfonyl)phenyl]-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (7)

Yield: 40%. Mp 139°C. Anal. calcd. for $C_{19}H_{20}N_2O_5S$: C, 58.75; H, 5.19; N, 7.21; S, 8.26. Found: C, 58.17; H, 5.23; N, 7.20; S, 8.13. ^{1}H NMR δ ppm, DMSO-d^6: ArH (2d: 7.96 and 7.51, $J = 7.4$ Hz); -CH═CH- (2d: 6.62 and 6.44, $J = 5.9$ Hz); -CH-O- (s: 5.16); H_{6a} and -CH_2-N-CH_2- (m: 3.26–3.18); H_{10a} (d: 2.99 and 2.96, $J = 6.7$ Hz); -CH_3 and -$(CH_2)_2$- (s broad: 1.66). ^{13}C NMR δ ppm, DMSO-d^6: CH_3 (15.61); NCH_2CH_2-CH_2 (24.80); CH_2-N-CH_2- (47.91); CH-10 (49.68); CH-6 (50.87); CH-O (80.06); C-O (80.64); C Ar (127.49; 128.18); C3 (135.81); C4 (135.95); -HC-SO_2 Ar (137.12); -CH-N-Ar (140.52), C═O-7 (174.05); C═O-9 (175.37).

(2*R*,6*S*)-1-Methyl-4-[4-(morpholin-4-ylsulfonyl)phenyl]-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (8)

Yield: 62%. Mp 138.1–139.3°C. Anal. calcd. for $C_{19}H_{20}N_2O_6S$: C, 56.42; H, 4.98; N, 6.93; S, 7.93. Found: C, 55.92; H, 5.04; N, 6.80; S, 7.73. ^{1}H NMR δ ppm, DMSO-d^6: ArH (2d: 7.87 and 7.55; $J = 7.4$ Hz); -CH═CH- (2d: 6.61 and 6.38; $J = 5.9$ Hz); -CH-O- (s: 5.33); -CH_2-O-CH_2- (t: 3.79–3.73, $J = 3.7$ Hz); H_{6a} (d: 3.19 and 3.16; $J = 7.4$ Hz); -CH_2-N-CH_2- (m: 3.06–3.01); H_{10a} (d: 2.93 and 2.90; $J = 7.4$ Hz); -CH_3 (s: 1.80). ^{13}C NMR δ ppm, DMSO-d^6: CH_3 (15.66); CH_2-N-CH_2 (45.84); CH-10 (49.55); CH-6 (50.66); CH_2-O-CH_2 (65.97); -C-O- (81.19); CH-O- (88.73); C Ar (126.80; 128.49); C3 (134.88); C4 (135.82); -HC-SO_2 Ar (137.06); -CH-N-Ar (140.71); C═O-7 (173.34); C═O-9 (175.61).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl] benzenesulfonohydrazide (9)

Compound **9** was obtained as previously described in the literature.[11] Yield: 63%. Mp 210.5–213.8°C. IR (KBr)ν_{Max}: 3370 (-NH_2), 3294 (ν-NH), 1780, 1718 (C═O), 1375, 1166 (-SO_2), 1201 (-C-N-), 850 (arom.).

4-[(2*R*,6*S*)-1-Methyl-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$] dec-8-en-4-yl]benzenesulfonohydrazide (10)

Compound **10** was obtained as previously described in the literature.[11] Yield: 69%. Mp 141.1–143.0°C. IR (KBr)ν_{Max}: 3383 (-NH_2), 3192 (-NH), 1777, 1708 (C═O), 1387, 1193 (-SO_2), 1173(-C-N-), 837 (arom.).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-methoxyfenyl)methylene]benzenesulfonohydrazide (11)

4-Methoxybenzaldehyde (0.23 g, 1.64 mmol) was added to a mixture of 4-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl)benzenesulfonohydrazide (4) (0.50 g, 1.49 mmol) in ethanol (10 mL), along with a drop of hydrochloric acid as the catalyst. The reaction was left under stirring at room temperature for 1 h. The solid formed was filtered off with suction. The product was crystallized from ethanol–ethyl acetate (2:1). Yield: 72%. Mp 155.2–155.5°C. Anal. calcd. for $C_{22}H_{19}N_3O_6S$: C, 58.27; H, 4.22; N, 9.27; S, 7.07. Found: C, 58.19; H, 4.30; N, 9.10; S, 6.94. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N═ (s: 11.44); ArH (2d: 7.97 and 7.50 $J = 9.0$ Hz); -N═CH-Ph (s: 7.82); ArH (2d: 7.47 and 6.97 $J = 9.0$ Hz); -CH═CH- (s: 6.60); -CH-O-CH- (s: 5.25); -OCH_3 (s: 3.77); H_{6a} and H_{10a} (s: 3.18). ^{13}C NMR δ ppm, DMSO-d^6: OCH_3 (47.64); CH-6 and 10 (55.28); CH-O-CH (80.87); C Ar (114.29; 126.13; 127.34; 128.15; 135.72); -CH═CH- (128.51); -HC-SO_2 Ar (136.66); -CH-N-Ar (138.59); CH-O-Ar

(147.77); -N=C- (160.89); C=O (175.33). Using this procedure the following sulfonylhydrazides were prepared.

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]-*N*′;-[(1*E*)-(4-nitrophenyl)methylene]benzenesulfonohydrazide (12)

Yield: 69%. Mp >270°C. Anal. calcd. for $C_{21}H_{16}N_4O_7S$: C, 53.84; H, 3.44; N, 11.96; S, 6.85. Found: C, 53.16; H, 3.48; N, 11.74; S, 6.71. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N= (s: 12.11); ArH (2d: 8.26–8.02; J = 10.0 Hz); -N=CH-Ph (s: 8.06); ArH (2d: 7.88 and 7.50; J = 10.0 Hz); -CH=CH- (s: 6.60); -CH-O-CH- (s: 5.25); H_{6a} and H_{10a} (s: 3.11). ^{13}C NMR δ ppm, DMSO-d^6: CH-6 and 10 (55.28); CH-O-CH (80.87); C Ar (124.03; 127.48; 127.62; 128.10; 136.64); -CH=CH- (135.94); -HC-SO_2 (138.36); -CH-NO_2 (139.66); N-CH Ar (145.06); -N=C- (147.92); C=O (175.31).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-hydroxyphenyl)methylene]benzenesulfonohydrazide (13)

Yield: 79%. Mp 141.0–143.7°C. Anal. calcd. for $C_{21}H_{17}N_3O_6S$: C, 57.40; H, 3.90; N, 9.56; S, 7.30. Found: C, 57.34; H, 3.93; N, 9.50; S, 7.22. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N= (s: 11.32); -OH (s broad: 9.92); ArH (2d: 8.02 and 7.48, J = 9.1 Hz); -N=CH- (s: 7.84); ArH (2d: 7.43 and 6.75, J = 9.1 Hz); -CH=CH- (s: 6.60); -CH-O-CH- (s: 5.24); H_{6a} and H_{10a} (s: 3.11). ^{13}C NMR δ ppm, DMSO-d^6: CH-6 and 10 (48.77); CH-O-CH (81.23); C Ar (116.98; 125.25; 127.48; 128.55; 128.95); -CH=CH- (128.71); -HC-SO_2 Ar (136.37); -CH-N-Ar (139.33); CH-OH Ar (149.70); -N=C- (160.09); C=O (176.03).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]-*N*′-[(1*E*)-phenylmethylene]benzenesulfonohydrazide (14)

Yield: 48%. Mp 142.6–143.4°C. Anal. calcd. for $C_{22}H_{19}N_3O_5S$: C, 60.40; H, 4.38; N, 9.61; S, 7.33. Found: C, 60.16; H, 4.44; N, 9.47; S, 7.24. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N= (s: 11.64); ArH and -N=CH-Ph (m: 8.04–7.40); -CH=CH- (2d: 6.61 and 6.42, J = 6.7 Hz); -CH-O- (s: 5.13); H_{6a} and H_{10a} (2d: 3.24 and 2.94, J = 4.8 Hz); -CH_3 (s: 1.62). ^{13}C NMR δ ppm, DMSO-d^6: CH_3 (15.54); CH-10 (49.67); CH-6 (50.81); C-O (80.54); CH-O (87.98); C Ar (126.86; 127.42; 128.09; 128.12; 130.21; 134.91); HC-SO_2 Ar(135.83); C3 (138.50); C4 (140.46); -CH-N-Ar (147.67); -C=N- (169.38); C=O-7 (173.90); C=O-9 (175.25).

4-[(2*R*,6*S*)-3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-methylphenyl)methylene]benzenesulfonohydrazide (15)

Yield: 76%. Mp 134.8–135.3°C. Anal. calcd. for $C_{23}H_{21}N_3O_5S$: C, 61.18; H, 4.69; N, 9.31; S, 7.10. Found: C, 60.83; H, 4.78; N, 9.12; S, 7.06. ^{1}H NMR δ

ppm, DMSO-d^6: -NH-N═ (s: 11.54), ArH (2d: 8.03–7.49, $J = 10.0$ Hz); -N═CH-Ph (s: 7.92); ArH (2d: 7.46–7.19, $J = 9.0$ Hz); -CH═CH- (2d: 6.60 and 6.42, $J = 6.0$ Hz), -CH-O- (s: 5.13), H_{6a} and H_{10a} (2d: 3.24 and 2.94, $J = 8.00$ Hz), -CH_3-Ph (s: 1.92); -CH_3 (s: 1.62). ^{13}C NMR δ ppm, DMSO-d^6: CH_3-CH-O (15.55); CH_3 –CH Ar (21.02); CH-10 (49.63); CH-6 (50.82); C-O (80.55); CH-O (87.99); C Ar (126.56; 128.10; 129.40; 130.21; 134.91; 138.53); HC-SO_2 Ar (135.83); C3 (140.08); C4 (140.46); -CH-N-Ar (147.81); -C═N- (172.04); C═O-7 (173.91); C═O-9 (175.26).

1-Methyl-4-[(2*R*,6*S*)-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-methoxyphenyl)methylene] benzenesulfonohydrazide (16)

Yield: 84%. Mp 136.4–137.4°C. Anal. calcd. for $C_{23}H_{21}N_3O_6S$: C, 59.09; H, 4.53; N, 8.99; S, 6.86. Found: C, 58.75; H, 4.60; N, 8.87; S, 6.74. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N═ (s: 11.44); ArH (2d: 8.02 and 7.51, $J = 9.1$ Hz); -N═CH-Ph (s: 7.89); ArH (2d: 7.48 and 6.93, $J = 9.1$ Hz); -CH═CH- (2d: 6.58 and 6.42, $J = 4.5$ Hz); -CH-O- (s: 5.13); -OCH_3 (s: 3.77); H_{6a} (d: 3.24 and 3.21, $J = 7.3$ Hz); H_{10a} (d: 2.97 and 2.94, $J = 7.3$ Hz); -CH_3 (s: 1.62). ^{13}C NMR δ ppm, DMSO-d^6: CH_3- (16.52); O-CH_3 (50.68); CH-6 and 10 (50.70); C-O (80.71); CH-O (81.77); C Ar (115.69; 127.54; 128.59; 128.70; 136.46); C3 (128.92); C4 (129.70); HC-SO_2 Ar (138.04); -CH-N- Ar (139.26); Ar-CH-O-CH_3 (148.30); -C═N- (161.58); C═O-7 (174.60); C═O-9 (175.95).

1-Methyl-4-[(2*R*,6*S*)-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-nitrophenyl)methylene]benzenesulfonohydrazide (17)

Yield: 84%. Mp 130.9–131.6°C. Anal. calcd. for $C_{22}H_{18}N_4O_7S$: C, 54.77; H, 3.76; N, 11.61; S, 6.65. Found: C, 54.52; H, 3.83; N, 11.43; S, 6.54. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N═ (s: 12.18); ArH (2d: 8.25 and 8.02, $J = 7.9$ Hz); -N═CH-Ph (s: 8.02); ArH (2d: 7.87 and 7.51, $J = 8.9$ Hz); -CH═CH- (2d: 6.57 and 6.42, $J = 3.0$ Hz); -CH-O- (s: 5.14); H_{6a} (d: 3.23–3.20, $J = 5.9$ Hz); H_{10a} (d: 2.92–2.89, $J = 5.9$ Hz); -CH_3 (s: 1.63). ^{13}C NMR δ ppm, DMSO-d^6: CH_3- (15.70); CH-6 and 10 (51.54); C-O (80.57); CH-O (80.96); C Ar (124.81; 128.35; 128.67; 128.77, 128.88); C3 (136.78); C4 (139.02); -CH-SO_2 Ar (137.16); -CH-NO_2 Ar (140.37); -CH-N-Ar (145.96); -C═N- (148.22); C═O-7 (174.10); C═O-9 (176.11).

1-Methyl-4-[(2*R*,6*S*)-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-hydroxyphenyl)methylene] benzenesulfonohydrazide (18)

Yield: 68%. Dec. 185°C. Anal. calcd. for $C_{22}H_{19}N_3O_6S$: C, 58.27; H, 4.22; N, 9.27; S, 7.07. Found: C, 57.97; H, 4.29; N, 9.08; S, 6.96. ^{1}H NMR δ ppm,

DMSO-d^6: -NH-N= (s: 13.33); ArH (2d: 8.02 and 7.53; $J = 9.1$ Hz); -N=CH-Ph (s: 7.84); -OH (s broad: 7.63); ArH (d: 7.48 and 6.75; $J = 9.1$ Hz); -CH=CH- (d: 6.61–6.42, $J = 5.4$ Hz); -CH-O- (s: 5.14); H_{6a} and H_{10a} (2d: 3.21–2.93, $J = 7.3$ Hz); -CH_3 (s: 1.62); ^{13}C NMR δ ppm, DMSO-d^6: CH_3- (15.80); CH-6 and 10 (51.85); C-O (80.70); CH-O (81.70); C Ar (116.98; 125.24; 127.52; 128.57; 128.90); -CH-*C*H=CH- (128.80); -C-*C*H=CH- (129.81); -CH-SO_2 Ar (136.39); -CH-N-Ar (139.25); -CH-OH-Ar (149.13); -C=N- (160.10); C=O-7 (174.63); C=O-9 (175.99).

1-Methyl-4-[(2*R*,6*S*)-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]-*N*′-[(1*E*)-(4-chlorophenyl)methylene] benzenesulfonohydrazide (19)

Yield: 63%. Mp 131.4–132.2°C. Anal. calcd. for $C_{22}H_{18}Cl\,N_3O_5S$: C, 55.99; H, 3.84; Cl, 7.51; N, 8.90; S, 6.79. Found: C, 55.71; H, 3.89; N, 8.74; S, 6.67. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N= (s: 11.75); -N=CH-Ph (s: 8.73); ArH (m: 8.03 and 7.90); -ArH (m: 7.61 and 6.48); -CH=CH- (d: 6.61–6.49, $J = 5.5$ Hz); -CH-O- (s: 5.14); H_{6a} and H_{10a} (2d: 3.23–2.96, $J = 7.5$ Hz); -CH_3 (s: 1.63). ^{13}C NMR δ ppm, DMSO-d^6: CH_3- (16.18); CH-6 and 10 (51.89); C-O (80.55); CH-O (81.59); C Ar (127.60; 128.87; 129.36; 129.64; 130.54); -CH-Cl Ar (135.35); C3 (136.54); C4 (139.12); -CH-SO_2 Ar (141.32); -CH-N-Ar (146.91); -C=N- (147.18); C=O-7 (174.60); C=O-9 (175.94).

1-Methyl-4-[(2*R*,6*S*)-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]-*N*′-[(1*E*)-(3,4-dichlorophenyl)methylene] benzenesulfonohydrazide (20)

Yield: 81%. Mp 127.5–128.0°C. Anal. calcd. for $C_{22}H_{17}Cl_2N_3O_5\,S$: C, 52.18; H, 3.38; Cl, 14.00; N, 8.30; S, 6.33. Found: C, 51.84; H, 3.44; N, 8.14; S, 6.29. ^{1}H NMR δ ppm, DMSO-d^6: -NH-N= (s: 11.91); ArH (m: 8.04 and 7.95); -N=CH-Ph (s: 7.44); ArH (m: 7.82 and 7.52); -CH=CH- (d: 6.61–6.44, $J = 5.4$ Hz); -CH-O- (s: 5.14); H_{6a} and H_{10a} (2d: 3.24–2.96, $J = 7.4$ Hz); -CH_3 (s: 1.63). ^{13}C NMR δ ppm, DMSO-d^6: CH_3- (16.25); CH-6 and 10 (51.85); C-O (80.55); CH-O (81.70); C Ar (127.68; 128.88; 131.33; 132.37); -CH-*m*-Cl Ar (133.15); -CH-*p*-Cl Ar (134.65); C3 (134.99); C4 (138.61); -CH-SO_2 Ar (139.07); -CH-N- Ar (145.52); -C=N- (145.81); C=O-7 (174.62); C=O-9 (175.96).

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