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Chemistry of 1,3-Dioxepins. XIII.[#] (*E*)/(*Z*) Configurational Assignment of 4,7-Dihydro-4-hydroxyimino-6-nitro-1,3-dioxepins

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The configuration of oximes **1a** and **1b** was investigated by chemical and spectroscopic methods. Under the Beckmann rearrangement conditions, using sulfonyl chlorides as reagents, the sulfonic esters **2a-c** were obtained. Under more drastic conditions, using PCl_5 or P_2O_5, the only isolated product was 4-nitro-5H-furan-2-on (**3**). It was also formed as the sole product by hydrolysis of oximes **1a-b**, as well as sulfonic ester **2a**.
The structure of all compounds was determined by one- and two-dimensional homo- and hetero-nuclear ^{1}H and ^{13}C NMR correlated spectra: COSY, NOESY, HETCOR and HMBC. Gradient selected differential NOE measurements confirmed that, in dimethylsulfoxide solution, oximes **1a** and **1b** exist in *E*-configuration, irrespective of the route of their formation.

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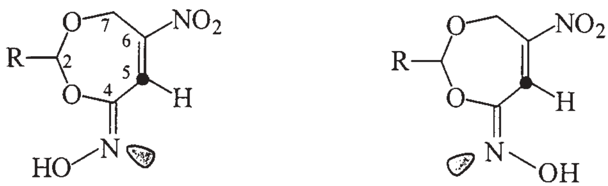
# For part XII see Ref. 1a.

INTRODUCTION

In the course of syntheses and/or application of 5-substituted-4,7-dihydro-1,3-dioxepins to the chemistry of pyridoxine,[1] we recently obtained 4,7-dihydro-4-hydroxyimino-6-nitro-1,3-dioxepins **(1)**, as by-products of the Diels-Alder reaction of 4,7-dihydro-5-nitro-1,3-dioxepins with 4-methyloxazole.[1a]

Their structure were confirmed by parallel synthesis, *i.e.* by nitrosation of 4,7-dihydro-5-nitro-1,3-dioxepins with ethylnitrite in dimethylsulfoxide.[1a]

Here, we present the synthetic and NMR spectroscopic investigations aimed at *E*/*Z* configurational assignment[2] of **1** (Figure 1).



***Z*-** ***E*-**

Figure 1. *Z*- and *E*-configurations of 4,7-dihydro-4-hydroxyimino-6-nitro-1,3-dioxepins, **(1)**.

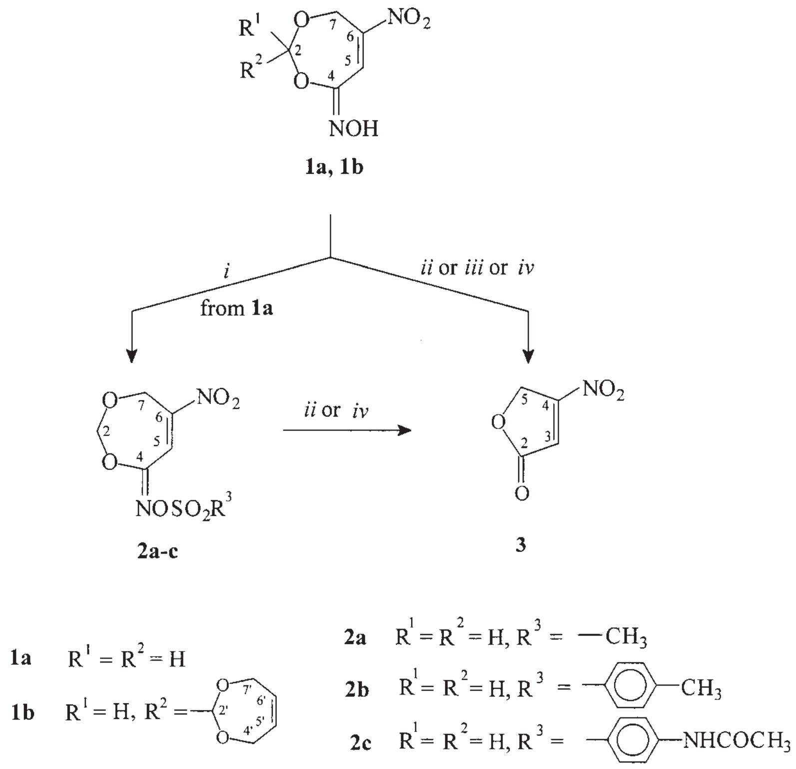
RESULTS AND DISCUSSION

Oximes **1a** and **1b** (Scheme 1) obtained either as by-products in Diels-Alder reaction or prepared by direct nitrosation have shown similar spectroscopic features, indicating the existence of only one configurational isomer in both cases. Therefore, we aimed our investigations at the chemical and spectroscopic determination of their structure and configuration.

Chemical Investigation

The Beckmann rearrangement is a well known standard procedure for elucidation of oxime stereochemistry.[3–5] Thus, by treatment of **1a** with methane-, *p*-toluene- or *p*-acetylaminobenzenesulfochlorides and sodium hydrogencarbonate in acetone, only *O*-sulfonates **2a-c** were isolated (Scheme 1).

Under more drastic conditions, using either PCl_5 or P_2O_5 in chloroform, both oximes **1a** and **1b**, and sulfonic ester **2a** furnished none of the two possible dioxaazocines **A** or **B** (Figure 2). In all studied cases, the only isolated product was 4-nitro-5H-furanon-2-on (**3**) (Scheme 1). The structure of **3** was



Reagents and conditions:

i, R^3SO_2Cl, $NaHCO_3$, acetone, rt, 1 hr

ii, $PCl_5/CHCl_3$, rt, 15 min.

iii, $P_2O_5/CHCl_3$, rt, 2 hrs

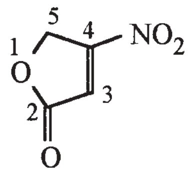
iv, HCl : H_2O(1:1), 50-60°C, 30 min.

Scheme 1

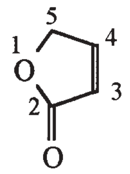
characterized by strong infrared absorption bands (doublet) in the region of carbonyl stretching at 1780 and 1750 cm^{-1}, and symmetrical and unsymmetrical (1540 and 1360 cm^{-1}) stretching vibrations of the nitro group. Electron impact (70 eV) and chemical ionization (NH_3) mass spectra showed molecular ion M^+ at 128 m/z and $M+1^+$ at 129 m/z, respectively. In addition, chemical shifts and coupling constants in ^1H and ^{13}C NMR spectra of **3** are in agreement with those of 5H-furan-2-one (**4**) (Table I).[6] Attempts of preparing **3** from **4** by nitromercuration and demercuration procedures failed in the first step, giving no chloromercury-nitro adduct.

TABLE I

^{1}H and ^{13}C NMR chemical shifts (δ/ppm), H-H and C-H coupling constants (J/Hz) of 4-nitro-5H-furan-2-on (**3**) and 5H-furan-2-on (**4**).



4-nitro-5H-furan-2-on (**3**)



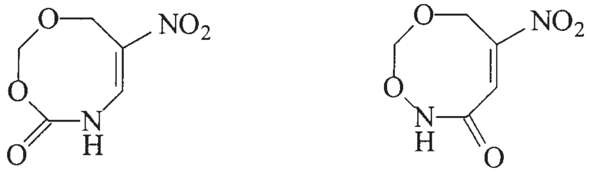
5H-furan-2-on (**4**)

Atom	^{13}C, δ/ppm[a]	$^{n}J_{C\text{-}H}$/Hz[b]	^{13}C, δ/ppm[a]	$^{n}J_{C\text{-}H}$/Hz
C-2	169.45	–	174.09	–
C-3	120.89	$^{1}J_{C\text{-}3,H\text{-}3}$ = 190.85 (d) $^{3}J_{C\text{-}3,H\text{-}5}$ = 3.5 (t)	121.22	$^{1}J_{C\text{-}3,H\text{-}3}$ = 180.9 (d)
C-4	168.25	–	155.21	$^{1}J_{C\text{-}4,H\text{-}4}$ = 176.5 (d)
C-5	68.47	$^{1}J_{C\text{-}5,H\text{-}5}$ = 158.0 (t) $^{3}J_{C\text{-}5,H\text{-}3}$ = 3.5 (t)	73.00	$^{1}J_{C\text{-}5,H\text{-}5}$ = 152.2 (d) $^{2}J_{C\text{-}5,H\text{-}4}$, $^{3}J_{C\text{-}5,H\text{-}3}$ = 10.0 (t)

Atom	1H, δ/ppm[c]	$^{n}J_{H\text{-}H}$/Hz	1H, δ/ppm[a]	$^{n}J_{H\text{-}H}$/Hz
H-3	7.09(1H)	$^{4}J_{H\text{-}3,H\text{-}5}$ = 2.2 (t)	7.83(1H)	$^{3}J_{H\text{-}3,H\text{-}4}$ = 5.8 (d) $^{4}J_{H\text{-}3,H\text{-}5}$ = 1.8 (t)
H-4	–	–	6.14(1H)	$^{3}J_{H\text{-}4,H\text{-}3}$ = 5.8 (d) $^{3}J_{H\text{-}4,H\text{-}5}$ = 2.2 (t)
H-5	5.24(2H)	$^{4}J_{H\text{-}5,H\text{-}3}$ = 2.2 (d)	4.94(2H)	$3J_{H\text{-}5,H\text{-}4}$, $^{4}J_{H\text{-}5,H\text{-}3}$ = 1.8(t)[d]

[a] Acetone-d_6 solution.
[b] n denotes the number of intervening bonds.
[c] CD_3OD solution.
[d] Triplet of H-5 arises from two overlapping doublets due to coupling with H-3 and H-4, three and four bonds away, respectively. Digital resolution 0.20 Hz.

Obtained results suggested formation of **3** simply by hydrolysis of **1** rather than by hydrolysis of the possible Beckmann product **B**. This was supported by the ease of hydrolysis of **1a, 1b** and **2a-c** in aqueous hydrochloric acid (1:1). However, it is important to note that the course of Beckmann rearrengement of **1** and **2a** by TLC indicated only **3** as the product. Therefore, it is possible that hydrolysis occurred on the TLC plate.



A **B**

Figure 2. Possible Beckmann rearrangement products **A** and **B**.

Unfortunately, Beckmann rearrangement did not give an answer on the configuration of oxime group in **1a** and **1b**. Therefore, to figure it out, we have investigated these compounds by various one- and two-dimensional ^{1}H and ^{13}C NMR techniques.

NMR Investigation

Assignments of ^{1}H and ^{13}C NMR spectra were performed using chemical and substituent shifts, H-H and C-H coupling constants and selected irradiation as well as connectivities in two-dimensional homo- and hetero-nuclear correlated spectra. The ^{1}H NMR data for **1a** and **1b** are collected in Table II. In Scheme 1, structures and the enumeration of atoms are displayed.

The ^{1}H spectra of **1a** showed four signals, whose chemical shifts, integrals and multiplicities support the 4,7-dihydro-4-hydroxyimino-6-nitro-1,3-dioxepinic structure. In the 1D spectrum only spin-spin coupling between H-7 and H-5 (see Scheme 1), *i.e.* through four bonds, is visible, amounting to 1.60 Hz. However, in the long-range COSY-45 spectrum very weak cross-signals between H-7 and H-2 were also observed, corresponding to four-bond coupling with a magnitude less than the signal width.

The ^{1}H spectra of **1b** displayed eleven signals out of possible twelve, since olefinic protons H-5' and H-6' showed only one signal. Due to the electronic effect of NO_2 group, the neighbouring olefinic H-5 is more deshielded than the more remote olefinic H-5',6'. This was confirmed by the HETCOR spectrum and by greater magnitude of one-bond C-H coupling at C-5 (164.0 Hz) with respect to that at C-5',6' (158.2 Hz). In NOESY spectrum, the weak cross-signal of H-2 was ascribed to the interaction with one of geminal H-7' since *ab initio* HF/3-21G* calculations showed that the closest spatial distance between H-2 and H-7' is 3.05 Å, while that between H-2 and H-4' is 4.00 Å. The strong geminal NOE cross-signal revealed the second geminal H-7', thus in turn enabling the determination of H-4' protons. It means that the geminal H-4' and H-7' protons are chemically nonequivalent and mutu-

TABLE II

^{1}H chemical shifts (/ppm)[a] and H-H coupling constants ($^nJ_{H-H}$/Hz)[b] in nitrooximes **1a** and **1b**

Molecule	**1a**		**1b**	
H-atom	δ/ppm	$^nJ_{H-H}$/Hz	δ/ppm	$^nJ_{H-H}$/Hz
NOH	11.74 (1H)	(s)	11.77 (1H)	(s)
H-2	5.36 (2H)	(s)	5.47 (1H)	^3J = 4.2(d)
H-5	7.33 (1H)	^4J=1.60(t)	7.33 (1H)	(s)
H-7	4.98 (2H)	^4J=1.65(t)	4.89 (1H) 5.10 (1H)	^2J = 17.52(d) ^2J = 17.58(d)
H-2'	–	–	4.82 (1H)	^3J = 4.2(d)
H-4'	–	–	4.18 (1H) 4.54 (1H)	^2J = 15.22(d) ^2J = 15.22(d)
H-5',6'	–	–	5.72 (2H)	(s)
H-7'	–	–	4.20 (1H) 4.50 (1H)	^2J = 16.12(d) ^2J = 16.01(d)

[a] DMSO-d_6 solutions. Chemical shifts refer to TMS. Number of equivalent protons is given in brackets.
[b] The multiplicity of coupling is as follows: s = singlet, d = doublet, t = triplet and m = complex multiplet. Digital resolution 0.20 Hz; *n* denotes the number of intervening bonds.

ally overlapped (see Table II), which was confirmed by the HETCOR spectra displayed in Figure 3.

The methine H-2 is much more deshielded than the H-2', which was supported by the NOESY, HETCOR and gated decoupled spectra as well as by comparison with **1a**. In the NOESY spectrum, H-2 displays only spatial contact to H-7', while H-2' shows spatial contacts to H-4' (3.76 Å) and H-7' (3.69 Å). Gated decoupled spectrum of C-2' showed a doublet of multiplets, while that of C-2 doublets of doublets, which is in agreement with their different proton environment. In contrast to **1a,** the H-7 protons in **1b** are chemically nonequivalent, displaying a typical geminal splitting pattern. They are shifted downfield with respect to H-7' protons, due to the effect of NO_2 group. The assignment of H-7 was substantiated by the strong NOE signal with H-2 (calculated distance 2.59 Å) and by four-bond coupling to H-5 in the long-range COSY-45 spectrum.

The presence of one signal for oxime hydroxyl proton in **1a** (11.74 ppm) and **1b** (11.77 ppm) confirms the existence of only one geometric isomer in the DMSO-d_6 solution. Differential NOE measurements revealed that the

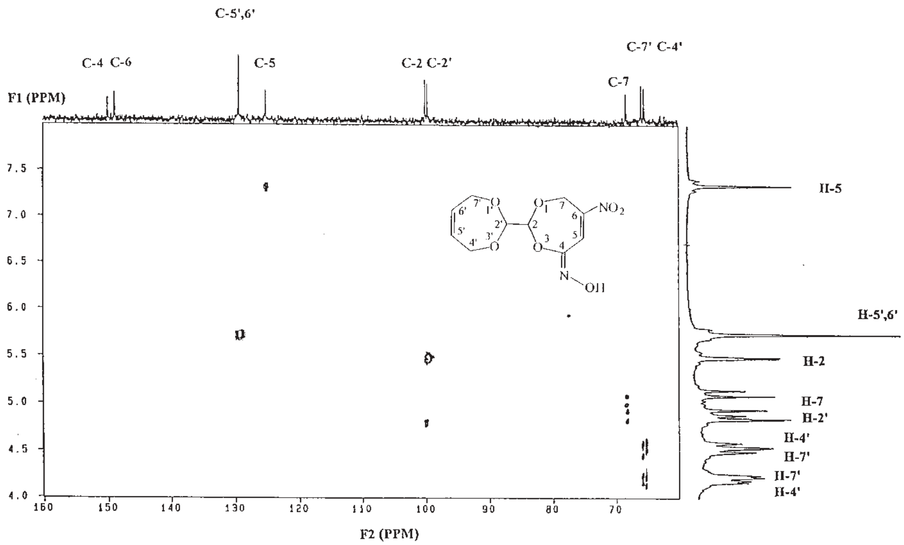


Figure 3. One-bond C-H correlated spectrum (HETCOR) of **1b**.

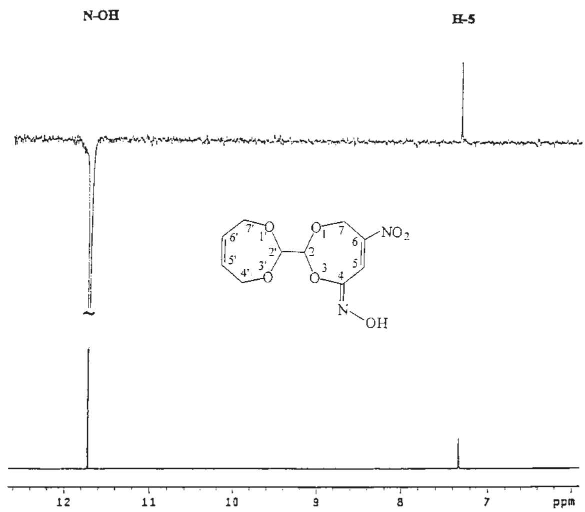


Figure 4. A part of the gradient selected differential NOE proton spectrum (above) and the normal proton spectrum (below) of **1b**, displaying spatial interaction between N-OH and H-5 protons.

hydroxyl proton is oriented towards the olefinic H-5, but not towards the ring oxygen atom. It means that **1a** and **1b** exist in the form of *E*-isomer in the DMSO-d_6 solution. In Figure 4, a part of the differential NOE spectrum of **1b** is given, displaying spatial interaction between N-OH and H-5. The NOE between N-OH and H-5 is in agreement with the *ab initio* calculated distance between these protons, amounting to 3.21 Å.[7]

The ^{13}C NMR data of **1a** and **1b** are collected in Table III. The broad-band proton decoupled ^{13}C NMR spectra of **1a** display five signals. C-2 is more deshielded than C-7 because of two oxygen atoms directly bonded to the former, while only one to the latter. For the same reason, one-bond C-H coupling at C-2 is greater than at C-7. The quarternary C-4 and C-6 were distinguished from their long-range C-H coupling patterns in the gated de-coupled spectrum. C-4 displays a doublet of poorly resolved triplets due to two-bond coupling with H-5 and three-bond coupling with both H-2, respectively, while C-6 appears as a quartet, which is in fact a doublet of doublets, due to two-bond coupling with both H-7 and H-5. The assignment was confirmed by heteronuclear multiple bond correlated (HMBC) spectra. A part of HMBC spectrum of **1a** is displayed in Figure 5. One can recognize the two-

TABLE III

^{13}C chemical shifts (δ/ppm)[a] and C-H coupling constants ($^nJ_{C\text{-}H}$/Hz)[b] in nitrooximes **1a** and **1b**

Molecule	**1a**		**1b**	
C-atom	δ/ppm	$^nJ_{C\text{-}H}$/Hz	δ/ppm	$^nJ_{C\text{-}H}$/Hz
C-2	93.28	^1J = 170.8 (t) ^3J = 6.3 (t)	99.95	^1J = 168.0 (d) ^2J = 9.8 (d)
C-4	151.23	^2J = 7.3 (d)	150.32	^2J = 7.6 (d)
C-5	125.31	^1J = 163.7 (d) ^3J = 4.4 (t)	125.47	^1J = 164.0 (d) ^3J = 9.8 (t)
C-6	149.31	^2J = 8.1 (q)	149.23	^2J = 7.2 (q)
C-7	68.84	^1J = 153.0 (t) ^3J = 7.6 (q)	68.46	^1J = 153.3 (t) ^3J = 7.2 (t)
C-2'	–	–	100.31	^1J = 168.0 (d)[c]
C-4'	–	–	65.61	^1J = 146.0 (t)
C-5',6'	–	–	129.65	^1J = 158.2 (d) ^2J = 5.4 (t)
C-7'	–	–	66.05	^1J = 146.3 (t)

[a] DMSO-d_6 solutions. Chemical shifts refer to TMS.

[b] Digital resolution 0.60 Hz. The multiplicity of coupling is as follows: s = singlet, d = doublet, t = triplet and q = quartet; *n* denotes the number of intervening bonds.

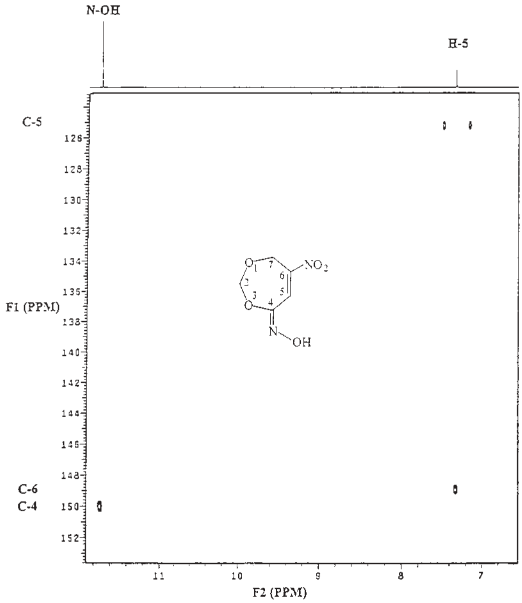


Figure 5. A part of the gradient selected multiple bond C-H correlated spectrum (HMBC) of **1a**. Besides the two- and three-bond C-H correlation of C-6 and C-4, respectively, the undecoupled one-bond correlation of C-5 is also visible.

bond correlation of C-6 with H-5 and three-bond correlation of C-4 with N-OH. In addition, the undecoupled one-bond correlation of C-5 with H-5 is also visible. The two-dimensional assignment of C-4 and C-6 confirmed previous data on related molecules having hydroxylimino and nitro groups.[8,9]

The ^{13}C spectrum of **1b** displayed nine signals out of possible ten, since olefinic carbons C-5',6' are chemically equivalent. The olefinic C-5 and C-5',6' were distinguished on the basis of their one-bond C-H coupling. The $^1J_{C,H}$ at C-5 is greater (164.0 Hz) than the $^1J_{C,H}$ at C-5',6' (158.2 Hz) due to the electron influence of NO_2 group in the former case.[8] Contrary to the situation in ^{1}H spectra, in ^{13}C spectra the NO_2 gives rise to C-5 shielding. Thus, C-5',6' is more deshielded than C-5, which was confirmed by HETCOR measurements. The quatrernary C-4 and C-6 showed the same features as in **1a**. The C-2 and C-2' were assigned straightforwardly from the HETCOR spectrum, since H-2 is easily distinguished on the basis of **1a** data (see Table II). For both C-2 and C-2', the one-bond C-H coupling is the same, amounting to 168.0 Hz. However, additional long-range C-H splittings are different: C-2' shows a complex multiplet due to interactions with H-2, H-4' and H-7', while C-2 displays only a doublet due to coupling with H-2'. The chemical shift of C-7 is similar to that in **1a**, but greater than those of C-7' and C-4' in the unsubstituted ring in **1b**.

The configuration of oximes **1a** and **1b** may be assumed from ^{13}C gated decoupled spectra as well. It is generally known that the *Z*-orientation of the lone electron pair to C-H bond gives rise to an increase in magnitude of the corresponding one-bond C-H coupling (*ca.* 10–15 Hz), as compared to the *E*-orientation.[9] The magnitude of $^{1}J_{C\text{-}5,H\text{-}5}$ in **1a** (163.7 Hz) and **1b** (164.0 Hz) might correspond to *E*-arrangement of the nitrogen lone electron pair to C-5-H bond (Figure 1), in parallelism with acetaldoxime, where the corresponding $^{1}J_{C,H}$ is 163.0 Hz for *E*-isomer, while it is even 177.0 Hz for *Z*-isomer.[10] This is in agreement with the differential NOE measurements, which unambiguously proved that both oximes **1a** and **1b** have *E*-configuration.

In conclusion, one can say that the analysis of ^{1}H and ^{13}C chemical shifts, magnitudes and patterns of couplings and nitro group substituent effects, as well as differential NOE and connectivities in COSY, NOESY, HETCOR and HMBC spectra, enabled determination of the structure and configuration of the compounds investigated here, proving that the 4,7-dihydro-4-hydroxyimino-6-nitro-1,3-dioxepins, **1a** and **1b**, exist in *E*-form in DMSO-d_6 solution. The energetical preference of *E*-form over *Z*-form was also confirmed by *ab initio* calculations.[7] It might the consequence of a more favourable balance between repulsive and attractive forces (*e.g.* H-bonding) in the former than in the latter isomer.

EXPERIMENTAL

Chemistry. General Information

Melting points were determined on the Boëtius Michroheating Stage and are uncorrected. The IR spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer from a KBr pelleted sample or as film.

The ^{1}H and ^{13}C one- and two-dimensional NMR spectra were recorded with a Varian Gemini 300 spectrometer, operating at 75.5 MHz for the ^{13}C nucleus. The differential NOE spectra and HMBC spectra were recorded using gradient selection spectroscopy (pulsed field gradients) on a Varian UNITY Inova 500 spectrometer (operating at 125.7 MHz for the ^{13}C nucleus). All samples were measured from DMSO-d_6 solution at 20 °C in 5 mm NMR tubes. Chemical shifts, in ppm, refer to TMS. Digital resolution in ^{1}H NMR spectra was 0.20 Hz, while in ^{13}C NMR spectra it was 0.60 Hz per point. The following spectra were recorded on a Gemini 300 spectrometer: broadband proton decoupling, gated proton decoupling, COSY-45, long-range (delayed) COSY-45, NOESY and HETCOR. In all experiments, proton decoupling was performed by Waltz-16 modulation. In two-dimensional experiments, standard pulse sequences were used. The COSY-45 and delayed COSY-45 spectra were measured in a magnitude mode, while NOESY spectra in a phase-sensitive mode. In COSY-45, delayed COSY-45 and NOESY spectra, 1024 points in F2 dimension and 256 increments in F1 dimension, subsequently zero-filled to 1024 points, were used.

Each increment was obtained with 16 scans, 3000 Hz spectral width and a relaxation delay of 1 s. Thus, the digital resolution was 5.9 Hz/point and 11.7 Hz/point in F2 and F1 dimension, respectively. The delayed COSY-45 spectra were measured with delay time, D3, of 0.25 s. The NOESY spectra were measured with several mixing times (0.45–1.2 s). The HETCOR spectra were recorded with 2048 points in F2 dimension and 256 increments in F1 dimension, zero-filled to 512 points. Increments were recorded with 180 scans, relaxation delay of 1 s and spectral width of 20000 Hz in F2 and 4500 Hz in F1 dimensions. The corresponding digital resolution was 19.53 and 17.6 Hz/point in F2 and F1 dimensions, respectively.

Mass spectra were scanned on a Shimadzu GC-MS QP-1000 instrument operating at 70 eV. TLC was performed using Merck Kieselgel 60 F_{254} silica plates and components were visualized using UV light (UV 254) and NH_3 vapor (yellow or brown spots). Compounds were purified by column chromatography using Merck Kieselgel 60 (0.063–0.200 mm, 70–230 mesh), and were homogenous by TLC. Solvents *p.a.* grade were used without further purification. All chemicals used were commercially available and were supplied by Merck. The yields were not optimized.

*General Procedure for the Preparation of Sulfonyl Esters of 4,7-Dihydro-4-hydroxyimino-6-nitro-1,3-dioxepin (**2a-c**)*

To a solution of 4,7-dihydro-4-hydroxyimino-6-nitro-1,3-dioxepin (**1a**) in acetone and sodium hydrogencarbonate in water, a suspension or solution of methanesulfonyl, *p*-toluenesulfonyl or *p*-acetylaminobenzenesulfonyl chloride in acetone was added under stirring in small portions. Reaction mixture was stirred at room temperature for 0.5, 1.5 or 1 hour, and extracted with ethylacetate. The combined extracts were washed with saturated water solution of sodium hydrogencarbonate, and subsequently with water, dried (anhydrous sodium sulfate) and concentrated *in vacuum*. Obtained yellow oils were purified by crystallization from the acetone-water mixture (**2b**, **2c**) or by silica-gel chromatography with benzene-acetone (7:3) (**2a**).

*4,7-Dihydro-4-mesyloxyimino-6-nitro-1,3-dioxepin (**2a**)*

According to the general procedure a mixture of **1a** (0.10 g, 0.57 mmol) in 6 mL acetone, sodium hydrogencarbonate (0.19 g, 2.20 mmol) in 6 mL water, and methane sulfonylchloride (0.230 g, 2.00 mmol) in 6 mL acetone was stirred at room temperature for 0.5 h. The crude oily **2a** (0.140 g; 96.61%) was purified by column chromatography using a benzene-acetone (7:3) mixture to yield pure **2a** (0.12 g; 82.73%). The analytical sample of **2a** (decomp. by warming up to 50–60 °C) was obtained by repeated column chromatography using the benzene-acetone (7:3) mixture. IR (film) ν_{max}/cm^{-1}: 3095w, 3020w, 2945w, 1600s, 1545vs, 1490w, 1450w, 1430m, 1370vs, 1335vs, 1305m, 1265w, 1185vs, 1130s, 1050s, 1025m, 980s, 940s, 910w, 880vs, 780vs, 760s, 730m, 695vs, 650w; ^1H NMR (acetone-d_6), δ/ppm: 4.09 (s, 3H, CH_3), 5.29 (d, 2H, J = 1.9 Hz, H–7), 5.71 (s, 2H, H-2) and 7.57 (t, 1H, J = 1.9 Hz, H-5); ^{13}C NMR (acetone-d_6) δ/ppm: 35.78 (CH_3), 69.53 (C-7), 94.87 (C-2), 121.73 (C-5), 155.08 (C-6) and 156.44 (C-4).

*Anal.*calcd. for $C_6H_8N_2O_7S$ (M_r=252.16): C 28.57, H 3.20, N 11.11%; found: C 28.39, H 3.47, N 10.92%.

4,7-Dihydro-6-nitro-4-tosyloxyimino-1,3-dioxepin (**2b**)

According to the general procedure, a mixture of **1a** (0.22 g, 1.26 mmol) in 15 mL acetone, sodium hydrogencarbonate (0.36 g, 4.28 mmol) in 15 mL water, and *p*-toluene sulfonylchloride (0.45 g, 2.36 mmol) in 15 mL acetone was stirred at 0–5 °C for 1.5 h. Reaction mixture was acidified and extracted with ethylacetate. The crude product was crystallized from the acetone-water mixture to yield **2b** (0.21 g; 50.91%), m.p. 89–91 °C. After recrystallization from the acetone-water mixture, the sample showed m.p. 90–92 °C.

IR (KBr) ν_{max}/cm^{-1}: 3035w, 3025w, 3015w, 2990w, 2960w, 2850w, 1590vs, 1535vs, 1480w, 1450m, 1430m, 1370vs, 1360vs, 1330vs, 1310s, 1195vs, 1180vs, 1130s, 1095m, 1050vs, 1015w, 960m, 950m, 925m, 880vs, 845m, 810m, 790m, 775vs, 720m, 700vs, 690vs and 660s; ^{1}H NMR ($CDCl_3$) δ/ppm: 2.46 (s, 3H, CH_3), 4.98 (d, 2H, J = 1.8 Hz, H-7), 5.34 (s, 2H, H-2), 7.37 (d, 2H, J = 8.1 Hz, ar.H-3', 5'), 7.45 (t, 1H, J = 1.8 Hz, H-5) and 7.88 (d, 2H, J = 8.1 Hz, ar. H-2', 6'); ^{13}C NMR ($CDCl_3$) δ/ppm: 21.73 (CH_3), 68.58 (C-7), 94.36 (C-2), 123.19 (C-5), 129.06 (C-2' & C6'), 129.90 (C-3' & C5'), 131.61 (C-1'), 145.77 (C-4'), 153.16 (C-6) and 155.19 (C-4); MS, m/z: 328 (M^+, 15.5%) 173 (21.0), 155 (100.0), 139 (31.5), 121 (20.8), 107 (23.3), 92 (30.1), 91 (99.9), 89 (26.4), 77 (27.2), 67 (71.5), 65 (99.9), 63 (32.0) and 52 (30.9).

*Anal.*calcd. for $C_{12}H_{12}N_2O_7S$ (M_r=328.27): C 43.90, H 3.68, N 8.53%; found: C 44.07, H 3.89, N 8.35%.

*4-(*N*-Acetylaminobenzensulfonyloxyimino)-4,7-dihydro-6-nitro-1,3-dioxepin* (**2c**)

According to the general procedure, a mixture of **1a** (0.30 g, 1.72 mmol) in 15 mL acetone, sodium hydrogencarbonate (0.49 g, 5.83 mmol) in 15 mL water, and *p*-acetylaminobenzenesulfonylchloride (0.75 g, 2.33 mmol) in 15 mL acetone, was stirred at room temperature for 1.0 h. The crude product was crystallized from the acetone-water mixture to yield **2c** (0.32 g; 50.10%) m.p. 152–154 °C. After recrystallization from the acetone-water mixture, the sample showed m.p. 153–155 °C. IR (KBr) ν_{max}/cm^{-1}: 3195s, 3050w, 3030w, 2960w, 2925w, 1715vs, 1590vs, 1530vs, 1445m, 1430m, 1405s, 1365vs, 1360vs, 1330s, 1315s, 1300m, 1260m, 1245m, 1195vs, 1175vs, 1125s, 1095m, 1040vs, 1020m, 1005m, 965m, 940m, 900m, 880s, 850s, 840m, 775vs, 720s, 715m, 690vs, 660m, 630s and 615vs; ^{1}H NMR (DMSO-d_6) δ/ppm: 2.11 (s, 3H, CH_3), 5.03 (d, 2H, J = 1.8 Hz, H-7), 5.50 (s, 2H, H-2), 7.19 (t, 1H, J = 1.8 Hz, H-5), 7.88 (s, 4H, ar. H-2', 3', 5' and 6') and 10.42 (s, 1H, NH); ^{13}C NMR (DMSO-d_6), δ/ppm: 24.27 (CH_3), 69.30 (C-7), 94.63 (C-2), 118.91 (C-3' and C-5'), 120.94 (C-5), 130.19 (C-2' and C-6'), 139.62 (C-1'), 145.09 (C-4'), 155.36 (C-6), 155.66 (C-4) and 169.47 (C=O); MS, m/z: 371 (M^+, 15.0%), 216 (43.5), 198 (100.0), 130 (60.3), 83 (73.2), 69 (33.3), 55 (97.7), 54 (46.6) and 53 (99.9).

*Anal.*calcd. for $C_{13}H_{13}N_3O_8S$ (M_r=371.28): C 42.05, H 3.53, N 11.32, S 8.64%; found: C 41.85, H 3.50, N 11.11, S 8.68%.

4-Nitro-5H-furan-2-on (**3**)

A – from **1a** with PCl_5

To the suspension of **1a** (0.20 g, 1.15 mmol) in 30 mL of chloroform, 0.73 g (3.5 mmol) phosphorus pentachloride was added. The reaction mixture was stirred at room temperature for 15 minutes and poured on 20 g ice. After separation of water-chloroform layers, the water layer was five times extracted with 10 mL chloroform. Collected chloroform layers were washed three times with water, dried on anhydrous sodium sulfate and evaporated under reduced pressure to dryness. The crude product (0.12 g ; m.p. 115–125 °C) was crystallized from benzene to yield **3** (0.09 g; 60.3%) m.p. 121–124 °C. After recrystallization from benzene, the sample showed m.p. 123–125 °C. IR (KBr) ν_{max}/cm^{-1}: 3130m, 2980w, 1780vs, 1750s, 1665w, 1540s, 1450m, 1380vs, 1360s, 1295s, 1160m, 1100s, 1030s, 880s, 790s and 750s; ^1H NMR (CD_3OD), δ/ppm: 7.09 (t, 1H, J = 2.3 Hz, H-3), 5.24 (d, 2H, J = 2.3 Hz, H-5); ^{13}C NMR (CD_3OD), δ/ppm: 169.54 (C-2), 168.25 (C-4), 120.86 (C-3) and 68.46 (C-5); MS, m/z: 129 (M^+, 33.5%) 99 (18.2), 83 (37.1), 69 (12.9), 55 (84.1), 53 (66.0) and 44 (100.0).

*Anal.*calcd. for $C_4H_3N_2O_2$ (M_r=129.07): C 37.22, H 2.34, N 10.85%, found: C 37.56, H 2.66, N 10.69%.

B – from **1a** with P_2O_5

To the suspension of **1a** (0.20 g, 1.5 mmol) in 30 mL of chloroform, 0.50 g (3.5 mmol) phosphorus pentoxyde was added. The reaction mixture was stirred at room temperature for 2 hours and poured on 20 g ice. Following water-chloroform layers separation, the water layer was five times extracted with 10 mL chloroform. Collected chloroform layers were washed three times with water, dried upon anhydrous sodium sulfate and evaporated under reduced pressure to dryness. The crude product (0.10 g; m.p. 115–125 °C) was crystallized from benzene to yield **3** (0.08 g; 56.67%) m.p. 121–124 °C. Its IR spectrum was identical to an authentic sample from **A**.

C – from **1b** with PCl_5

To the suspension of **1b** (0.20 g, 0.73 mmol) in 30 mL of chloroform, 0.46 g (2.2 mmol) phosphorus pentachloride was added. The reaction mixture was stirred at room temperature for 15 minutes and poured on 20 g ice. Following water-chloroform layers separation, the water layer was five times extracted with 10 mL chloroform. Collected chloroform layers were washed three times with water, dried upon anhydrous sodium sulfate and evaporated under reduced pressure to dryness. The crude product (0.07 g ; m.p. 115–125 °C) was crystallized from benzene to yield **3** (0.05 g; 54.4%) m.p. 121–124 °C. After recrystallization from benzene, the sample showed m.p. 123–125 °C. Its IR spectrum was identical to an authentic sample from **A**.

D – from **1b** with P_2O_5

To the suspension of **1b** (0.20 g, 0.73 mmol) in 30 mL of chloroform, 0.31 g (2.2 mmol) phosphorus pentoxide was added. The reaction mixture was stirred at room temperature for 15 minutes and poured on 20 g ice. Following water-chloroform layers separation, the water layer was five times extracted with 10 mL of chloroform. Collected chloroform layers were washed three times with water, dried upon anhydrous sodium sulfate and evaporated under reduced pressure to dryness. The crude product (0.08 g ; m.p. 115–125 °C) was crystallized from benzene to yield **3** (0.047 g; 50.2%) m.p. 121–124 °C. After recrystallization from benzene, the sample showed m.p. 123–125 °C. Its IR spectrum was identical to an authentic sample from **A**.

E – from **1a** with HCl

The suspension of **1a** (0.05 g, 0.3 mmol) in 5 mL hydrochloric acid (1:1), was stirred at 50–60 °C for 0.5 h. The reaction mixture was evaporated under reduced pressure to dryness. The residue (0.036 g) was extracted with benzene. Benzene extract was dried over anhydrous sodium sulfate and concentrated, furnishing crude, TLC pure **3** (0.03 g; 80.9%). Its IR spectrum was identical to an authentic sample from **A**.

F – from **1b** with HCl

The suspension of **1b** (0.05 g, 0.2 mmol) in 5mL hydrochloric acid (1:1), was stirred at 50–60 °C for 0.5 h. After isolation of product according the procedure **E**, the **3** (0.02 g; 84.3 %) m.p. 123–125 °C was obtained. Its IR spectrum was identical of an authentic sample from **A.**

G – from **2a** with PC_5

To the suspension of **2a** (0.20 g, 0.79 mmol) in 30 mL of chloroform, phosphorus pentachloride (0.73 g) was added. The reaction mixture was stirred at room temperature for 15 minutes and poured on ice (20 g). Following the water-chloroform layers separation, the water layer was five times extracted with 10 mL chloroform. Collected chloroform layers were washed three times with water, dried upon anhydrous sodium sulfate and evaporated under reduced pressure to dryness. The crude product (0.06 g; 55.7%), m. p. 121–124 °C. Its IR spectrum was identical to an authentic sample from **A**.

H – from **2a** with HCl

The suspension of **2a** (0.05 g, 0.2 mmol) in 5 mL hydrochloric acid (1:1) was stirred at 50–60 °C for 0.5 h. After product isolation according the procedure **E**, the **3** (0.02 g; 73.8%), m.p. 122–124 °C, was obtained. Its IR spectrum was identical to an authentic sample from **A.**

According to TLC, the **3** was the sole product of sulfonic esters **2b-c** hydrolysis, under the same conditions as reported in procedure **H**. Unfortunately, **3** was not isolated.

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SAŽETAK

Kemija 1,3-dioksepina. XIII. Određivanje (*E*)/(*Z*) konfiguracije 4,7-dihidro-4-hidroksiimino-6-nitro-1,3-dioksepina

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Konfiguracija oksima **1a** i **1b** istraživana je kemijskim i spektroskopskim metodama. Uporabom sulfonil-klorida kao reagensa, u uvjetima Beckmannove pregradnje dobiveni su esteri **2a-c**. Pri mnogo žeščim uvjetima, uporabom PCl_5 ili P_2O_5, izoliran je 4-nitro-5H-furan-2-on (**3**). Hidrolizom oksima **1a-b**, kao i sulfonskog estera **2a**, 4-nitro-5H-furan-2-on također je nastajao kao jedini produkt.

Strukture svih spojeva određene su iz jedno- i dvodimenzijskih homo- i heteronuklearnih NMR spektara: COSY, NOESY, HETCOR i HMBC. Gradijentno pobuđena NMR mjerenja diferencijalnog nuklearnog Overhauserova efekta (NOE) potvrdila su da su oksimi **1a** i **1b** u otopini dimetilsulfoksida u *E*-konfiguraciji, bez obzira na način njihova nastanka.