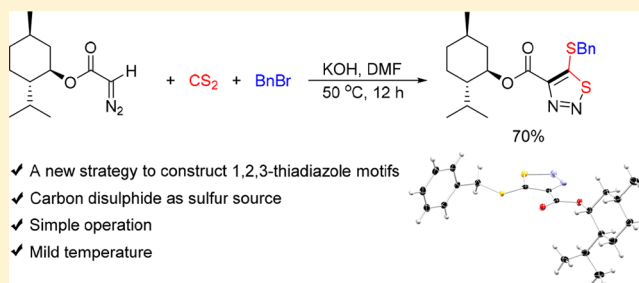# Addition of Diazo Compounds *ipso*-C−H Bond to Carbon Disulfide: Synthesis of 1,2,3-Thiadiazoles under Mild Conditions

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S *Supporting Information*

ABSTRACT: We describe here an operationally simple and straightforward synthesis method for a series of diverse 4,5-disubstituted 1,2,3-thiadiazoles via the nucleophilic addition of α-diazo carbonyl compounds to carbon disulfide. This method features using abundant and inexpensive carbon disulfide under mild reaction conditions.


✓ A new strategy to construct 1,2,3-thiadiazole motifs
✓ Carbon disulphide as sulfur source
✓ Simple operation
✓ Mild temperature

The 1,2,3-thiadiazoles[1] are versatile heterocycles present in various pharmaceutical molecules.[2] Because of their biological activities, many derivatives of 1,2,3-thiadiazoles are important in industry, medicine, and agriculture (Scheme 1A).[3] To date, the known methods for synthesizing 1,2,3-thiadiazoles can be summarized as shown in Scheme 1B: (a) cyclization of hydrazones with thionyl chloride (Hurd−Mori synthesis),[4] (b) treatment of α-diazo carbonyl compounds with Lawesson's reagent (Wolff synthesis),[5] (c) addition of diazomethane (Pechmann synthesis)[6] or lithium (trimethylsilyl)-diazomethane[7] to thiocarbonyl compounds, (d) diazotization of α-enolicdithioesters,[8] and (e) oxidative cyclization of N-tosylhydrazones and sulfur.[9] Although these techniques are frequently used, the synthesis of 1,2,3-thiadiazoles remains an active research area.

Recently, we have reported transition-metal-free diazo compounds *ipso*-C−H bond addition to carbon dioxide (CO_2) under very mild reaction conditions with the diazo group retained.[10] The resulting α-diazo carboxylate intermediate is readily converted to esters and amides in a one-pot manner (Scheme 2A). CO_2 is a greenhouse gas that has been attracting much attention as an inexpensive, nontoxic, non-flammable, renewable, and abundant C1 building block for organic synthesis.[11] Meanwhile, carbon disulfide (CS_2), an analogue of CO_2, has long been used as a sulfur source for a variety of useful chemicals for agricultural, medicinal, and pharmaceutical applications.[12] As an extension of our previous

Scheme 1. Introduction of 1,2,3-Thiadiazoles

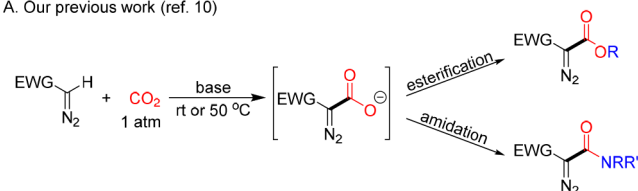

A. Commercial 1,2,3-thiadiazoles in medicine and agriculture

Cefuzonam

Bion

Thidiazuron
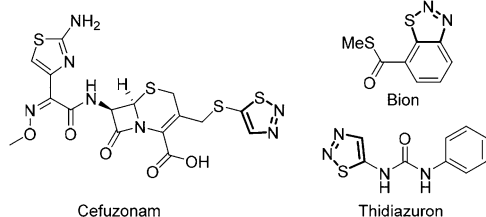
B. Known methods for synthesizing 1,2,3-thiadiazoles
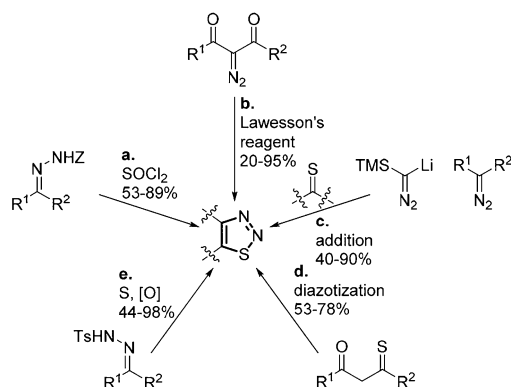
Scheme 2. Diazo Compound *ipso*-C−H Bond Addition to CO_2 and CS_2
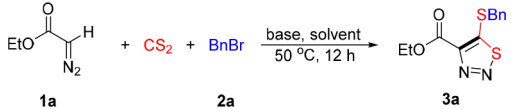

A. Our previous work (ref 10)

B. This work
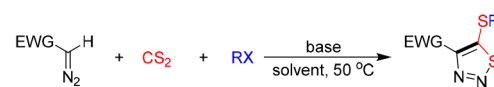
work, we report here on diazo compound *ipso*-C−H bond addition to CS_2 for the synthesis of 1,2,3-thiadiazoles under mild conditions (Scheme 2B).

To probe the feasibility of the nucleophilic addition of the diazo group to CS_2, we initiated our studies with ethyl diazoacetate (EDA) **1a** and benzyl bromide (BnBr) **2a** as the standard substrates. Various organic and inorganic bases were examined in the initial studies. As shown in Table 1, with

**Table 1. Selected Optimization of Reaction Conditions**[a]

entry	base	solvent	equivalency of CS_2	yield (%)[b]
1	Cs_2CO_3	MeCN	1.5	38
2	CsF	MeCN	1.5	17
3	KO^{t}Bu	MeCN	1.5	20
4	DBU	MeCN	1.5	trace
5	Et$_3$N	MeCN	1.5	n. d.
6	KOH	MeCN	1.5	41
7	KOH	DMF	1.5	73
8	KOH	DMSO	1.5	36
9	KOH	THF	1.5	12
10	KOH	1,4-dioxane	1.5	8
11	KOH	DMF	2.0	81 (69[c])
12	KOH	DMF	5.0	78

[a]Reaction conditions: EDA (0.5 mmol), BnBr (1.5 equiv), base (1.2 equiv), solvent (2 mL), reaction time 12 h, temperature 50 °C, sealed; n.d., not detected. [b]Yields were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane used as internal standard. [c]Isolated yield.

Cs_2CO_3 as the base, the desired product ethyl 5-(benzylthio)-1,2,3-thiadiazole-4-carboxylate **3a** was obtained with 38% NMR yield (entry 1). CsF and KO^{t}Bu turned out to be less effective in this transformation (entries 2 and 3), and organic bases such as DBU and Et$_3$N were inactive (entries 4 and 5). This suggested that bases with proper basicity might be a key issue for the desired transformation. Indeed, the yield was slightly improved with the use of KOH as the base (entry 6). Product **3a** was thus obtained with 73% yield by switching the solvent from MeCN to DMF (entry 7). Other solvents, such as DMSO, THF, and 1,4-dioxane, were less efficient (entries 8−10). Finally, an improved yield (81%) was obtained by using 2.0 equiv of CS_2 (entry 11). The yield was not further improved by increasing the equivalency of CS_2 to 5.0 (entry 12). However, product **3a** was not very stable during handling, and the isolated yield diminished to ∼10% compared with the NMR yield.

After obtaining the optimal yield for **3a**, we next conducted substrate scope studies with the results shown in Table 2. Various benzyl bromides were evaluated with various substituent groups for this reaction. Both *para*- and *ortho*-substituents (**3b**−**3e**) on benzyl bromides were tolerated, giving good yields. Additionally, allyl bromide (**3f**) was also a good reagent to facilitate the construction of 1,2,3-thiadiazoles. To further demonstrate the expansibility of this methodology, we synthesized and tested various α-diazo carbonyl compounds using this transformation. In general, all of these types of diazo substrates were suitable for the reaction with the products obtained with moderate to good yields. Menthyl diazoacetate

Table 2. Substrate Scope[a]

3a, 69%   3b, 68%   3c, 59%
3d, 64%   3e, 56%   3f, 50%
3g, 70%   XRD of 3g
3h, 64%   3i, 62%
3j, 47%   3k, 39%
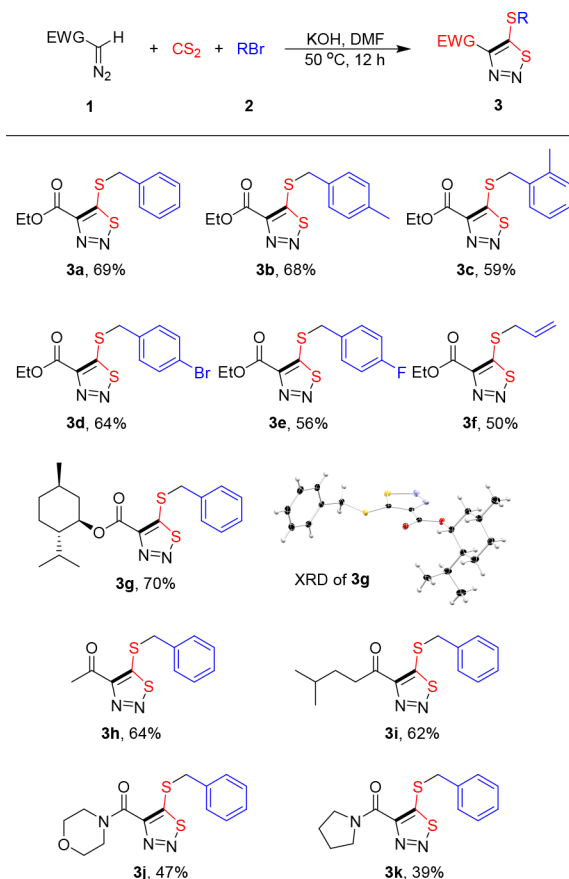
[a]Reaction conditions: diazo compound (0.5 mmol), RBr (1.5 equiv), KOH (1.2 equiv), solvent (2 mL), reaction time 12 h, temperature 50 °C, sealed.

was converted to 1,2,3-thiadiazole (**3g**) with 70% yield. XRD data was obtained for **3g**. Furthermore, α-diazo alkyl ketones (**3h** and **3i**) also worked well, whereas α-diazo amides (**3j** and **3k**) gave relatively low yields.

Compared with the known methods shown in Scheme 1B, our synthetic strategy is more close to the catalog c: addition of diazo compounds to the C=S bond. In ref 7, Aoyama suggested a nucleophilic addition/cyclization mechanism for the conversion of lithium (trimethylsilyl)diazomethane and carbon disulfide to the 1,2,3-thiadiazole product. Meanwhile, as a good electrophile, carbon disulfide has ready reactivity with a variety of nucleophiles, ranging from carbon-centered nucleophiles (e.g., Grignard reagents) to oxygen-centered nucleophiles (e.g., alkoxy) and amines.[12c] On this basis, we proposed that our reaction mechanism is also a normal deprotonation-nucleophilic addition/cyclization process (Scheme 3).

Scheme 3. Proposed Reaction Pathway
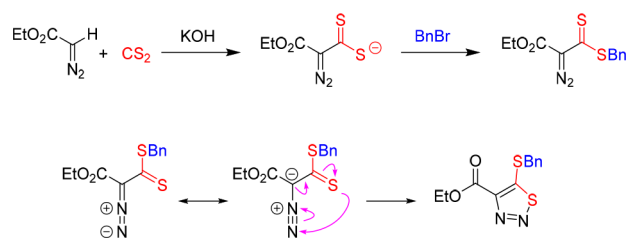
In summary, we have developed an operationally simple method for the synthesis of 4,5-disubstituted 1,2,3-thiadiazoles via the nucleophilic addition of α-diazo carbonyl compounds to carbon disulfide. This method can be applied as an alternative to traditional synthesis methods of 1,2,3-thiadiazoles with carbon disulfide as the C1 building block under mild reaction conditions.

■ EXPERIMENTAL SECTION

General Information. All of the solvents were purchased from ENERGY CHEMICAL and kept dry by molecular sieves. The products were purified by column chromatography on silica gel (300–400 mesh, from Qingdao, China). NMR spectra were measured on a Bruker ARX400 (^{1}H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 377 MHz) magnetic resonance spectrometer. The chemical shifts (δ) are reported as ppm using tetramethylsilane as the internal standard (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet), and the coupling constants (J) are reported in hertz (Hz). Infrared spectra were recorded on a Thermal Fisher Nicolet iS50 Fourier transform spectrometer (FT-IR) and are reported as wave numbers (cm^{-1}). The HRMS data was obtained on a VG ZAB-HS mass spectrometer and a Bruker Apex IV FTMS spectrometer. The diazo starting materials were synthesized in the lab. For details, see the Supporting Information.

General Procedure for the Synthesis of 1,2,3-Thiadiazoles. In a glovebox, a 4 mL vial equipped with a stir bar was charged with potassium hydroxide (0.6 mmol, 1.2 equiv), dimethylformamide (2 mL), the diazo compound (0.5 mmol), carbon disulfide (1.0 mmol, 2.0 equiv), and bromide (0.75 mmol, 1.5 equiv) in succession. Then, the vial was sealed, and the mixture was stirred at 50 °C for 12 h. Then, the reaction mixture was washed with 20 mL of ethyl acetate and water (3 × 20 mL). The organic layer was separated and dried over Na$_2$SO$_4$. After solvent removal, the residue was purified by column chromatography (silica gel) to afford the desired product.

Ethyl 5-(Benzylthio)-1,2,3-thiadiazole-4-carboxylate (3a).[13] Yellowish-green solid, yield 78% (110 mg); mp 83–84 °C; R_f = 0.25 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47–7.30 (m, 5H), 4.51 (q, J = 7.1 Hz, 2H), 4.26 (s, 2H), 1.46 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.4, 160.8, 146.4, 133.6, 129.14, 129.08, 128.6, 62.1, 42.3, 14.4.

Ethyl 5-((4-Methylbenzyl)thio)-1,2,3-thiadiazole-4-carboxylate (3b). White solid, yield 68% (100 mg); mp 93–94 °C; R_f = 0.25 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 4.51 (q, J = 7.1 Hz, 2H), 4.23 (s, 2H), 2.35 (s, 3H), 1.46 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.5, 160.8, 146.4, 138.6, 130.5, 129.8, 129.0, 62.1, 42.1, 21.2, 14.4; IR (film) 2984, 2921, 1732, 1701, 1439, 1309, 1271, 1209, 1065, 1021, 842; HRMS (ESI) calcd for C$_{13}$H$_{15}$N$_2$O$_2$S$_2^+$ [M + H]$^+$ 295.0569, found 295.0563.

Ethyl 5-((2-Methylbenzyl)thio)-1,2,3-thiadiazole-4-carboxylate (3c). White solid, yield 59% (87 mg); mp 90–91 °C; R_f = 0.25 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41–7.15 (m, 4H), 4.50 (q, J = 7.1 Hz, 2H), 4.25 (s, 2H), 2.43 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.8, 160.8, 146.2, 137.2, 131.6, 131.0, 130.0, 129.0, 126.6, 62.1, 41.0, 19.3, 14.4; IR (film) 2980, 2932, 1730, 1701, 1439, 1310, 1272, 1209, 1065, 1020, 842, 780; HRMS (ESI) calcd for C$_{13}$H$_{15}$N$_2$O$_2$S$_2^+$ [M + H]$^+$ 295.0569, found 295.0562.

Ethyl 5-((4-Bromobenzyl)thio)-1,2,3-thiadiazole-4-carboxylate (3d). White solid, yield 64% (115 mg); mp 93–94 °C; R_f = 0.20 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.55–7.48 (m, 2H), 7.32 (d, J = 8.5 Hz, 2H), 4.51 (q, J = 7.1 Hz, 2H), 4.21 (s, 2H), 1.46 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 163.8, 160.7, 146.5, 132.7, 132.3, 130.7, 122.8, 62.2, 41.6, 14.3; IR (film) 2984, 1730, 1700, 1487, 1440, 1310, 1271, 1210, 1066, 1012, 842, 780; HRMS (ESI) calcd for C$_{12}$H$_{12}$BrN$_2$O$_2$S$_2^+$ [M + H]$^+$ 358.9518, found 358.9512.

Ethyl 5-((4-Fluorobenzyl)thio)-1,2,3-thiadiazole-4-carboxylate (3e). White solid, yield 56% (84 mg); mp 63–64 °C; R_f = 0.20 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.42 (dd, J = 8.5, 5.2 Hz, 2H), 7.06 (t, J = 8.5 Hz, 2H), 4.51 (q, J = 7.1 Hz, 2H), 4.24 (s, 2H), 1.46 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.0 (d, J = 2.1 Hz), 161.5, 160.8, 146.4, 130.9 (d, J = 8.4 Hz), 129.4 (d, J = 3.3 Hz), 116.2, 116.0, 62.2, 41.6, 14.3; ^{19}F NMR (377 MHz, CDCl$_3$) δ −112.5 to −112.6 (m); IR (film) 2984, 1730, 1700, 1508, 1439, 1310, 1271, 1210, 1159, 1064, 1017, 842, 780; HRMS (ESI) calcd for C$_{12}$H$_{12}$FN$_2$O$_2$S$_2^+$ [M + H]$^+$ 299.0319, found 299.0311.

Ethyl 5-(Allylthio)-1,2,3-thiadiazole-4-carboxylate (3f). Yellow oil, yield 50% (58 mg); R_f = 0.25 (petroleum ether:EtOAc = 10:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.90 (m, 1H), 5.50 (dd, J = 17.0, 0.7 Hz, 1H), 5.38 (d, J = 10.1 Hz, 1H), 4.52 (q, J = 7.1 Hz, 2H), 3.71 (d, J = 6.7 Hz, 2H), 1.47 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.3, 160.8, 146.7, 129.9, 121.7, 62.1, 40.6, 14.4; IR (film) 2984, 1730, 1701, 1438, 1307, 1271, 1207, 1063, 1020, 930, 842; HRMS (ESI) calcd for C$_8$H$_{11}$N$_2$O$_2$S$_2^+$ [M + H]$^+$ 231.0256, found 231.0254.

(1S,2R,5S)-2-Isopropyl-5-methylcyclohexyl 5-(Benzylthio)-1,2,3-thiadiazole-4-carboxylate (3g). White solid, yield 70% (136 mg); mp 102–103 °C; R_f = 0.30 (petroleum ether:EtOAc = 20:1); petroleum ether:EtOAc = 100:1–50:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.50–7.29 (m, 5H), 5.08–5.01 (m, 1H), 4.25 (s, 2H), 2.23–2.11 (m, 1H), 2.07–2.00 (m, 1H), 1.80–1.48 (m, 4H), 1.23 (dd, J = 23.2, 12.0 Hz, 1H), 1.18–1.07 (m, 1H), 0.92 (dd, J = 10.8, 6.8 Hz, 6H), 0.80 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.2, 160.4, 146.7, 133.7, 129.1, 129.1, 128.6, 76.5, 46.8, 42.4, 40.8, 34.1, 31.6, 26.2, 23.4, 22.0, 20.8, 16.3; IR (film) 2954, 2926, 2869, 1729, 1698, 1436, 1311, 1272, 1214, 1064, 980, 837, 704; HRMS (ESI) calcd for C$_{20}$H$_{27}$N$_2$O$_2$S$_2^+$ [M + H]$^+$ 391.1508, found 391.1502.

1-(5-(Benzylthio)-1,2,3-thiadiazol-4-yl)ethan-1-one (3h). Yellow solid, yield 64% (80 mg); mp 100–101 °C; R_f = 0.20 (petroleum ether:EtOAc = 20:1); petroleum ether:EtOAc = 100:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 m, 5H), 4.23 (s, 2H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 192.4, 164.1, 154.0, 133.6, 129.2, 129.1, 128.6, 42.8, 28.8; IR (film) 3063, 3032, 2915, 1672, 1413, 1273, 1175, 1066, 910, 790, 705, 604; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$OS$_2^+$ [M + H]$^+$ 251.0307, found 251.0308.

1-(5-(Benzylthio)-1,2,3-thiadiazol-4-yl)-4-methylpentan-1-one (3i). Yellow oil, yield 62% (95 mg); R_f = 0.20 (petroleum ether:EtOAc = 40:1); petroleum ether:EtOAc = 100:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.48–7.28 (m, 5H), 4.23 (s, 2H), 3.28 (t, J = 7.2 Hz 2H), 1.68 (m, 3H), 0.95 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.4, 164.0, 153.7, 133.7, 129.2, 129.0, 128.6, 42.7, 39.3, 32.9, 27.8, 22.4; IR (film) 2954, 2927, 2867, 1669, 1495, 1414, 1271, 1139, 1112, 1044, 1026, 908, 703; HRMS (ESI) calcd C$_{15}$H$_{18}$N$_2$NaOS$_2^+$ [M + Na]$^+$ 329.0753, found 329.0753.

(5-(Benzylthio)-1,2,3-thiadiazol-4-yl)(morpholino)methanone (3j). White solid, yield 47% (75 mg); mp 96–97 °C; R_f = 0.50 (petroleum ether:EtOAc = 1:1); petroleum ether:EtOAc = 10:1–5:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45–7.29 (m, 5H), 4.23 (s, 2H), 4.08 (s, 2H), 3.79 (m, J = 25.0 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.6, 160.2, 150.1, 134.2, 129.2, 129.0, 128.5, 67.2, 66.9, 48.0, 43.3, 42.2; IR (film) 2964, 2913, 2859, 1616, 1472, 1443, 1302, 1269, 1218, 1114, 1076, 1030, 968, 705; HRMS (ESI) calcd for C$_{14}$H$_{16}$N$_3$O$_2$S$_2^+$ [M + H]$^+$ 322.0678, found 322.0671.

(5-(Benzylthio)-1,2,3-thiadiazol-4-yl)(pyrrolidin-1-yl)methanone (3k). White solid, yield 39% (60 mg); mp 124–125 °C; R_f = 0.60 (petroleum ether:EtOAc = 1:1); petroleum ether:EtOAc = 10:1–5:1 as eluent; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43 (m, 2H), 7.38–7.28 (m, 3H), 4.21 (s, 2H), 4.02 (t, J = 6.6 Hz, 2H), 3.72 (t, J = 6.7 Hz, 2H), 2.08–1.85 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 163.0, 159.8, 150.6, 134.3, 129.2, 128.9, 128.3, 49.4, 47.2, 42.3, 26.6, 23.9; IR (film) 2970, 2875, 1610, 1468, 1454, 1374, 1256, 1079, 843, 710; HRMS (ESI) calcd for C$_{14}$H$_{16}$N$_3$OS$_2^+$ [M + H]$^+$ 306.0729, found 306.0729.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b00383.

> Preparation of substrates and NMR spectra (PDF)
> X-ray single-crystal structure of compound **3g** (CIF)

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Notes
The authors declare no competing financial interest.

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REFERENCES

(1) Bakulev, V. A.; Dehaen, W. *The Chemistry of 1,2,3-Thiadiazoles*; John Wiley & Sons, Inc., 2004.

(2) (a) Li, Z.; Wu, Z.; Luo, F. Synthesis and Antifungal Activities of Alkyl N-(1,2,3-Thiadiazole-4-Carbonyl) Carbamates and S-Alkyl N-(1,2,3-Thiadiazole-4-Carbonyl) Carbamothioates. *J. Agric. Food Chem.* **2005**, *53*, 3872−3876. (b) Hayat, F.; Salahuddin, A.; Zargan, J.; Azam, A. Synthesis, Characterization, Antiamoebic Activity and Cytotoxicity of Novel 2-(Quinolin-8-Yloxy) Acetohydrazones and Their Cyclized Products (1,2,3-Thiadiazole and 1,2,3-Selenadiazole Derivatives). *Eur. J. Med. Chem.* **2010**, *45*, 6127−6134. (c) Wang, Z.-H.; Guo, Y.-Z.; Zhang, J.; Ma, L.; Song, H.-B.; Fan, Z.-J. Synthesis and Biological Activity of Organotin 4-Methyl-1,2,3-Thiadiazole-5-Carboxylates and Benzo[1,2,3]Thiadiazole-7-Carboxylates. *J. Agric. Food Chem.* **2010**, *58*, 2715−2719. (d) Zheng, Q.; Mi, N.; Fan, Z.; Zuo, X.; Zhang, H.; Wang, H.; Yang, Z. 5-Methyl-1,2,3-Thiadiazoles Synthesized Via Ugi Reaction and Their Fungicidal and Antiviral Activities. *J. Agric. Food Chem.* **2010**, *58*, 7846−7855. (e) Fan, R. Z.; Wang, D.; Fan, Z. J.; Wang, S. X.; Hua, X. W.; Ji, X. T.; Huang, Y.; Song, H. B. Synthesis, Crystal Structure, and Biological Activity of N-((1-Cyclohexyl-1h-Tetrazol-5-Yl)(5-Methyl-1,2,3-Thiadiazol-4-Yl)Methyl) −4-Nitroben-zenamine. *Jiegou Huaxue* **2012**, *31*, 803−808.

(3) (a) Yasuda, M.; Nakashita, H.; Yoshida, S. Tiadinil, a Novel Class of Activator of Systemic Acquired Resistance, Induces Defense Gene Expression and Disease Resistance in Tobacco. *J. Pestic. Sci.* **2004**, *29*, 46−49. (b) Fan, Z.; Shi, Z.; Zhang, H.; Liu, X.; Bao, L.; Ma, L.; Zuo, X.; Zheng, Q.; Mi, N. Synthesis and Biological Activity Evaluation of 1,2,3-Thiadiazole Derivatives as Potential Elicitors with Highly Systemic Acquired Resistance. *J. Agric. Food Chem.* **2009**, *57*, 4279−4286. (c) Morzherin, Y.; Prokhorova, P. E.; Musikhin, D. A.; Glukhareva, T. V.; Fan, Z. 2-Hydroxypropyl Derivatives of 1,2,3-Thiadiazole and 1,2,3-Triazole: Synthesis and Antifungal Activity. *Pure Appl. Chem.* **2011**, *83*, 715−722. (d) Du, Q.; Zhu, W.; Zhao, Z.; Qian, X.; Xu, Y. Novel Benzo-1,2,3-Thiadiazole-7-Carboxylate Derivatives as Plant Activators and the Development of Their Agricultural Applications. *J. Agric. Food Chem.* **2012**, *60*, 346−353. (e) Flygare, J. A.; Beresini, M.; Budha, N.; Chan, H.; Chan, I. T.; Cheeti, S.; Cohen, F.; Deshayes, K.; Doerner, K.; Eckhardt, S. G.; Elliott, L. O.; Feng, B.; Franklin, M. C.; Reisner, S. F.; Gazzard, L.; Halladay, J.; Hymowitz, S. G.; La, H.; LoRusso, P.; Maurer, B.; Murray, L.; Plise, E.; Quan, C.; Stephan, J.-P.; Young, S. G.; Tom, J.; Tsui, V.; Um, J.; Varfolomeev, E.; Vucic, D.; Wagner, A. J.; Wallweber, H. J. A.; Wang, L.; Ware, J.; Wen, Z.; Wong, H.; Wong, J. M.; Wong, M.; Wong, S.; Yu, R.; Zobel, K.; Fairbrother, W. J. Discovery of a Potent Small-Molecule Antagonist of Inhibitor of Apoptosis (Iap) Proteins and Clinical Candidate for the Treatment of Cancer (Gdc-0152). *J. Med. Chem.* **2012**, *55*, 4101−4113. (f) Xu, J.; Li, Z.; Luo, J.; Yang, F.; Liu, T.; Liu, M.; Qiu, W.-W.; Tang, J. Synthesis and Biological Evaluation of Heterocyclic Ring-Fused Betulinic Acid Derivatives as Novel Inhibitors of Osteoclast Differentiation and Bone Resorption. *J. Med. Chem.* **2012**, *55*, 3122−3134. (g) Krishnaraj, T.; Muthusubramanian, S. Synthesis of Biologically Important N-Heteroaryl-2-(Heteroarylthio)Acetamides. *J. Heterocycl. Chem.* **2014**, *51*, 1012−1019.

(4) Hurd, C. D.; Mori, R. I. On Acylhydrazones and 1,2,3-Thiadiazoles. *J. Am. Chem. Soc.* **1955**, *77*, 5359−5364.

(5) (a) Wolff, L. Ueber 1,2,3-Thiodiazole. *Justus Liebigs Ann. Chem.* **1904**, *333*, 1−21. (b) Caron, M. Convenient Preparation of 5-Alkyl-4-Carbalkoxy-1,2,3-Thiadiazoles. *J. Org. Chem.* **1986**, *51*, 4075−4077.

(6) Pechmann, H.; Nold, A. Ueber Die Einwirkung Von Diazomethan Auf Phenylsenföl. *Ber. Dtsch. Chem. Ges.* **1896**, *29*, 2588−2593.

(7) Aoyama, T.; Iwamoto, Y.; Shioiri, T. New Methods and Reagents in Organic Synthesis. 59. Lithium Trimethylsilyldiazomethane: A New Synthon for the Preparation of 5-Substituted 1,2,3-Thiadiazoles. *Heterocycles* **1986**, *24*, 589−592.

(8) (a) Singh, M. S.; Nagaraju, A.; Verma, G. K.; Shukla, G.; Verma, R. K.; Srivastava, A.; Raghuvanshi, K. Eco-Efficient, Regioselective and Rapid Access to 4,5-Disubstituted 1,2,3-Thiadiazoles Via [3 + 2] Cycloaddition of [Small Alpha]-Enolicdithioesters with Tosyl Azide under Solvent-Free Conditions. *Green Chem.* **2013**, *15*, 954−962. (b) Nagaraju, A.; Ramulu, B. J.; Shukla, G.; Srivastava, A.; Verma, G. K.; Raghuvanshi, K.; Singh, M. S. A Facile and Straightforward Synthesis of 1,2,3-Thiadiazoles from A-Enolicdithioesters Via Nitro-sation/Reduction/Diazotization/Cyclization Cascade in One-Pot. *Tetrahedron Lett.* **2014**, *55*, 2430−2433.

(9) Chen, J.; Jiang, Y.; Yu, J.-T.; Cheng, J. Tbai-Catalyzed Reaction between N-Tosylhydrazones and Sulfur: A procedure toward 1,2,3-Thiadiazole. *J. Org. Chem.* **2016**, *81*, 271−275.

(10) Liu, Q.; Li, M.; Xiong, R.; Mo, F. Direct Carboxylation of the Diazo Group Ipso-C(Sp2)−H Bond with Carbon Dioxide: Access to Unsymmetrical Diazomalonates and Derivatives. *Org. Lett.* **2017**, *19*, 6756−6759.

(11) Aresta, M.; Dibenedetto, A.; Angelini, A. Catalysis for the Valorization of Exhaust Carbon: From CO$_2$ to Chemicals, Materials, and Fuels. Technological Use of CO$_2$. *Chem. Rev.* **2014**, *114*, 1709−1742.

(12) (a) Yokoyama, M.; Imamoto, T. Organic Reactions of Carbon Disulfide. *Synthesis* **1984**, *1984*, 797−824. (b) Tominaga, Y. Synthesis of Heterocyclic Compounds Using Carbon Disulfide and Their Products. *J. Heterocycl. Chem.* **1989**, *26*, 1167−1204. (c) Schmitt, C.; Murai, T. Carbon Disulfide. In *Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons, Ltd, 2001. (d) Ho, T.-L.; Fieser, M.; Fieser, L.; Fieser, L. F.; Fieser, M.; Ho, T.-L. Carbon Disulfide. In *Fieser and Fieser's Reagents for Organic Synthesis*; John Wiley & Sons, Ltd, 2006.

(13) Hinz, W.; Just, G. The Synthesis of 4-Carbalkoxy-5-Thioalkyl-1,2,3-Thiadiazoles. *Synth. Commun.* **1986**, *16*, 917−927.