Synthesis of new azepanedione oximes

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Abstract : Synthesis and physico-chemical properties of some 1-benzyl-azepane-2,3-dione 3-(*O*-substituted oximes) with attribution of their Z and E configurations and 4-(phenylhydrazono)azepane-2,3-dione 3-(*O*-substituted oximes) resulting of condensation with various *O*-aryl-hydroxylamines are described. These azepanedione-oxime compounds are prepared from the corresponding azepan-2-ones and 1-benzylazepan-2-ones.

Introduction

Through studies of amide or lactame derivatives highlighted the interesting pharmacological properties, in particular actions on central nervous system via stimulation of various ion channels [1]. The synthesis of 3-[*O*-(benzyl)oximinoether] hexahydroazepin-2,3-diones previously reported [2] showed that they are capable to relax both rat trachea and human bronchus. The oximinoether or oxime derivatives exhibited marked antinociceptive and anticonvulsant activities [3]. This work describes synthesis and physicochemical properties of 1-benzylazepane-2,3-dione 3-(*O*-substituted oximes) with attribution of their Z and E configurations and 4-(phenylhydrazono)azepane-2,3-dione 3-(*O*-substituted oximes) resulting of condensation with various *O*-arylhydroxylamines from the corresponding azepan-2-ones and 1-benzylazepan-2-ones.

Synthesis and structural study

Strategy for the synthesis of target compounds **8a-f** and **10a-g** (Scheme 1) was based on the construction of the azepane-2,3-dione skeleton 7, 9 followed by attachment of the *O*-substituted hydroxylamines in presence of pyridine.

The 1-benzylazepan-2-one 2, starting compound for the preparation of the 1-benzylazepane-2,3-dione 7, was prepared from cyclohexanone [4]. Chlorination of 2 by phosphorus pentasulphide [5] leads to the 1-benzyl-3,3-dichloroazepan-2-one 4. This compound, after treatment by morpholine and acidic hydrolysis in cold hydrochloric acid led to the azepanedione 7.

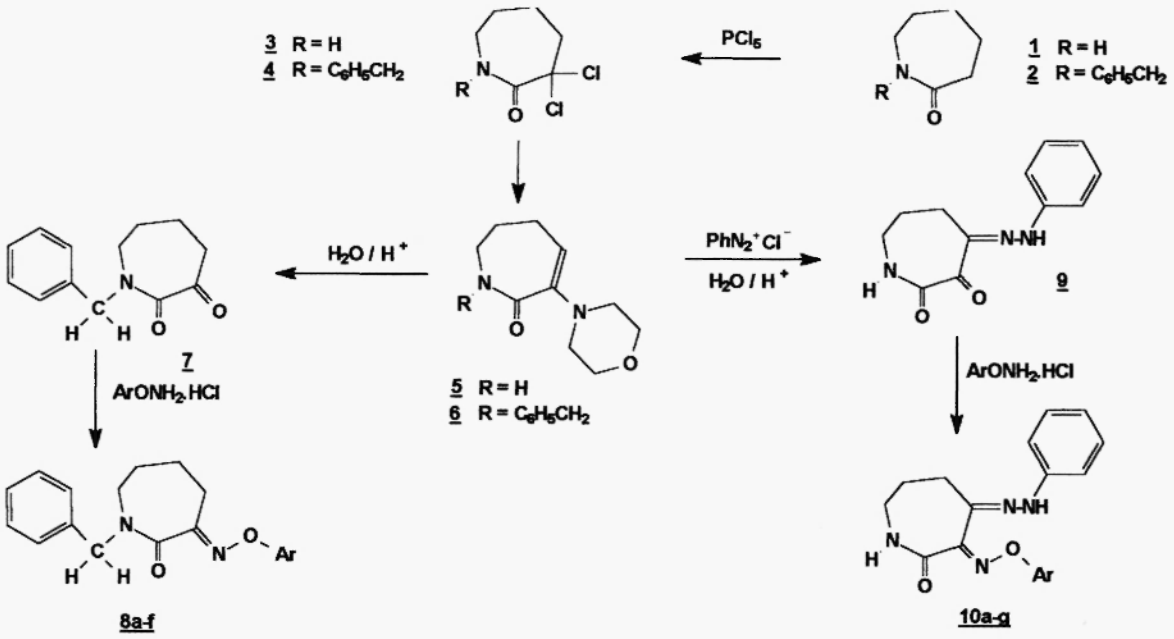

Figure 1. Synthesis of azepanedione oxime compounds.

Several methods can be used for the preparation of 4-(phenylhydrazono)azepane-2,3-dione **9**. Initially, the 3,3-dichloroazepan-2-one **3** was prepared using phosphorous pentachloride. Treatment of **3** with morpholine [6] followed by condensation with phenyldiazonium chloride [7] leads to the azepane **9**.

The *O*-aryl-hydroxylamines used for the synthesis of the azepanedione oximes, were prepared according to Garoufalias et al. [8] and their physicochemical properties were reported in a previous work [2].

1-Benzylazepane-2,3-dione 3-(*O*-substituted oximes) **8a-f** were isolated as mixture of *Z* and *E* isomers (Table 1) in which the *E* isomer predominates. Ratio of isomers were assessed by NMR spectroscopy on the basis of the chemical shifts observed for protons on carbon adjacent to the oxime double bond [9]. In accordance with assignments reported in literature for several oximes and alkylated oximes [10], *Z* isomers are more downfield than their *E* counterparts. The 4-(phenylhydrazono)azepane-2,3-dione 3-(*O*-substituted oximes) **10a-g** were isolated in the form of only one isomer.

Fragmentations observed and intensity of the peaks of isotopes under electronic impact in MS are in agreement with the structures suggested.

Experimental

Melting points were measured with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Pye-Unicam SP3-100 (Philips) spectrometer. Wavelengths are expressed in cm^{-1}. Nuclear magnetic resonance spectra were recorded on an AC 200 FT (Bruker) spectrometer ^{1}H NMR at 200 MHz and ^{13}C NMR at 50 MHz. Chemical shifts (δ) are expressed in part per million (ppm) and coupling constants (J) are given in hertz (Hz).

Table 1. Physicochemical data

Compound	Ar	bp°C *	mp°C	Isomer Yield %	Formula
8a (*E*)	CH_3	128		90	$C_{14}H_{18}N_2O_2$
8a (*Z*)	CH_3	110		10	$C_{14}H_{18}N_2O_2$
8b (*E*)	$C_6H_5CH_2$	134		70	$C_{20}H_{22}N_2O_2$
8b (*Z*)	$C_6H_5CH_2$	158		30	$C_{20}H_{22}N_2O_2$
8c (*E*)	2-$NO_2C_6H_4CH_2$	168		58	$C_{20}H_{21}N_3O_4$
8c (*Z*)	2-$NO_2C_6H_4CH_2$	195		42	$C_{20}H_{21}N_3O_4$
8d (*E*)	3-$NO_2C_6H_4CH_2$	194		67	$C_{20}H_{21}N_3O_4$
8d (*Z*)	3-$NO_2C_6H_4CH_2$	184		33	$C_{20}H_{21}N_3O_4$
8e (*E*)	4-$NO_2C_6H_4CH_2$	134		65	$C_{20}H_{21}N_3O_4$
8e (*Z*)	4-$NO_2C_6H_4CH_2$	164		35	$C_{20}H_{21}N_3O_4$
8f (*E*)	4-$CNC_6H_4CH_2$	155		75	$C_{21}H_{21}N_3O_2$
8f (*Z*)	4-$CNC_6H_4CH_2$	157		25	$C_{21}H_{21}N_3O_2$
10a	H		194		$C_{12}H_{14}N_4O_2$
10b	CH_3		162		$C_{13}H_{16}N_4O_2$
10c	$C_6H_5CH_2$		140		$C_{19}H_{20}N_4O_2$
10d	2-$NO_2C_6H_4CH_2$		196		$C_{19}H_{19}N_5O_4$
10e	3-$NO_2C_6H_4CH_2$		149		$C_{19}H_{19}N_5O_4$
10f	4-$NO_2C_6H_4CH_2$		155		$C_{19}H_{19}N_5O_4$
10g	4-$CNC_6H_4CH_2$		161		$C_{20}H_{19}N_5O_2$

* 760 mm/Hg

Mass spectra obtained by 70eV electronic impact, were recorded on a Delsi-Nermag R-1010 C apparatus. Intensity of the molecular peaks is given compared to the most intense peak M^+(%). Elemental analyses (C, H, N) were determined at the CNRS-Centre in Vernaison, France, and are within ± 0.4% of the calculated values.

Synthesis and physico-chemical characteristics of *O*-aryl-hydroxylamines,**1**,**3**,**5** [2] and compound **2** [11] were previously described.

1-Benzyl-3,3-dichloro-azepan-2-one **4** was obtained by chlorination of the 1-benzyl-azepan-2-one **2** with phosphorus pentachloride [5]. Action of morpholine transformed this dihalo compound in the 1-benzyl-3-morpholin-4-yl-1,5,6,7-tetrahydro-azepin-2-one **6** [6]. This one can lead either to the 1-benzyl-azepane-2,3-dione **7** by treatment with hydrochloric acid or to the 4-(phenylhydrazono)azepane-2,3-dione **9** by condensation with phenyldiazonium hydrochloride [7].

In the series of 1-benzyl-azepane-2,3-dione 3-[*O*-(nitrobenzyl)oximes] **8c-e**, IR absorption of CO, CN and NO and ^1H and ^{13}C NMR chemical shifts as well are similar from one compound to the other. Variations of physical constants for **8d** and **8e** are only compared to those of **8c**.

1-benzylazepane-2,3-dione 3-(O-substituted oxime) 8a-f and 4-(phenylhydrazono)azepane-2,3-dione 3-(O-substituted oxime) 10a-g : General procedure.

Substituted *O*-hydroxylamines and pyridine (1 mL) were added to a solution of azepane-2,3-dione **7** or **9** (8 mmol) in absolute EtOH (10 mL). The mixture was heated under reflux for 4h. The solvent was evaporated in vacuo and water (25 mL) was added. The aqueous solution was extracted by CH_2Cl_2 (3 x 10 mL). The organic phase was dried ($MgSO_4$), filtered, and evaporated. The mixture of isomers **8a-f** was separated on silica gel column chromatography (ethyl acetate) to afford corresponding *Z* and *E* isomers. The compounds **10a-g** was purified by silica gel column chromatography (ethyl acetate/cyclohexane 8/2).

1-Benzylazepane-2,3-dione 3-(O-methyl oxime) 8a

IR (film): ν 1680 (CO), 1660 (CN), 890 (NO) cm^{-1}. *E* isomer NMR ^1H ($CDCl_3$): δ 1.44 (m, 2H, 2H5), 1.69 (m, 2H, 2H6), 2.6 (m, 2H, 2H4), 3.28 (t, 2H, 2H7, J=6 Hz), 4.02 (s, 3H, CH_3), 4.8 (s, 2H, $CH_2C_6H_5$), 7.31 (m, 5H, C_6H_5); NMR ^{13}C (DMSO-d_6, DEPT): δ 20.6 (C5), 24.4 (C4), 25.2 (C6), 45.1 (C7), 49.6 ($CH_2C_6H_5$), 62.4 (CH_3), 127.6 (2CH *o*C_6H_5), 128.4 (3CH *m,p*C_6H_5) 139.6 (C C_6H_5), 157.2 (C3), 165.6 (C2). *Z* isomer NMR ^1H ($CDCl_3$): δ 1.43 (m, 2H, 2H5), 1.69 (m, 2H, 2H6), 2.51 (m, 2H, 2H4), 3.26 (t, 2H, 2H7, J=6 Hz), 4 (s, 3H, CH_3), 4.62 (s, 2H, $CH_2C_6H_5$), 7.3 (m, 5H, C_6H_5); NMR ^{13}C (DMSO-d_6, DEPT): δ 24.4 (C4), 28.5 (C6), 29 (C5), 47.1 (C7), 50.2 ($CH_2C_6H_5$), 62.8 (CH_3), 127.6 (2CH *o*C_6H_5), 128.3 (3CH *m,p*C_6H_5) 136.8 (C C_6H_5), 157.5 (C3), 165.8 (C2). MS (EI 70 eV, m/z(%): 246 (M^+ 33.65), 91 (100).

1-Benzylazepane-2,3-dione 3-(O-benzyl oxime) 8b

IR (film): ν 1680 (CO), 1660 (CN), 890 (NO) cm^{-1}. *E* isomer NMR ^1H ($CDCl_3$): δ 1.45 (m, 2H, $2H_5$), 1.69 (m, 2H, $2H_6$), 2.59 (m, 2H, $2H_4$), 3.29 (t, 2H, $2H_7$, J=6 Hz), 4.65 (s, 2H, $NCH_2C_6H_5$), 5.25 (s, 2H, $OCH_2C_6H_5$), 7.36 (m, 10H, $2C_6H_5$); NMR ^{13}C (DMSO-d_6, DEPT): δ 20.6 (C5), 24.4 (C4), 25.3 (C6), 45.2 (C7), 49.9 (NCH_2), 75.1 (OCH_2), 127.4-137.3 (C and CH aromatics), 157.2 (C3), 165.6 (C2). *Z* isomer NMR ^1H ($CDCl_3$): δ 1.42 (m, 2H, $2H_5$), 1.69 (m, 2H, $2H_6$), 2.52 (m, 2H, $2H_4$), 3.25 (t, 2H, $2H_7$, J=6 Hz), 4.63 (s, 2H, $NCH_2C_6H_5$), 5.22 (s, 2H, $OCH_2C_6H_5$), 7.35 (m, 10H, $2C_6H_5$); NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C6), 29 (C4, C5), 47.1 (C7), 50.2 (NCH_2), 74.5 (OCH_2), 127.6-137.2 (C and CH aromatics), 157.1 (C3), 165.4 (C2). MS (EI 70 eV, m/z(%): 322 (M^+ 8), 91 (100).

1-Benzylazepane-2,3-dione 3-[O-(2-nitrobenzyl)oxime] 8c

IR (film): ν 1700 (CO), 1680 (CN), 900 (NO) cm^{-1}. *E* isomer NMR ^1H ($CDCl_3$): δ 1.48 (m, 2H, 2H5), 1.69 (m, 2H, 2H6), 2.62 (m, 2H, 2H4), 3.32 (t, 2H, 2H7, J=6 Hz), 4.8 (s, 2H, $NCH_2C_6H_5$), 5.3 (s, 2H, $OCH_2C_6H_5$), 7.3 (m, 5H, C_6H_5), 7.44 (m, 1H, *p*NO_2), 7.52 (m, 2H, *m*NO_2), 8.1 (m, 1H, *o*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 20.5 (C5), 24.4 (C4), 25.3 (C6), 45.3 (C7), 49.9 (NCH_2), 75.5 (OCH_2), 123.5-136.4 (C and CH aromatics), 145.5 (C, NO_2), 158.6 (C3), 166.2 (C2). *Z* isomer NMR ^1H ($CDCl_3$): δ 1.48 (m, 2H, 2H5), 1.69 (m, 2H, 2H6), 2.57 (m, 2H, 2H4), 3.28 (t, 2H, 2H7, J=6 Hz), 4.64 (s, 2H, $NCH_2C_6H_5$), 5.25 (s, 2H, $OCH_2C_6H_5$), 7.3 (m, 5H, C_6H_5), 7.44 (m, 1H, *p*NO_2), 7.52 (m, 2H, *m*NO_2), 8.1 (m, 1H, *o*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C6), 29 (C4, C5), 47.1 (C7), 50.2 (NCH_2), 75.5 (OCH_2), 123.5-136-4 (C and CH aromatics), 144.5 (C, NO_2), 157.2 (C3), 165.2 (C2). MS EI 70 eV, m/z(%): 367 (M^+ 18.94), 91 (100).

1-Benzylazepane-2,3-dione 3-[O-(3-nitrobenzyl)oxime] 8d

E isomer NMR ^1H ($CDCl_3$): δ 4.8 (s, 2H, $NCH_2C_6H_5$), 5.3 (s, 2H, $OCH_2C_6H_5$), 7.49 (m, 1H, *o*NO_2 and *o*OCH_2), 7.66 (m, 1H, *o*NO_2), 8.2 (m, 2H, *m,p*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 145.5 (C, NO_2). *Z* isomer NMR ^1H ($CDCl_3$): δ 4.64 (s, 2H, $NCH_2C_6H_5$), 5.25 (s, 2H, $OCH_2C_6H_5$), 7.49 (m, 1H, *o*NO_2 and *o*OCH_2), 7.66 (m, 1H, *o*NO_2), 8.2 (m, 2H, *m,p*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 144.7 (C, NO_2). MS EI 70 eV, m/z(%): 367 (M^+ 33.67), 91 (100).

1-Benzylazepane-2,3-dione 3-[O-(4-nitrobenzyl)oxime] 8e

E isomer NMR ^1H ($CDCl_3$): δ 4.8 (s, 2H, $NCH_2C_6H_5$), 5.3 (s, 2H, $OCH_2C_6H_5$), 7.5 (m, 2H, *m*NO_2), 8.19 (m, 2H, *o*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 145.5 (C, NO_2). *Z* isomer NMR ^1H ($CDCl_3$): δ 4.64 (s, 2H, $NCH_2C_6H_5$), 5.25 (s, 2H, $OCH_2C_6H_5$), 7.5 (m, 2H, *m*NO_2), 8.19 (m, 2H, *o*NO_2); NMR ^{13}C (DMSO-d_6, DEPT): δ 144.8 (C, NO_2). MS EI 70 eV, m/z(%): 367 (M^+ 45.5), 91 (100).

***1-Benzylazepane-2,3-dione 3-[O-(4-cyanobenzyl)oxime]* 8f**

IR (film): ν 1640 (CN) cm^{-1}. *E* isomer NMR ^1H ($CDCl_3$): δ 1.51 (m, 2H, $2H_5$), 1.74 (m, 2H, $2H_6$), 2.61 (m, 2H, 2H4), 3.28 (t, 2H, 2H7, J=6 Hz), 4.62 (s, 2H, $NCH_2C_6H_5$), 5.32 (s, 2H, $OCH_2C_6H_5$), 7.31 (m, 5H, C_6H_5), 7.51 (m, 2H, *m*CN), 7.82 (m, 2H, *o*CN); NMR ^{13}C (DMSO-d_6, DEPT): δ 20.7 (C5), 24.2 (C4), 25.6 (C6), 45.1 (C7), 49.6 (NCH_2), 75.2 (OCH_2), 118.6 (CN), 123.6-136.7 (C and CH aromatics), 145.1 (C, CN), 157.8 (C3), 166.2 (C2). *Z* isomer NMR ^1H ($CDCl_3$): δ 1.48 (m, 2H, $2H_5$), 1.72 (m, 2H, $2H_6$), 2.58 (m, 2H, $2H_4$), 3.26 (t, 2H, $2H_7$, J=6 Hz), 4.64 (s, 2H, $NCH_2C_6H_5$), 5.24 (s, 2H, $OCH_2C_6H_5$), 7.32 (m, 5H, C_6H_5), 7.52 (m, 2H, *m*CN), 7.85 (m, 2H, *o*CN); NMR ^{13}C (DMSO-d_6, DEPT): δ 28.9 (C5, C6), 29 (C4), 47.6 (C7), 49.9 (NCH_2), 74.5 (OCH_2), 118.5 (CN), 123.5-136-3 (C and CH aromatics), 144.6 (C, CN), 157.1 (C3), 165.1 (C2). MS EI 70 eV, m/z(%): 347 (M^+ 17.8), 91 (100).

***4-(Phenylhydrazono)azepane-2,3-dione 3-oxime* 10a**

Yield % 77. IR (KBr 2%): ν 3240 (OH), 3200 (NH), 1670 (CO), 940 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.71 (m, 2H, $2H_6$), 2.6 (t, 2H, 2H5, $J_{5,6}$=6.6Hz), 3.32 (m, 2H, 2H7, $J_{7,6}$=6.6Hz, $J_{7,1}$=6.5Hz), 6.65 (m, 1H, *p*H), 7.71 (m, 2H, *m*2CH), 7.24 (m, 2H, *o*2CH), 11.43 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 20.9 (C5), 25.5 (C6), 39.1 (C7), 113.6 (*m*2CH), 122 (*p*CH), 129.4 (*o*2CH), 130.1 (C phenyl), 143.2 (C4), 154.4 (C3), 166.6 (C2). MS EI 70 eV, m/z(%): 246 (M^+ 8.5), 229 (100).

***4-(Phenylhydrazono)azepane-2,3-dione 3-(O-methyl-oxime)* 10b**

Yield % 73. IR (KBr 2%): ν 3200 (NH), 1700 (CO), 1610 (CN), 910 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.9 (m, 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.66 (t, 2H, 2H5, $J_{5,6}$=6.5Hz), 3.3 (m, 2H, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 4.1 (s, 3H, CH_3), 6.66 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.9 (m, 1H *p*CH), 7.15 (m, 2H, *m*2CH), 7.29 (m, 2H, *o*2CH), 11.60 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C5), 30.5 (C6), 38.9 (C7), 63.6 (OCH_3), 113.5 (*m*2CH), 121.6 (*p*CH), 126.4 (C phenyl), 129.2 (*o*2CH), 143.9 (C4), 150.3 (C3), 164.1 (C2). MS EI 70 eV, m/z(%): 260 (M^+ 34.58), 229 (100).

***4-(Phenylhydrazono)azepane-2,3-dione 3-(O-benzyl-oxime)* 10c**

Yield % 75. IR (KBr 2%): ν 3200 (NH), 1700 (CO), 1610 (CN), 900 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.66 (m, 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.66 (t, 2H, 2H5, $J_{5,6}$=6.5Hz), 3.27 (td, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 5.3 (s, 2H, OCH_2), 6.61 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.93 (m, 3H *m,p*3CH phenylhydrazono), 7.24 (m, 2H, *o*2CH phenylhydrazono), 7.37 (m, 5H, C_6H_5 benzyhdene), 11.51 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C5), 30.4 (C6), 38.9 (C7), 77.4 (OCH_2), 113.4 (*m*2CH phenylhydrazono), 121.5 (*p*CH phenylhydrazono), 126.5 (C phenylhydrazono), 128 (*o*2CH benzylidene), 128.2 (*p*CH benzylidene), 128.6 (*m*2CH benzylidene), 129.1 (*o*2CH phenylhydrazono), 136.8 (C benzylidene), 143.6 (C4), 150.8 (C3), 164.2 (C2). MS EI 70 eV, m/z(%): 336 (M^+ 82.64), 92 (100).

***4-(Phenylhydrazono)azepane-2,3-dione 3-[O-(2-nitro-benzyl)oxime]* 10d**

Yield % 80. IR (KBr 2%): ν 3200 (NH), 1700 (CO), 1610 (CN), 900 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.92 (tt 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.7 (t, 2H, 2H5, $J_{5,6}$=6.5Hz), 3.33 (td, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 5.75 (s, 2H, OCH_2), 6.34 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.91 (m, 3H *m,p*3CH phenylhydrazono), 7.24 (m, 2H, *o*2CH phenylhydrazono), 7.48 (m, 1H, CH *p*NO_2), 7.65 (m, 1H, CH *m*NO_2 *o*OCH_2), 7.73 (m, 1H, CH *m*NO_2), 8.15 (m, 1H, CH *o*NO_2), 11.47 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C5), 30.4 (C6), 39 (C7), 74.2 (OCH_2), 113.4 (*m*2CH phenylhydrazono), 121.6 (*p*CH phenylhydrazono), 124.8 (CH *p*NO_2), 126 (C phenylhydrazono), 128.5 (CH *m*NO_2 *o*OCH_2), 129 (CH *m*NO_2), 129.2 (*o*2CH phenylhydrazono), 133.6 (C benzylidene), 134 (CH *o*NO_2), 143.5 (C4), 147.2 (CNO_2), 151.3 (C3), 163.9 (C2). MS EI 70 eV, m/z(%): 381 (M^+ 39.07), 229 (100).

***4-(Phenylhydrazono)azepane-2,3-dione 3-[O-(3-nitro-benzyl)oxime]* 10e**

Yield % 67. (KBr 2%): ν 3200 (NH), 1700 (CO), 1610 (CN), 900 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.92 (tt 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.66 (t, 2H, 2H5, $J_{5,6}$=6.5Hz), 3.29 (td, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 5.39 (s, 2H, OCH_2), 6.62 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.92 (m, 3H *m,p*3CH phenylhydrazono), 7.24 (m, 2H, *o*2CH phenylhydrazono), 7.57 (m, 1H, CH *o*NO_2), 7.78 (m, 1H, CH *m*NO_2), 8.17 (m, 1H, CH *p*NO_2), 8.31 (m, 1H, CH *o*NO_2, *o*OCH_2), 11.44 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.4 (C5), 30.3 (C6), 38.9 (C7), 75.9 (OCH_2), 113.4 (*m*2CH phenylhydrazono), 121.9 (*p*CH phenylhydrazono), 126.1 (C phenylhydrazono), 128 (CH *m*NO_2), 128.2 (*o*2CH phenylhydrazono), 132.4 (CH *p*NO_2), 142.4 (CNO_2), 143.5 (C4), 151.3 (C3), 163.7 (C2). MS EI 70 eV, m/z(%): 381 (M^+ 40.2), 229 (100).

4-(Phenylhydrazono)azepane-2,3-dione 3-[O-(4-nitro-benzyl)oxime] **10f**

Yield % 78. (KBr 2%): ν 3200 (NH), 1700 (CO), 1610 (CN), 910 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.91 (tt 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.69 (t, 2H, 2H5, $J_{5,6}$=6.5Hz), 3.31 (td, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 5.4 (s, 2H, OCH_2), 6.3 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.91 (m, 3H *m,p*3CH phenylhydrazono), 7.24 (m, 2H, *o*2CH phenylhydrazono), 7.6 (dd, 2H, 2CH *m*NO_2), 8.27 (dd, 2H, 2CH *o*NO_2), 11.42 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C5), 30.3 (C6), 39 (C7), 75.9 (OCH_2), 113.4 (*m*2CH phenylhydrazono), 121.9 (*p*CH phenylhydrazono), 123.9 (2CH *m*NO_2), 126.1 (C phenylhydrazono), 128.1 (2CH *o*NO_2), 129.2 (*o*2CH phenylhydrazono), 143.5 (CNO_2), 144.2 (C4), 151.7 (C3), 163.6 (C2). MS EI 70 eV, m/z(%): 381 (M^+ 27.86), 229 (100).

4-(Phenylhydrazono)azepane-2,3-dione 3-[O-(4-cyano-benzyl)oxime] **10g**

Yield % 74. (KBr 2%): ν 3200 (NH), 1690 (CO), 1620 (CN), 900 (NO) cm^{-1}. NMR ^1H ($CDCl_3$): δ 1.9 (tt 2H, $2H_6$, $J_{6,5}$=6.5Hz, $J_{6,7}$=6.5Hz), 2.62 (t, 2H, 2H5, $J_{5,6}$=6.6Hz), 3.32 (td, 2H7, $J_{7,6}$=6.5Hz, $J_{7,1}$=6.6Hz), 5.35 (s, 2H, OCH_2), 6.4 (t, 1H, NH1, $J_{1,7}$=6.6Hz), 6.92 (m, 3H *m,p*3CH phenylhydrazono), 7.22 (m, 2H, *o*2CH phenylhydrazono), 7.53 (m, 2H, 2CH *m*CN), 7.68 (m, 2H, 2CH *o*CN), 11.42 (s, 1H, NNH). NMR ^{13}C (DMSO-d_6, DEPT): δ 28.5 (C5), 30.3 (C6), 39 (C7), 76.2 (OCH_2), 113.4 (*m*2CH phenylhydrazono), 121.9 (*p*CH phenylhydrazono), 126.1 (C phenylhydrazono), 128 (2CH *m*CN), 129.2 (*o*2CH phenylhydrazono), 132.4 (2CH *o*CN), 142.2 (CN), 143.5 (C4), 151.3 (C3), 163.7 (C2). MS EI 70 eV, m/z(%): 361 (M^+ 10.47), 84 (100).

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