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Short Note

4-Methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene) benzenesulfonohydrazide

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Abstract

4-Methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene)benzenesulfonohydrazide was synthesized via *N*-alkylation. The compound was characterized by nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS). Its molecular structure was unambiguously established by single-crystal X-ray diffraction analysis. The comprehensive spectral and crystallographic data conclusively verify the successful synthesis and structural integrity of this newly prepared compound.

Keywords: tosylhydrazone; sulfonohydrazide; *N*-alkylation reaction; crystal structure

1. Introduction

N-alkyl-*N*′-alkylidene sulfonohydrazides can be synthesized via carbene insertion reactions of aryl tosylhydrazones [1–3] and nucleophilic substitution reactions between tosylhydrazones and alkyl halides [4]. Initially, these compounds attracted research attention as byproducts in the Bamford–Stevens reaction [5,6] and Shapiro reaction [7]. In recent years, typical synthetic strategies for constructing valuable organic compounds employing *N*-alkyl-*N*′-alkylidene sulfonohydrazides are summarized as follows: (I) aluminum chloride-mediated highly regioselective synthesis of 1,3,5-trisubstituted pyrazoles using terminal alkynes [8]; (II) regioselective preparation of highly functionalized pyrazoles [9]; (III) synthesis of *N*-tosylhydrazonyl chlorides [10]; (IV) solvent-free synthesis of 1,2,4-triazoles via reactions with nitriles [11].

Previously, our research group reported a synthetic route to 1-arylprop-1-ynes employing aromatic aldehyde *p*-toluenesulfonyl hydrazones as starting materials and calcium carbide as a solid acetylide surrogate. [12] As a follow-up to our ongoing work, we herein investigate the *N*-alkylation reaction of tosylhydrazones.

Herein, we report the successful synthesis of 4-methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene)benzenesulfonohydrazide, together with its single-crystal structure and detailed structural characterizations.

2. Results

The structure of the target compound was unambiguously confirmed by comprehensive spectral and crystallographic characterization, including melting point measurement, ^{1}H NMR, ^{13}C NMR, mass spectrometry, and single-crystal X-ray diffraction.

The ^{1}H NMR spectrum confirms the presence of all 24 expected protons. The three methyl groups appear at δ 2.29 ppm, δ 2.30 ppm, δ 2.39 ppm as a single integrating for nine

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protons. A singlet signal at δ 4.75 ppm was observed in the ^{1}H NMR spectrum and assigned to the methylene group belonging to the benzyl moiety formed during *N*-alkylation reaction (see Supplementary Figure S1). The presence of a signal at δ 52.3 ppm in the ^{13}C NMR spectrum associated with the methylene group was also evidence (see Supplementary Figure S2). HRMS: *m*/*z* [M + Na]$^{+}$ calcd for $C_{23}H_{24}N_2NaO_2S^{+}$: 415.1451; Found: 415.1452. Dimeric species ionized [M + Na]$^{+}$ calcd for $C_{46}H_{48}N_4NaO_4S_2^{+}$: 807.3009; Found: 415.1452. 807.3010. (See Supplementary Figure S3).

Compound **2** was obtained as a crystalline solid from an ethyl acetate/n-hexane (*v*/*v* 6/1) solution through slow evaporation. Single-crystal X-ray crystallography was used to study it, allowing this compound to be unequivocally identified. Crystallographic data and structural refinement parameters of **2** are summarized in Table 1 and an ORTEP representation of the structure of compound **2** is shown in Figure 1.

Table 1. Crystallographic data for the structural analysis of compound **2**.

Crystal Data	2
Empirical formula	$C_{23}H_{24}N_2O_2S$
Formula weight	392.50
Temperature/K	293.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	19.2784(11)
b/Å	6.1133(3)
c/Å	19.2234(11)
α/°	90
β/°	108.513(2)
γ/°	90
Volume/Å^3	2148.3(2)
Z	4
Density (calculated, Mg/m^3)	1.214
Absorption coefficient μ (mm^{-1})	0.170
F(000)	832.0
Crystal size/mm^3	0.32 × 0.28 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.456 to 52.12
Index ranges	$-22 \leq h \leq 23$, $-7 \leq k \leq 7$, $-23 \leq l \leq 23$
Reflections collected	19,812
Independent reflections	4247 [R_{int} = 0.0584, R_{sigma} = 0.0424]
Data/restraints/parameters	4247/0/256
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ(I)]	R_1 = 0.0623, wR_2 = 0.1246
Final R indexes [all data]	R_1 = 0.0942, wR_2 = 0.1450
Largest diff. peak/hole/e Å^{-3}	0.19/−0.36

Compound **2** crystallized in the monoclinic centrosymmetric $P2_1/c$ space group, with four molecules in the asymmetric unit. The characteristic C=N bond angles were present in this molecule, displaying angles N(2)-C(16)-H(16) and N(2)-C(16)-C(17) of 120.01° and 119.98(12)°, respectively (see Table 2). Furthermore, the N(1)-N(2) bond distance (1.383(15) Å) aligned with that reported for other hydrazides in the literature. [13,14] The crystal packing depicted in Figure 2.

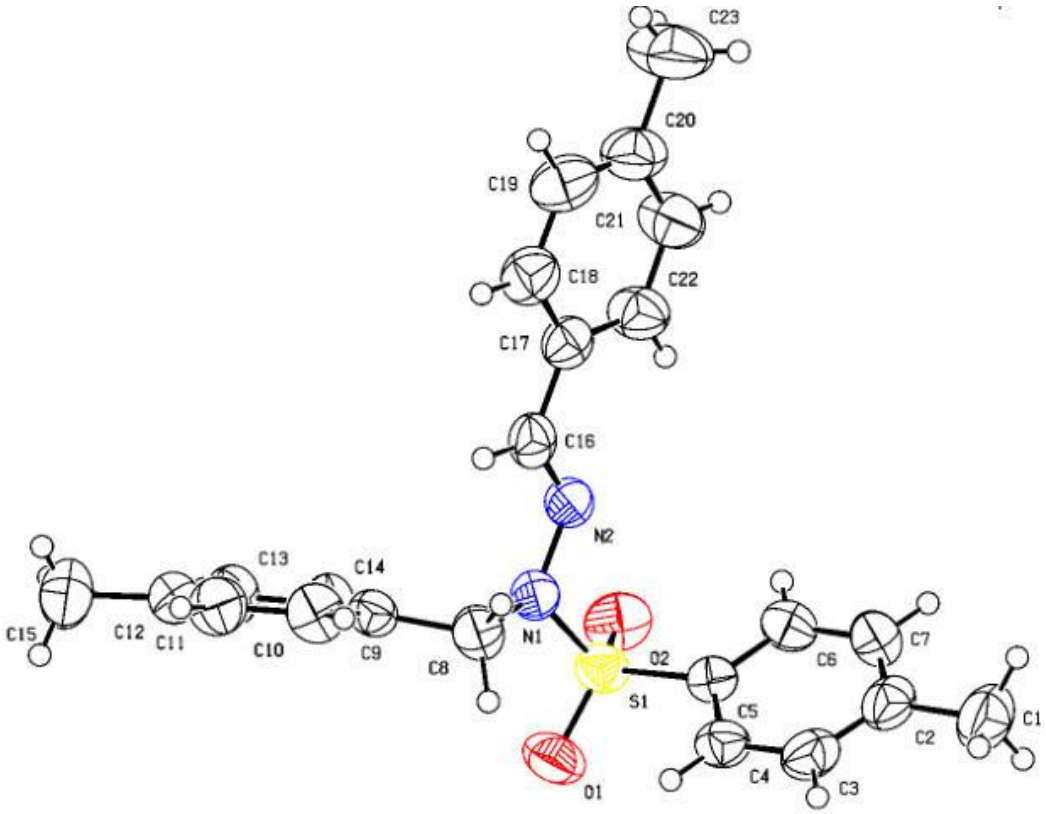


Figure 1. Geometric structures of **2** obtained by X-ray diffraction; displacement ellipsoids are drawn at the 50% probability level.

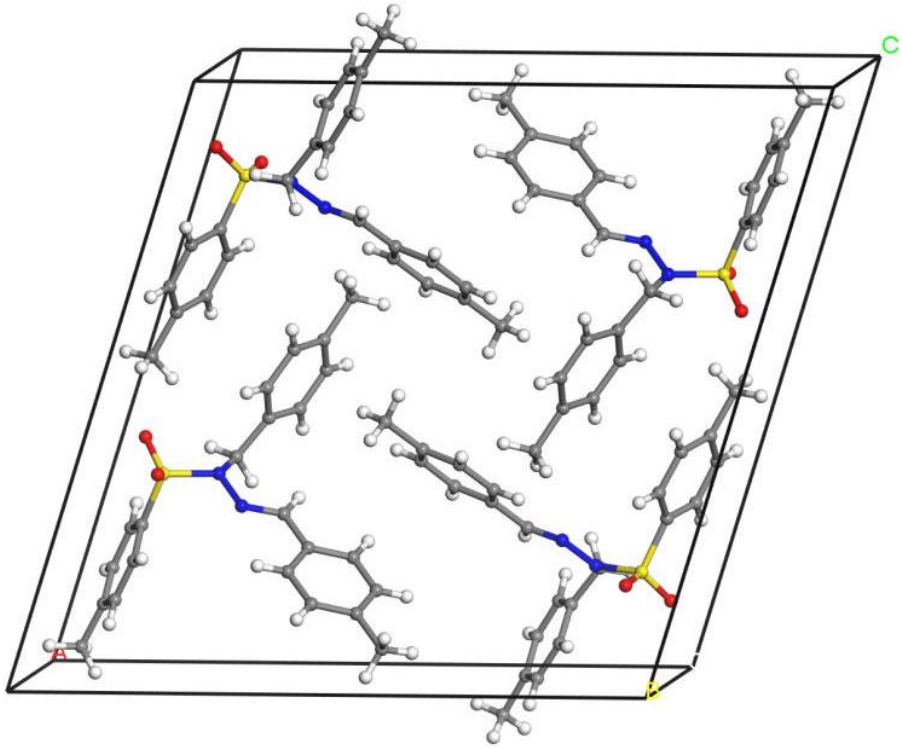


Figure 2. Crystal packing of compound **2**.

Table 2. Selected bond distances (Å) and bond angles (deg) for compound **2**.

Bond	Distance (Å)	Bond	Angle (°)
N(1)-N(2)	1.383(15)	N(2)-C(16)-H(16)	120.01
N(1)-C(8)	1.460(16)	N(2)-C(16)-C(17)	119.98(12)
N(2)-C(16)	1.277(19)	C(8)-N(1)-N(2)	122.00(11)
S(1)-C(5)	1.752(13)	C(16)-N(2)-N(1)	119.45(11)
S(1)-N(1)	1.663(12)	N(2)-N(1)-S(1)	112.19(8)
S(1)-O(1)	1.425(10)	C(8)-N(1)-S(1)	120.34(9)
S(1)-O(2)	1.420(10)	O(1)-S(1)-O(2)	120.54(6)
C(8)-H(8)	0.970	O(1)-S(1)-N(1)	104.86(6)
C(8)-C(9)	1.506(18)	O(1)-S(1)-C(5)	108.13(6)

3. Materials and Methods

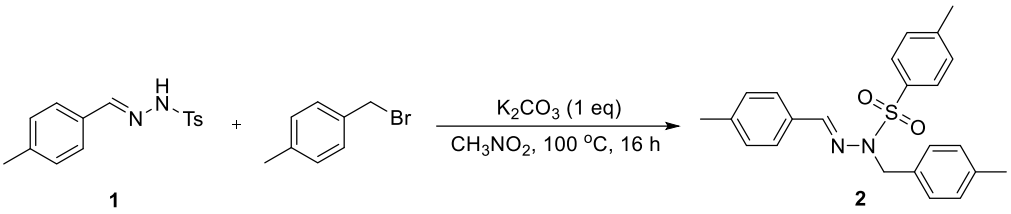
^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker NEO 400 MB instrument (Bruker, Billerica, MA, USA) using $CDCl_3$ as solvent and Me4Si as internal standard. For analytical purposes, the mass spectra were recorded on a Shimadzu GCMS-QP2010 Plus (Shimadzu, Kyoto, Japan) device in the EI mode with 70 eV and 200 _C via a direct inlet probe. Only the molecular and parent ions (m/z) were reported. The starting materials were purchased from Macklin Biochemical Company (Shanghai, China). Unless otherwise noted, the solvents and reagents were reagent grade and were used without any further purification. Column chromatographic separations were carried out on a flash chromatographic system using silica gel, and petroleum ether (60–90 °C) and ethyl acetate as eluent. For thin layer chromatography (TLC), silica gel plates precoated with GF-254 were used.

For the X-ray diffraction studies, crystals of compound **2** were obtained by the slow evaporation of a dilute hexane solution, and the reflections were acquired with a Bruker APEX DUO (Bruker, Billerica, MA, USA) diffractometer equipped with an Apex II CCD detector, with Mo Kα radiation (λ = 0.71073 Å) at 100 K. Frames were collected using omega scans and integrated with SAINT, and multi-scan absorption correction (SADABS) was applied [15]. Direct methods (SHELXS-97) were employed to solve the structure [16]. Subsequent difference-Fourier syntheses revealed the remaining atoms, which were then refined anisotropically against F2 by full-matrix least-squares fitting using SHELXL [17] and the ShelXle GUI [18]. The C-H hydrogen atoms were positioned geometrically at idealized locations.

4-Methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene)benzenesulfonohydrazide **2**

White Solid (272 mg, 70% yield), mp = 149–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.63 (s, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.10 (d, J = 7.9 Hz, 4H), 4.75 (s, 2H), 2.39 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 144.1, 140.5, 137.3, 134.6, 132.6, 131.4, 129.6, 129.3, 128.3, 127.5, 127.1, 52.2, 21.6, 21.5, 21.1. HRMS: m/z $(M + Na)^+$ calcd for $C_{23}H_{24}N_2NaO_2S^+$: 415.1451; Found: 415.1452.

Methylbenzaldehyde *p*-methylbenzenesulfonyl hydrazone (1 mmol 0.288 g) 1-(bromomethyl)-4-methylbenzene (1.2 mmol 0.221 g) and K_2CO_3 (1 mmol 0.138 g) were dissolved in nitromethane (6 mL). The mixture was heated at 100 °C for 16 h. After the reaction was complete, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3 × 10 mL), and washed with saturated sodium chloride solution (3 × 10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using ethyl acetate/petroleum ether (v/v 5/1) as eluent for 4-methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene)benzenesulfonohydrazide (Scheme 1).



1 **2**

Scheme 1. Synthesis of 4-methyl-*N*-(4-methylbenzyl)-*N*′-(4-methylbenzylidene)benzenesulfonohydrazide (**2**).

Supplementary Materials: The following supporting information can be downloaded online. Figure S1: ^{1}HNMR spectrum of compound **2**; Figure S2: ^{13}CNMR spectrum of compound **2**; Figure S3: ESI-HRMS of compound **2**. CDDC 2538528 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/Search?access=referee&ccdc=2538528&Author=Yue+Zhang (accessed on 28 May 2026) (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Liu, J.B.; Yan, H.; Lu, G. *N*-Alkylation of tosylhydrazones via a metal-free reductive coupling procedure. *Tetrahedron Lett.* **2013**, *54*, 891–895. [CrossRef]
2. Sha, Q.; Wei, Y. Base and solvent mediated decomposition of tosylhydrazones: Highly selective synthesis of *N*-alkyl substituted hydrazones, dialkylidenehydrazines, and oximes. *Tetrahedron* **2013**, *69*, 3829–3835. [CrossRef]
3. Kong, Y.; Zhang, W.; Tang, M.; Wang, H. *N*-Alkylation of tosylhydrazones in the presence of triphenylphosphine. *Tetrahedron* **2013**, *69*, 7487–7491. [CrossRef]
4. Benstead, D.J.; Hulme, A.N.; McNab, H.; Wight, P. An Efficient Synthesis of Substituted Hydrazides. *Synlett* **2005**, *2005*, 1571–1574. [CrossRef]
5. Bamford, W.R.; Stevens, T.S.J. The Decomposition of Toluene-*p*-sulphonylhydrazones by Alkali. *J. Chem. Soc. (Resumed)* **1952**, 4735–4740. [CrossRef]
6. Ji, Y.Z.; Wu, Q.X.; Li, H.J.; Luo, D.H.; Wu, Y.C. Base-Promoted Direct Synthesis of Sulfinates from *N*-Sulfonyl-hydrazones under Metal-Free Conditions. *Synthesis* **2020**, *52*, 755–762. [CrossRef]
7. Shapiro, R.H.; Lipton, M.F.; Kolonko, K.J.; Buswell, R.L.; Capuano, L.A. Tosylhydrazones and alkyllithium reagents: More on the regiospecificity of the reaction and the trapping of three intermediates. *Tetrahedron Lett.* **1975**, *16*, 1811–1814. [CrossRef]
8. Tang, M.; Wang, Y.; Wang, H.; Kong, Y.F. Aluminum Chloride Mediated Reactions of *N*-Alkylated Tosylhydrazones and Terminal Alkynes: A Regioselective Approach to 1,3,5-Trisubstituted Pyrazoles. *Synthesis* **2016**, *48*, 3065–3070. [CrossRef]
9. Zhang, Q.; Tang, M. Regioselective Synthesis of Highly Functionalized Pyrazoles from *N*-Tosylhydrazones. *Org. Lett.* **2019**, *21*, 1917–1920. [CrossRef] [PubMed]
10. Zhang, Q.; Zhang, S.Y.; Tang, M. Method for Preparing *N*-Tosylhydrazonyl Chlorides. *J. Org. Chem.* **2022**, *87*, 6393–6396. [CrossRef] [PubMed]
11. Zhang, Q.; Zhang, S.Y.; Zhang, Q.; Xia, Y.W.; Tang, M. Solvent-Free Synthesis of 1,2,4-Triazols from *N*-Tosylhydrazonyl Chlorides and Nitriles. *Asian J. Org. Chem.* **2023**, *12*, e202300081. [CrossRef]

12. Gao, L.; Li, Z. Direct Synthesis of 1-Arylprop-1-ynes with Calcium Carbide as an Acetylene Source. *Synlett* **2019**, *30*, 1580–1584. [CrossRef]
13. Sivajeyanthi, P.; Jeevaraj, M.; Edison, B.; Balasubramani, K. Crystal structure and Hirshfeld surface analysis of (*E*)-2-(5-bromo-2-hydroxybenzylidene)hydrazinecarbothioamide dimethyl sulfoxide monosolvate. *Acta Cryst.* **2018**, *74*, 119–123. [CrossRef] [PubMed]
14. Wang, L.; Xu, K.; Wang, N. Synthesis and Crystal Structure of *N*, *N*′-Bisphenylacetic Hydrazide. *IOP Conf. Ser. Earth Environ. Sci.* **2020**, *440*, 022055. [CrossRef]
15. Chauhan, D.P.; Varma, S.J.; Vijeta, A.; Banerjee, P.; Talukdar, P. A 1,3-amino group migration route to form acrylamidines. *Chem. Commun.* **2014**, *50*, 323–325. [CrossRef] [PubMed]
16. APEX; Bruker. *SAINT, and SADABS*; Bruker AXS Inc.: Madison, WI, USA, 2007.
17. Sheldrick, G.M. A short history of SHELX. *Acta Crystallogr.* **2008**, *64*, 112–122. [CrossRef] [PubMed]
18. Sheldrick, G.M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* **2015**, *71*, 3–8. [CrossRef] [PubMed]