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Short Note

4-(8-Propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one)

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Abstract: A number of 1D and 2D NMR techniques, such as ^{1}H, ^{13}C, DEPT 135, ^{1}H-^{1}H COSY, HSQC, and HMBC, were utilized for the structure verification of 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one). The NMR spectra provided evidence for the tautomeric conversion of the compound. The completely assigned NMR data was supported additionally by ATR.

Keywords: heterocycle synthesis; heterocyclic tautomers; benzodiazepines; NMR spectroscopy

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1. Introduction

Isatin, 1,5-benzodiazepine, and 5-spirocyclohexyl-2,4-dithiohydantoin are chemical building blocks possessing several reaction centers, which allow them to be used as precursors in numerous organic syntheses of heterocyclic compounds [1–5]. For example, the carbonyl groups in isatin can participate in addition reactions at the C-O bond as well as in condensation reactions. Meanwhile, the NH group in isatin enters into N-alkylation and N-acylation reactions. Various polar (e.g., hydroxyl, carbonyl) and non-polar groups (e.g., alkyl) can be incorporated into the benzene and diazepine rings of the 1,5-benzodiazepine fragment, leading to the production of a broad range of derivatives with versatile biological activity. Furthermore, 1,5-benzodiazepines are famous for their tautomerism due to the presence of NH groups in their structure, which additionally modifies their biochemical properties [6–8]. The 5-spirocyclohexyl-2,4-dithiohydantoin fragment has two NH and two C=S groups, which can participate in substitution and addition organic reactions, respectively. Most of the heterocycles produced containing some or all of the abovementioned fragments possess antimicrobial [3,9–14], antifungal [14], antiepileptic [15], and anticancer [16] activity. The high interest towards the isatin-, 1,5-benzodiazepine- and/or 5-spirocyclohexyl-2,4-dithiohydantoin-based derivatives have led to a significant amount of reported IR, NMR, and MS data supporting their structures [1–5,9–14]. Thus, spectral or structural data for such newly synthesized compounds can be found in some spectral databases and interpretative libraries [17–19].

The main aim of the work was to verify the structure of 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one) synthesized by combining isatin, 1,5-benzodiazepine, and 5-spirocyclohexyl-2,4-dithiohydantoin. The structure verification was performed mainly by using 1D and 2D NMR techniques—^{1}H, ^{13}C, DEPT 135, ^{1}H-^{1}H COSY, HSQC, and HMBC.

2. Results and Discussion

The suggested structures of the synthesized compound and its tautomer are presented in Figure 1.

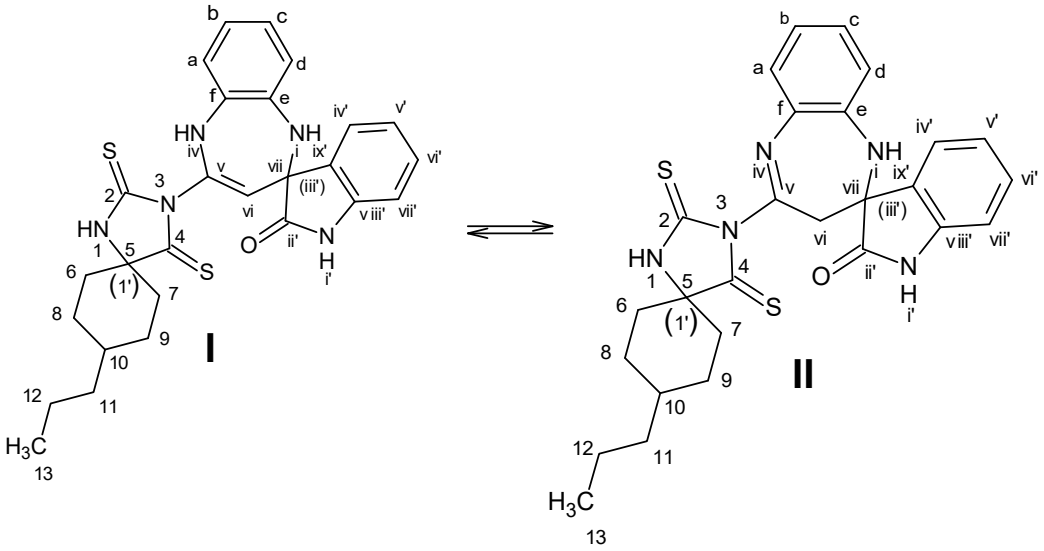

Figure 1. Suggested structure of 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one) (**I**) and its tautomer (**II**). The numbering and lettering of the atoms in both structures were used only for the spectral assignments.

The molecular formula of compound **I** and its tautomer **II** is $C_{27}H_{29}N_5S_2O$. The reason for presenting the tautomer of compound **I** was the missing signal of NH-iv proton in the ^{1}H NMR spectrum (Table 1) (Figure S1). However, the ^{1}H singlet at 2.72 ppm, with an area of 1.81, indicated the transfer of the NH-iv proton to the C-vi carbon, forming the CH_2 group in the structure of tautomer **II**. Moreover, the HSQC spectrum showed two correlations involving the signal at 2.72 ppm–(2.72–28.90 ppm) and (2.72–32.09 ppm). The former HSQC correlation was positive, indicating the presence of the H-vi proton and C-vi carbon in the CH group in compound **I**. The latter HSQC correlation was negative, including the chemical shifts of the signals of the methylene protons and carbon in the CH_2-vi group that is present in compound **II**. Thus, the ^{1}H singlet at 2.72 ppm was assigned to both protons in CH_2-vi in tautomer **II**. Also, instead of observing 25 signals in the ^{13}C spectrum (Figure S2), there were 26 signals, where those at 29.17 ppm and 32.14 ppm, as already suggested by the HSQC spectrum, corresponded to the carbon C-vi in the tautomers **I** and **II**. Meanwhile, the DEPT 135 spectrum (Figure S3) showed a positive ^{13}C signal at 29.17 ppm as there was not any signal at 32.14 ppm. Consequently, the ^{1}H NMR spectrum showed the resonances specifically for compound **II** while the ^{13}C NMR and HSQC spectra showed some resonances for both tautomers. The DEPT 135 spectrum included the CH and C^6H_2, C^7H_2, C^8H_2, C^9H_2, $C^{11}H_2$, and $C^{12}H_2$ signals only for tautomer **I**. Evidently, the NMR data indicated the mutual presence of both tautomers **I** and **II** in the reaction mixture, as the mobile NH-iv proton participated in the tautomeric interconversion. For this reason, there was no NH-iv signal detected in the ^{1}H NMR spectrum (Table 1).

Table 1. ^{1}H and ^{13}C NMR data assignment for compounds **I** and **II**. [^{1}H [500.13 MHz] and ^{13}C [125.76 MHz]] [a].

Atom	δ (^{13}C), ppm	DEPT [b]	δ (^{1}H), ppm	Multiplicity (J, Hz)	^{1}H-^{1}H COSY [b]	HMBC [b]
2(C=S)	180.25	C				
4(C=S)	208.63	C				
1(NH)			13.91	s		
(1′)	79.79	C				
6/7	30.77	CH_2	2.66 [c] (H_a) [f]	td(13.4, 4.7)	H_b, H_c, H_d	(1′), 8/9, 4
			1.80 [c] (H_b) [f]	m	H_a, H_c, H_d	
8/9	21.13	CH_2	2.20 [c] (H_c) [f]	qd(13.2, 4.0)	H_d, H_a, H_b, 10	6/7 [d], 10 [e]
			1.59 [c] (H_d) [f]	m	H_c, H_a, H_b, 10	
10	45.05	CH	1.06 [c]	m	H_c, H_d	
11	20.31	CH_2	2.17 [c] (H_e) [f]	qd(13.2, 4.0)	H_f, 10, H_g, H_h	
			1.55 [c] (H_f) [f]	m	H_e, 10, H_h, H_g	
12	35.05	CH_2	1.86 [c] (H_g) [f]	m	H_e, H_f, H_h	
			1.63 [c] (H_h) [f]	m	H_e, H_f, H_g	
13	27.38	CH_3	0.86 [c]	s		10
ii′(C=O)	176.15	C				
v	171.30	C				
i(NH)			7.26	s		
(iii′)	74.30	C				
iv(NH)						
i′(NH)			10.34	s		(iii′), viii′, ix′
viii′	141.30	C				
ix′	129.78	C				
iv′	125.59	CH	7.55	d(7.4)	v′, vi′ [e]	(iii′), viii′, vi′
v′	122.44	CH	7.07 [c]	td(7.6, 0.9)	iv′, vi′, vii′ [e]	vii′, ix′
vi′	130.46	CH	7.29	td(7.7, 1.2)	v′, vii′, iv′ [e]	iv′, viii′
vii′	110.03	CH	6.84	d(7.8)	v′ [e], vi′	v′, ix′
vi	29.17/32.14	CH/CH_2	2.72	s		v
a	121.07	CH	7.04 [c,f]	dd(7.5,0.8)	b, c [e]	c, e
b	118.63	CH	6.63 [f]	td(7.5, 1.0)	a, c, d [e]	d, f
c	125.68	CH	6.90 [f]	td(7.7, 1.2)	a [e], b, d	a, e
d	108.41	CH	6.53 [f]	dd(7.8, 0.8)	b [e], c	b, f
e	147.19	C				
f	124.10	C				

[a] In DMSO-d_6 (solvent reference: ^{1}H δ_{ref} 2.50 ppm, ^{13}C δ_{ref} 39.51 ppm). All spectral assignments are in accordance with HSQC, HMBC, and COSY spectra. [b] Abbreviations: DEPT, Distortionless Enhancement by Polarization Transfer spectrum; ^{1}H-^{1}H COSY, proton–proton homonuclear correlation spectrum; HMQC, Heteronuclear Multiple Quantum Correlation experiment; HMBC, Long-range ^{1}H-^{13}C Heteronuclear Multiple Bond Correlation experiment. [c] The chemical shift was assigned from the HSQC spectrum. [d] Correlations are weak. [e] Correlations are extremely weak. [f] H-a, H-b, H-c, and H-d are the benzene protons while the chemically inequivalent methylene protons were expressed with capital letter H, accompanied by a letter as a lower subscript.

The ^{1}H singlet at 13.91 ppm was assigned to the NH-1 proton that is close to the C^{2}=S group, while the ^{1}H singlets at 10.34 ppm and 7.26 ppm were assigned to the NH-i′ and NH-i protons, respectively. Additionally, the strong HMBC correlations—

(10.34–74.30 ppm), (10.34 ppm–141.30 ppm) and (10.34–129.78 ppm)—indicating the interaction of the NH-i′ proton with the C-iii′, C-viii′, and C-ix′ carbons, respectively, supported the assignment of the ^{1}H signal at 10.34 ppm to the NH-i′ proton.

The DEPT 135 spectrum showed four negative signals at 20.05 ppm, 20.88 ppm, 30.51 ppm, and 34.79 ppm that were for the carbons of the six CH_2 groups in the 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl) fragment—C^6H_2, C^7H_2, C^8H_2, C^9H_2, $C^{11}H_2$ and $C^{12}H_2$. The carbon and both protons in C^6H_2 are chemically equivalent to the corresponding carbon and protons in C^7H_2. Similarly, the protons and carbons in C^8H_2 are chemically equivalent to the protons and carbon in the C^9H_2 group. However, the protons in each of these CH_2 groups are not chemically equivalent. Therefore, four HSQC correlations were found specifically for the C^6H_2, C^7H_2, C^8H_2, and C^9H_2 groups (Figure S4). The strong HMBC correlations, (2.66–79.79 ppm) and (2.66–208.63 ppm), indicated for the two-bond and three-bond interactions of the protons H_a in C^6H_2 and C^7H_2, respectively, with the spirocarbon, C-1′, and thiocarbonyl carbon, C-4. The COSY spectrum indicated that the protons H_c and H_d in C^8H_2 and C^9H_2, whose signals can be found at 2.20 ppm and 1.59 ppm, are neighbors to the protons H_a and H_b (Figure S5). Furthermore, a strong COSY correlation can be found for each of the signals of the protons, H_c and H_d, with the signal of the proton H-10. Additionally, HMBC correlations, (2.66–21.13 ppm), (2.20–30.77 ppm) and (2.20–45.05 ppm), indicated the interactions of the methylene protons H_a with the carbons C-8/9 as well as those interactions of the protons H_c with the carbons, C-6/7 and C-10. The strong COSY correlations of the signals of the methylene protons H_e and H_f with the signal of the proton H-10 indicated that H_e and H_f are bonded with the carbon atom, C-11. Consequently, the signals with the chemical shifts, 1.86 ppm and 1.63 ppm, were assigned to the signals of the protons H_g and H_h that were bonded with the carbon, C-12. The ^{1}H singlet of methyl protons has a chemical shift of 0.86 ppm. While there was one HMBC correlation (Figure S6), (0.86–45.05 ppm), indicating the interaction of the methyl protons with the C-10 carbon, there were no observable COSY correlations involving the signal of methyl protons.

The signals of all aromatic protons and carbons were assigned according to their strong HMBC correlations that resulted from the meta (vicinal) interactions between the protons and carbons in each benzene ring [20]. The COSY correlations, as well as the multiplicity of the ^{1}H signals, supported the assignment of the signals of the benzene protons.

The ATR-IR spectrum showed a band at 3313 cm^{-1} for the ν(N-H) (Table 2). In addition, there were some ATR-IR bands for $\nu_{as}(CH_2)$, $\nu_{as}(CH_3)$, and $\delta_s(CH_2)$ at 2937, 2953, and 1473 cm^{-1}. The ATR-IR bands for ν(C=O) and ν(C=S) can be found at 1705 cm^{-1} and 1257 cm^{-1}, respectively (Figure S7).

Table 2. Key ATR-IR bands.

ATR-IR Band	Wavenumber, cm^{-1}
ν(N-H)	3313
ν(C-H)	3136, 3085, 3070, 3060
$\nu_{as}(CH_3)$	2953
$\nu_{as}(CH_2)$	2937
ν(C=O)	1705
ν(C=C)	1603, 1493
$\delta_s(CH_2)$	1473
ν(C=S)	1257

3. Materials and Methods

3.1. Synthesis

The reaction of 8-propyl-1,3-diazaspiro[4.5]decane-2,4-dithione (**1**) with pyridine and acetic anhydride leads to the synthesis of 1-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethanone (**2**, m.p. 176–177 °C, yield 93%).

The reaction of compound **2** with isatin (1*H*-indole-2,3-dione, **3**) produced 3-hydroxy-3-[2-oxo-2-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethyl]indolin-2-one (**4**, m.p. 201–202 °C, yield 88%), which was converted into 3-[2-oxo-2-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethylidene]indolin-2-one after a treatment with AcOH/HCl (**5**, m.p. 217–218 °C, yield 91%).

The interaction of compound **5** with benzene-1,2-diamine produces 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one (**6**, m.p. 234–235 °C, yield 85%). The whole synthesis pathway is presented in Figure 2.

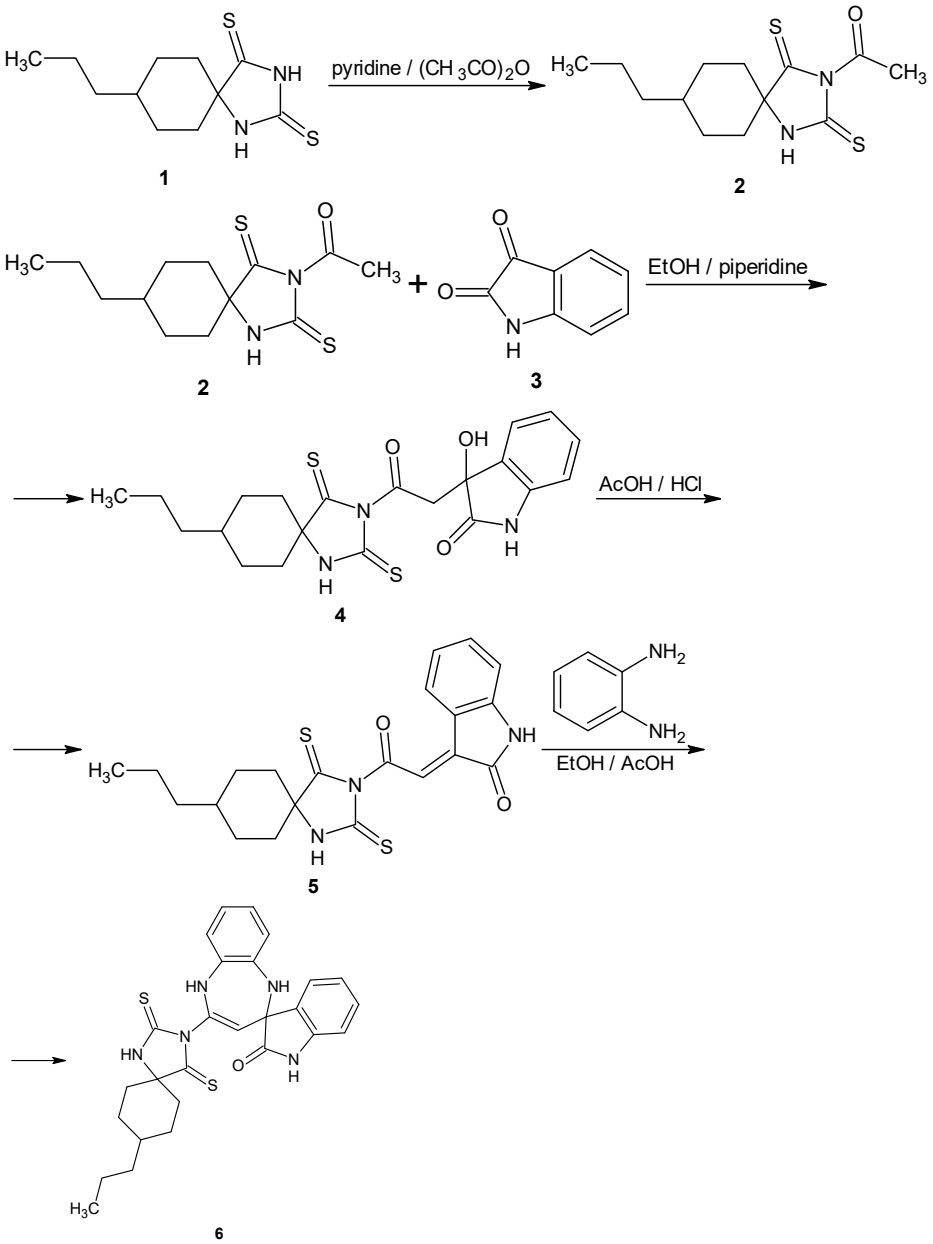

Figure 2. Synthesis of 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one).

*3.2. Synthesis of 3-Hydroxy-3-[2-oxo-2-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethyl]indolin-2-one (**4**)*

A mixture of 1-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethanone (**2**, 2.84 g, 0.01 mol), isatin (**3**, 1.47 g, 0.01 mol) in 100 mL absolute ethanol, and **4** drops of piperidine was shaken for 30 min at room temperature and it was left to stay overnight. The formed solid product was filtrated and recrystallized in ethanol/dioxane.

m.p. 201–202 °C. Yield 3.79 g (88%).

*3.3. Synthesis of 3-[2-Oxo-2-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)ethylidene]indolin-2-one (**5**)*

Compound **4** (4.31 g, 0.01 mol) was solved in 25 mL glacial CH_3COOH and 0.5 mL concentrated HCl. The reaction mixture was heated for 1 h in a boiling bath. A solid product was formed, which was filtered and recrystallized afterwards in ethanol/dioxane.

m.p. 217–218 °C. Yield 3.76 g (91%)

*3.4. Synthesis of 4-(8-Propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one (**6**)*

Benzene-1,2-diamin (0.60 g, 0.0055 mol) and 0.5 mL glacial CH_3COOH was added to the solution of compound **5** (2.07 g, 0.005 mol) prepared in 20 mL ethanol The reaction mixture was heated and boiled for 6 h. After cooling, a solid precipitate was produced, filtered, and recrystallized in ethanol/dioxane.

m.p. 234–235 °C. Yield 2.14 g (85%).

3.5. Apparatus

A Bruker Avance III HD spectrometer (Bruker Optics, Billerica, MA, USA)with frequencies 125.76 MHz and 500.130 MHz was used to measure the 1D and 2D NMR spectra. TMS was used as an internal standard and DMSO-d_6 as a solvent. ATR spectrum was registered with VERTEX 70 FT-IR instrument (Bruker Optics, Billerica, MA, USA) using MIRacleTM with a one-reflection ZnSe element (PIKE Technology, Madison, WI, USA). ATR data was measured in the range (4000–600) cm^{-1} with 25 scans and a resolution of 2 cm^{-1}.

4. Conclusions

The combination of isatin, 1,5-benzodiazepine, and 5-spirocyclohexyl-2,4-dithiohydantoin fragments led to the synthesis of 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3′-indoline]-2′-one) which, according to the assigned NMR data, exists in tautomeric equilibrium with its deprotonated form **II** in the reaction mixture. Further attempts to synthesize and verify the structures of new derivatives, including the same heterocyclic building blocks, will be made.

Supplementary Materials: Figure S1: ^{1}H NMR. Spectrometer frequency is 500.13 MHz. DMSO-d_6 is the used solvent. The expansion shows the singlet at 2.72 ppm, with area 1.81 corresponding to the protons of the CH_2 group in tautomer **II**; Figure S2: ^{13}C NMR. Spectrometer frequency is 125.76 MHz. DMSO-d_6 is the used solvent. The expansion shows the signals at 32.14 ppm and 29.17 ppm that correspond to the carbon C-vi in both tautomers; Figure S3: DEPT 135. Spectrometer frequency is 125.76 MHz. DMSO-d_6 is the used solvent; Figure S4: HSQC. The horizontal and vertical traces show ^{1}H NMR and DEPT 135 spectra, respectively. Spectrometer frequencies for ^{1}H NMR and DEPT 135 spectra are correspondingly 500.13 MHz and 125.76 MHz. DMSO-d_6 is the used solvent. The expansion shows the positive HSQC correlation, (2.72 ppm–28.90 ppm), registered for C-vi carbon and H-vi proton of the CH group in tautomer **I** as well as the negative HSQC correlation, (2.72 ppm–32.09 ppm), for the C-vi carbon and H-vi proton of the CH_2 group in tautomer **II**; Figure

S5: ^{1}H-^{1}H COSY. The horizontal and vertical traces show the ^{1}H NMR spectrum, respectively. Spectrometer frequency for 1H NMR is correspondingly 500.13 MHz. DMSO-d_6 is the used solvent; Figure S6: HMBC spectrum. The horizontal and vertical traces show ^{1}H and ^{13}C NMR spectra, respectively. Spectrometer frequencies for ^{1}H and ^{13}C NMR are correspondingly 500.13 MHz and 125.76 MHz. DMSO-d_6 is the used solvent. Figure S7: ATR-IR.

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References

1. Grewal, A. Isatin Derivatives with Several Biological Activities. *Int. J. Pharm. Res.* **2014**, *6*, 1–7.
2. Pakravan, P.; Kashanian, S.; Khodaei, M.; Harding, F. Biochemical and pharmacological characterization of isatin and its derivatives: From structure to activity. *Pharmacol. Rep.* **2013**, *65*, 313–335. [CrossRef] [PubMed]
3. An, Y.; Hao, Z.; Zhang, X.; Wang, L. Efficient Synthesis and Biological Evaluation of a Novel Series of 1,5-Benzodiazepine Derivatives as Potential Antimicrobial Agents. *Chem. Biol. Drug Des.* **2016**, *88*, 110–121. [CrossRef] [PubMed]
4. Caiana, E.; de Veras, B.O.; de Souzaa, A.L.; Queiroz, N. Synthesis of Hydroxybenzodiazepines with Potential Antioxidant and Antifungal Action. *J. Braz. Chem. Soc.* **2021**, *32*, 626–637. [CrossRef]
5. Elgazwy, A.S.; Atta-Allha, S.; Keshk, S. Synthesis of 5-spirocyclohexyl-2,4-dithiohydantoin derivatives: A potential anti-leishmaniasis agent. *Monatsh. Chem.* **2009**, *140*, 243–249. [CrossRef]
6. Lloyd, D.; Cleghorn, H. 1,5-Benzodiazepines. *Adv. Heterocycl. Chem.* **1974**, *17*, 27–43. [CrossRef]
7. Obydennov, D.; Sosnovskikh, V. The reaction of 6-substituted 4-pyrone-2-carboxylic acids with *o*-phenylenediamine. Synthesis and structure of 3-(1*H*-1,5-benzodiazepin-2(3*H*)-ylidenemethyl)quinoxalin-2(1*H*)-ones. *Chem. Heterocycl. Compd.* **2015**, *51*, 281–290. [CrossRef]
8. Obydennov, D.; Sosnovskikh, V. 3-(1*H*-1,5-Benzodiazepin-2(3*H*)-ylidenemethyl)-quinoxalin-2(1*H*)-ones in reactions with nucleophiles. Synthesis and structure of 3-(hetarylmethyl)quinoxalin-2-ones. *Chem. Heterocycl. Compd.* **2015**, *51*, 503–513. [CrossRef]
9. Kumar, R.; Joshi, Y. Synthesis, spectral studies and biological activity of 3*H*-1, 5-benzodiazepine derivatives. *ARKIVOC* **2007**, *xiii*, 142–149. [CrossRef]
10. Odame, F.; Madanhire, T.; Tettey, C.; Neglo, D.; Adzaho, F.; Sedohia, D.; Hosten, E. Anticancer and Antimicrobial Activity of Some New 2,3-Dihydro-1,5-benzodiazepine Derivatives. *Heteroat. Chem.* **2023**, *2023*, 3390122. [CrossRef]
11. Jaafar, Z.; Chniti, S.; Sassi, A.; Dziri, H.; Marque, S.; Lecouvey, M.; Gharbi, R.; Msaddek, M. Design and microwave-assisted synthesis of dimers of 1,5 benzodiazepine-1,2,3-triazole hybrids bearing alkyl/aryl spacers and their biological assessment. *J. Mol. Struct.* **2019**, *1195*, 689–701. [CrossRef]
12. Liu, J.B.; Lin, C.L.; Wan, Y.Q.; Song, H.C. Synthesis and Bioactivities of 1,5-Benzodiazepine Derivatives. *Chin. J. Org. Chem.* **2008**, *28*, 317–320.
13. Wang, L.; Li, X.; An, Y. 1,5-Benzodiazepine derivatives as potential antimicrobial agents: Design, synthesis, biological evaluation, and structure–activity relationships. *Org. Biomol. Chem.* **2015**, *13*, 5497–5509. [CrossRef] [PubMed]
14. Nsira, A.; Mtiraoui, H.; Chniti, S.; Al-Ghulikah, H.; Gharbi, R.; Msaddek, M. Regioselective One-Pot Synthesis, Biological Activity and Molecular Docking Studies of Novel Conjugates *N*-(p-Aryltriazolyl)-1,5-benzodiazepin-2-ones as Potent Antibacterial and Antifungal Agents. *Molecules* **2022**, *27*, 4015. [CrossRef] [PubMed]
15. Verma, R.; Bhatia, R.; Singh, G.; Kumar, B.; Mehan, S.; Monga, V. Design, Synthesis and Neuropharmacological Evaluation of New 2,4-Disbsituted-1,5 Benzodiazepines as CNS Active Agents. *Bioorg. Chem.* **2020**, *101*, 104010. [CrossRef] [PubMed]
16. Chen, Y.; Le, V.; Xu, X.; Shao, X.; Liu, J.; Li, Z. Discovery of novel 1,5-benzodiazepine-2,4-dionederivatives as potential anticancer agents. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 3948–3951. [CrossRef] [PubMed]
17. Penchev, P.N.; Schulz, K.-P.; Munk, M.E. INFERCNMR: A ^{13}C NMR Interpretive Library Search System. *J. Chem. Inf. Model.* **2012**, *52*, 1513–1528. [CrossRef] [PubMed]
18. Steinbeck, C.; Krause, S.; Kuhn, S. NMRShiftDBConstructing a Free Chemical Information System with Open-Source Components. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1733–1739. [CrossRef] [PubMed]

19. Steinbeck, C.; Kuhn, S. NMRShiftDB–compound identification and structure elucidation support through a free community-built web database. *Phytochemistry* **2004**, *65*, 2711–2717. [CrossRef] [PubMed]
20. Breitmaier, E. *Structure Elucidation by NMR in Organic Chemistry: A Practical Guide, Recognition of Structural Fragments by NMR*, 3rd ed.; John Wiley & Sons Ltd.: Chichester, UK, 2002; Volume 2, p. 27.