A Novel Convenient Synthesis of 1,3,4-Oxadiazol-2-ones and -thiones from *N*-tert-Butyldiacylhydrazines

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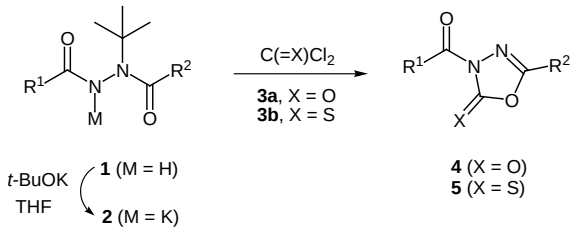
Abstract: An attractive, novel, convenient process for the preparation of 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones and -thiones from the reaction of various equivalent and non-equivalent *N*-*tert*-butyldiacylhydrazines with potassium *tert*-butoxide followed by treatment with phosgene or thiophosgene, respectively, has been discovered. The 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones and -thiones are confirmed both analytically and chemically. Various equivalent and non-equivalent *N*-*tert*-butyldiacylhydrazines are conveniently synthesized from the reaction of *tert*-butylhydrazine hydrochloride in the presence of *i*-Pr_2NEt, with acid chloride #1 followed by subsequent treatment with acid chloride #2. Both the syntheses of 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones and -thiones, as well as *N*-*tert*-butyldiacylhydrazines, are easily performed on multigram scales.

Key words: cyclization, heterocycles, regioselectivity, hydrazine, phosgene

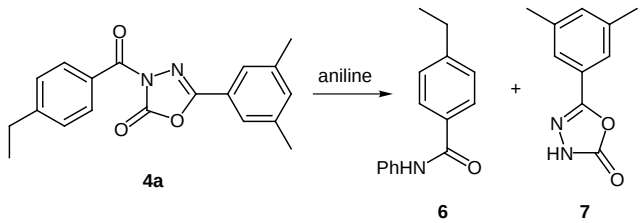
N-*tert*-Butyldiacylhydrazines **1** such as tebufenozide (**1a**),[1] methoxyfenozide (**1b**),[2] and halofenozide (**1c**)[3] are an important class of insecticidal compounds serving as environmentally safe, extremely selective insect growth regulators (Table 1).[4] 1,3,4-Oxadiazole derivatives **4** and **5** are also an important class of heterocyclic compounds displaying a wide range of biological activities.[5] Several novel and efficient routes toward their syntheses have been reported.[5–7] Normally, one would not necessarily assume a relationship between the two classes of compounds, however, this paper reports the novel cyclization reaction of *N*-*tert*-butyldiacylhydrazines **1** with phosgene as well as thiophosgene to afford 1,3,4-oxadiazol-2-ones and -thiones **4** and **5**, respectively, with loss of the *tert*-butyl moiety.

In studies, directed toward the synthesis of more insecticidally active *N*-*tert*-butyldiacylhydrazines, we discovered that 1,3,4-oxadiazol-2-one **4a** (where R^1 = 4-ethylphenyl, R^2 = 3,5-dimethylphenyl, and X = O) is produced in 95% yield. This is achieved when diacylhydrazine **1a** (where R^1 = 4-ethylphenyl and R^2 = 3,5-dimethylphenyl), is converted to its potassium salt **2a,** via treatment with potassium *tert*-butoxide, followed by reaction with phosgene (**3a**, X = O) at –78 °C. Similar reaction of potassium salt **2a** with thiophosgene (**3b**, X = S) afforded 1,3,4-oxadiazol-2-thione **5a** in 80% yield (Scheme 1 and Table 1).



Scheme 1 1,3,4-Oxadiazol-2-ones **4** and -thiones **5** from *N'*-*tert*-butyldiacylhydrazines **1**

Understanding from literature precedence that 3-benzoyl-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one readily underwent cleavage at the 3-benzoyl position when subjected to aniline to afford *N*-phenylbenzamide and 5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one,[6b] we decided to react our 3-(4-ethylbenozyl)-5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (**4a**) under the same conditions. We found that subjection of 3-(4-ethylbenozyl)-5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (**4a**) to aniline in THF smoothly afforded both expected products, 4-ethyl-*N*-phenylbenzamide (**6**) and 5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (**7**) (Scheme 2).[8]



Scheme 2 Reaction of 1,3,4-oxadiazol-2-one **4a** with aniline to afford benzamide **6** and 3*H*-[1,3,4]-oxadiazol-2-one **7**

After analytically and chemically establishing the structure of 5-(3,5-dimethylphenyl)-3-(4-ethylbenozyl)-3*H*-[1,3,4]-oxadiazol-2-one (**4a**) via both the Gogoi[8] and Saegusa method (Scheme 2), we began contemplating the mechanism for such a cyclization. We envisioned that the mechanism for the transformation of *N*-*tert*-butyldiacylhydrazine salt **2** to 1,3,4-oxadiazol-2-one **4** via reaction with phosgene involved *N*-acylation of *N*-*tert*-butyldiacylhydrazine **2** to afford the acyl adduct **8**, which after cyclization via attack of the R^2 carbonyl to give **9** and subsequent loss of *tert*-butyl afforded 1,3,4-oxadiazol-2-one **4** (Scheme 3).

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Table 1 1,3,4-Oxadiazol-2-ones **4** and -thiones **5** from *N-tert*-Butyldiacylhydrazines **1**

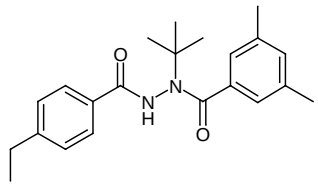
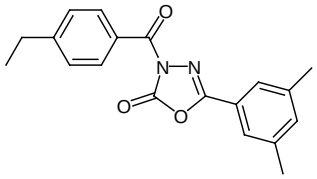
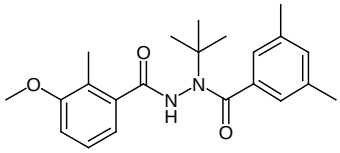
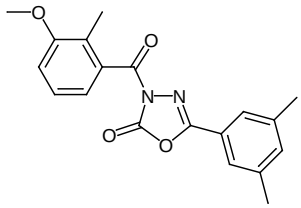
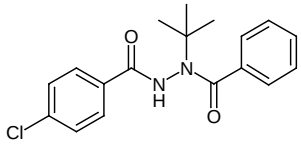
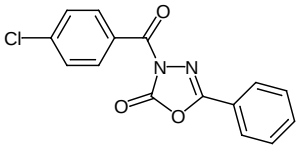
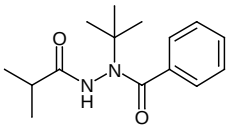
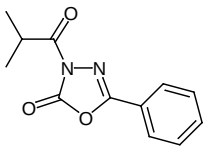
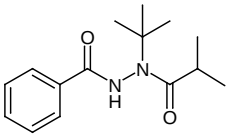
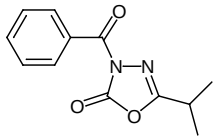
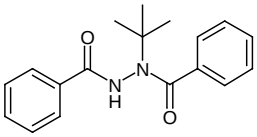
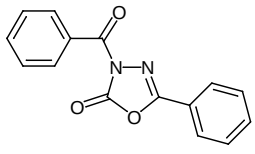
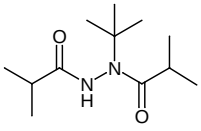
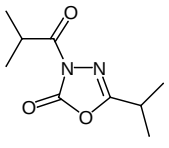
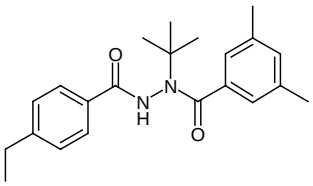
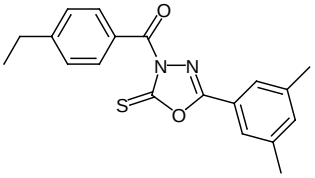
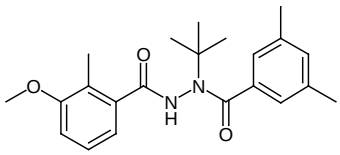
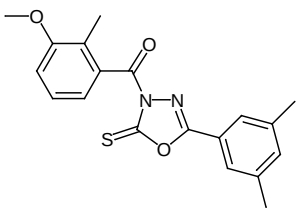
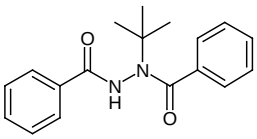
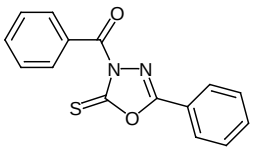
Entry	*N-tert*-Butyldiacylhydrazines **1**[a]	1,3,4-Oxadiazol-2-ones **4** and -thiones **5**[d]	Yield (%)	mp (°C)
1	 **1a**	 **4a**	95	134–135
2	 **1b**	 **4b**	95	152–153
3	 **1c**	 **4c**	60	138–139
4	 **1d**	 **4d**	95	82–84
5	 **1e**	 **4e**	92	Oil
6	 **1f**	 **4f**	90	134–136[b]
7	 **1g**	 **4g**	80	Oil

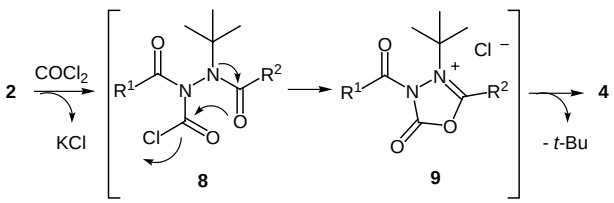
Table 1 1,3,4-Oxadiazol-2-ones **4** and -thiones **5** from *N-tert*-Butyldiacylhydrazines **1** (continued)

Entry	*N-tert*-Butyldiacylhydrazines **1**[a]	1,3,4-Oxadiazol-2-ones **4** and -thiones **5**[d]	Yield (%)	mp (°C)
8	 **1a**	 **5a**	80	142–144
9	 **1b**	 **5b**	75	166–168
10	 **1f**	 **5f**	70	135–136[c]

[a] *N-tert*-Butyldiacylhydrazines **1a**, **1b**, and **1c** are commercially available or can be prepared according to known procedures.[1–3]
[b] Lit.[6b] mp 136–137 °C.
[c] Lit.[6b] mp 136–137 °C.
[d] Reaction of *N-tert*-butyldiacylhydrazines **1c**, **1d**, **1e**, and **1g** with thiophosgene did not give satisfactory results.

In order to further test the scope of this process for the general preparation of 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones **4** and -thiones **5** from *N'-tert*-butyldiacylhydrazines **1**, we prepared a series of *N'-tert*-butyldiacylhydrazines **1a**–**g** and subjected them to potassium *tert*-butoxide in THF at –78 °C followed by treatment with phosgene or thiophosgene. The results are reported in Table 1 and the spectral data of compounds prepared are listed in Table 2. It should be noted that *tert*-butylhydrazine offers the versatility of a one-pot, two step regioselective diacylation process. This is due to the sterics associated with the *tert*-butyl moiety.[9] For example, benzoic acid *N'-tert*-butyl-*N'-iso*-butyrylhydrazide (**1e**) can be prepared from the reaction of *tert*-butylhydrazine hydrochloride salt (**10**) with 2 equivalents of *i*-Pr_2NEt and 1 equivalent of benzoyl chloride, followed by the addition of a third equivalent of *i*-Pr_2NEt and 1 equivalent of *iso*-butyryl chloride. On the other hand, benzoic acid *N-tert*-butyl-*N'-iso*-butyrylhydrazide (**1d**) can be prepared by reversing the order of addition of the acid chlorides to first charging the reaction with *iso*-butyryl chloride followed by benzoyl chloride. Further reaction of benzoic acid *N'-tert*-butyl-*N'-iso*-butyrylhydrazide (**1e**) with potassium *tert*-butoxide followed by treatment with phosgene afforded 3-benzoyl-5-*iso*-propyl-3*H*-[1,3,4]-oxadiazol-2-one (**4e**), while treatment of benzoic acid *N-tert*-butyl-*N'*-iso-butyrylhydrazide (**1d**) under identical conditions afforded 3-*iso*-butyryl-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one (**4d**) (Scheme 4).

In conclusion, we have developed a novel, convenient, and scaleable process toward the synthesis of 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones **4a**–**g** and -thiones **5a**,**b**,**f** by reacting *N-tert*-butyldiacylhydrazines **1a**–**g** with potassium *tert*-butoxide followed by the addition of phosgene **3a** or thiophosgene **3b**. We also determined the structure of 5-(3,5-dimethylphenyl)-3-(4-ethylbenozyl)-3*H*-[1,3,4]-oxadiazol-2-one (**4a**) not only through analyt-



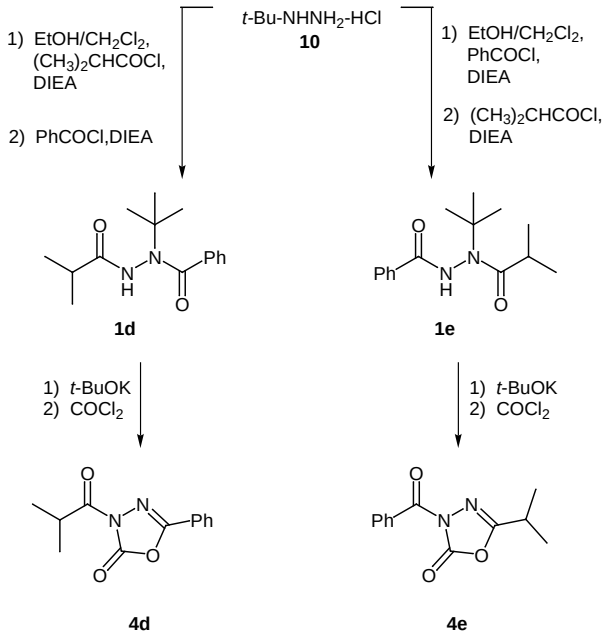
Scheme 3 Proposed mechanism for the transformation of diacylhydrazine **2** to 1,3,4-oxadiazol-2-one **4**

Table 2 Selected Spectra Data of Compounds **1d–g**, **4a–g**, **5a**, **5b**, **5f**, **6**, and **7**

Product[a]	^{1}H NMR (300 MHz, $CDCl_3$) δ, *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$) δ	IR (cm^{-1})
1d	0.45 (d, 3 H, *J* = 6.6), 0.89 (d, 3 H, *J* = 6.6), 1.50 (s, 9 H), 1.95 (m, 1 H), 7.21–7.34 (m, 5 H), 8.41 (br s, 1 H)	18.7, 19.2, 28.0, 33.3, 61.4, 126.6, 128.1, 129.6, 138.4, 174.2, 175.9	2900, 1706, 1684, 1637
1e	1.07 (d, 3 H, *J* = 6.0), 1.08 (d, 3 H, *J* = 6.0), 1.50 (s, 9 H), 2.80 (m, 1 H), 7.48 (m, 2 H), 7.56 (m, 1 H), 7.80 (d, 2 H, *J* = 6.0), 8.33 (s, 1 H)	19.2, 20.1, 28.1, 31.9, 61.3, 127.2, 129.0, 132.1, 132.6, 167.3, 179.4	2919, 1666, 1643
1f	1.60 (s, 9 H), 7.26–7.45 (m, 10 H), 7.85 (br s, 1 H)	28.1, 61.9, 126.6, 127.3, 128.2, 128.7, 129.6, 132.1, 132.6, 138.1, 167.9, 174.2	1666, 1638
1g	1.04 (t, 6 H, *J* = 6.6), 1.18 (t, 6 H, *J* = 6.6), 1.43 (s, 9 H), 2.57–2.67 (m, 1 H), 2.71–2.80 (m, 1 H), 9.11 (br s, 1 H)	19.7, 20.3, 28.2, 32.0, 33.4, 61.2, 177.4, 179.9	3283, 2910, 1689
4a	1.30 (t, 3 H, *J* = 7.5), 2.38 (s, 6 H), 2.75 (q, 2 H, *J* = 7.5), 7.18 (s, 1 H), 7.32 (d, 2 H, *J* = 8.1), 7.56 (s, 2 H), 7.92 (d, 2 H, *J* = 8.4)	15.0, 21.2, 29.1, 122.4, 124.3, 127.9, 128.0, 130.9, 134.6, 139.0, 149.9, 150.9, 154.1, 164.2	2927, 1831, 1703, 1301
4b	2.27 (s, 3 H), 2.36 (s, 6 H), 3.89 (s, 3 H), 7.05 (m, 2 H), 7.19 (s, 1 H), 7.26–7.30 (m, 1 H), 7.54 (s, 2 H)	13.0, 21.1, 55.7, 112. 9, 119.7. 122.2, 124.5, 125.8, 126.6, 133.0, 134.7, 138.9, 149.1, 154.8, 157.8. 164.9	2931, 1822, 1726, 1291
4c	7.50–7.61 (m, 5 H), 7.92–7.97 (m, 4 H)	122.4, 126.6, 128.7, 129.0, 129.2, 132.0, 133.0, 140.3, 149.4, 153.9, 163.3	2926, 2891, 1850, 1728
4d	1.30 (d, 3 H, *J* = 6.6), 1.32 (d, 3 H, *J* = 6.6), 3.53–3.63 (m, 1 H), 7.49–7.61 (m, 3 H), 7.94 (d, 2 H, *J* = 7.5)	18.4, 33.4, 122.6, 126.6, 129.2, 133.9, 149.2, 154.0, 172.9	1849, 1824, 1725
4e	1.34 (d, 6 H, *J* = 6.0), 2.94 (m, 1 H), 7.49 (m, 2 H), 7.63 (m, 1 H), 7.92 (d, 2 H, *J* = 6.0)	18.6, 27.1, 128.2, 130.4, 130.8, 133.6, 150.1, 161.2, 164.3	1833, 1805, 1711, 1307
4f	7.49–7.66 (m, 6 H), 7.93 (d, 2 H, *J* = 6.0), 7.99 (d, 2 H, *J* = 6.0)	122.5, 126.6, 128.3, 129.2, 130.5, 130.7, 132.9, 133.7, 149.6, 153.8, 164.3	2916, 1821, 1701, 1293
4g	1.26 (d, 6 H, *J* = 6.0), 1.33 (d, 6 H, *J* = 6.0), 2.92 (m, 1 H), 3.51 (m, 1 H)	18.4, 18.6, 27.1, 33.2, 149.8, 161.4, 172.8	1835, 1802, 1744, 1271
5a	1.32 (t, 3 H, *J* = 7.5), 2.38 (s, 6 H), 2.77 (q, 2 H, *J* = 7.5), 7.22 (s, 1 H), 7.36 (d, 2 H, *J* = 8.1), 7.59 (s, 2 H), 7.94 (d, 2 H, *J* = 8.1)	15.0, 21.2, 29.1, 121.3, 124.7, 128.0, 128.1, 131.4, 134.9, 139.1, 151.4, 158.3, 164.7, 175.0	2940, 1713, 1607, 1279
5b	2.27 (s, 3 H), 2.36 (s, 6 H), 3.90 (s, 3 H), 7.04–7.10 (m, 2 H), 7.21 (s, 1 H), 7.26–7.31 (m, 1 H), 7.55 (s, 2 H)	13.0, 21.1, 55.7, 113.1, 120.2, 121.2, 124.8, 126.3, 126.7, 133.3, 134.9, 139.1, 157.9, 158.6, 165.7, 174.2	2903, 1733, 1461, 1309
5f	7.50–7.68 (m, 6 H), 7.96–8.01 (m, 4 H)	121.6, 127.1, 128.4, 129.3, 130.8, 130.9, 133.2, 134.0, 158.0, 164.9, 174.8	2925, 1727, 1625, 1287
7[b]	2.37 (s, 6 H), 7.15 (s, 1 H), 7.48 (s, 2 H), 9.58 (br s, 1 H)	21.2, 123.48, 123.53, 133.5, 138.8, 154.9, 155.7	2932, 2906, 1777, 1734
6[c]	1.26 (t, 3 H, *J* = 9.0), 2.72 (q, 2 H, *J* = 9.0), 7.14 (t, 1 H, *J* = 9), 7.28–7.39 (m, 4 H), 7.64 (d, 2 H, *J* = 6.0), 7.79 (d, 2 H, *J* = 6.0), 7.85 (br s, 1 H)	15.3, 28.8, 120.1, 124.4, 127.1, 128.3, 129.1, 132.3, 138.0, 148.6, 165.7.	3303, 2908, 1648

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.24, N ±0. 29.
[b] Compound **7**, mp 182–183 °C.
[c] Compound **6**, mp 120–122 °C.

ical methods, but also through chemical means utilizing the methods of Gogoi and Saegusa as shown in Schemes 2 and Ref.[8] to synthesize both **4a** and 5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (**7**). We also demonstrated that various *N*-*tert*-butyldiacylhydrazines **1**, equivalent and non-equivalent in nature of their acyl groups, could be easily synthesized in a one-pot, two step regioselective acylation procedure involving the reaction of *tert*-butylhydrazine hydrochloride in the presence of *i*-Pr_2NEt with R^1COCl followed subsequently by R^2COCl. Also, it should be noted that the *tert*-butyl moiety, which is inconspicuously removed in situ during the cyclization process,



Scheme 4 Selective diacylation of *tert*-butylhydrazine **10** to afford *iso*-butyryl/benzoylhydrazine isomers **1d** and **1e**, respectively followed by cyclization to afford 1,3,4-oxadiazol-2-ones **4d** and **4e**

is especially attractive as it creatively serves a dual purpose in directing both the regioselective diacylation reaction as well as the subsequent cyclization reaction.

Reagents and solvents were used as received from commercial sources. TLC was performed on 4 × 8 cm, SIL 6UV/254, Lot 111989 silica gel plates with fluorescent indicator available from Alltech Associates, Inc. TLC plates were visualized with UV light. Column chromatography was performed on silica gel (Merck, 70–230 mesh). ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ on a Bruker 300 MHz spectrometer. All ^{1}H NMR spectra are reported in ppm relative to TMS. All ^{13}C NMR spectra are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.00 ppm. Melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were obtained by dissolving the compound in $CHCl_3$ and then applying the solution to a polyethylene film plate and spectra were obtained on a Mattson Genesis II FT-IR spectrophotometer and reported in cm^{-1}. Elemental analyses were performed by Robertson Microlit Laboratories, Inc., 29 Samson Avenue, P.O. Box 927, Madison, New Jersey 07940.

_N_-*tert*-Butyldiacylhydrazines 1d–g; Benzoic Acid _N_-*tert*-Butyl-_N'_-*iso*-butyrylhydrazide (1d); Typical Procedure

To a solution of *tert*-butylhydrazine hydrochloride (4.0 g, 32.0 mmol) in a mixture of CH_2Cl_2 (75 mL) and EtOH (75 mL) was added *i*-Pr_2NEt (11.2 mL, 64.0 mmol). The solution was cooled to 5 °C in an ice-water bath and then charged with *iso*-butyryl chloride (3.3 mL, 32.0 mmol) at once and allowed to warm to r.t. After stirring for 4 h, the solution was cooled to 5 °C in an ice bath, charged with *i*-Pr_2NEt (5.6 mL, 32.0 mmol) followed by benzoyl chloride (3.7 mL, 32.0 mmol) and then allowed to warm to r.t. After stirring for 4 h, the solvent was removed in vacuo and the solids were dissolved in EtOAc (100 mL) and washed with 5% HCl solution (80 mL), H_2O (2 × 80 mL) and then with brine (80 mL). The EtOAc layer was dried ($MgSO_4$), filtered and concentrated in vacuo to afford 7.5 g (90%) of the desired product **1d** as a white solid which was recrystallized from Et_2O (Table 1); mp 156–157 °C.

Benzoic Acid _N'_-*tert*-Butyl-_N'_-*iso*-butyrylhydrazide (1e)

Compound **1e** was prepared in 80% yield according to the typical procedure above except for charging the reaction first with benzoyl chloride followed by *iso*-butyryl chloride; mp 180–181 °C.

Benzoic Acid _N'_-Benzoyl-_N_-*tert*-butylhydrazide (1f)

Compound **1f** was prepared in 93% yield according to the typical procedure above except benzoyl chloride was used instead of *iso*-butyryl chloride; mp 172–173 °C.

***iso*-Butyric Acid _N_-*tert*-Butyl-_N'_-*iso*-butyrylhydrazide (1g)**

Compound **1g** was prepared in 90% yield according to the typical procedure above except for the addition of *iso*-butyryl chloride instead of benzoyl chloride; mp 151–152 °C.

3,5-Disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones 4a–g and -thiones 5a, 5b, and 5f; 5-(3,5-Dimethylphenyl)-3-(4-ethylbenzoyl)-3*H*-[1,3,4]-oxadiazol-2-one (4a); Typical Procedure

To a THF solution (30 mL) of **1a** (500 mg, 1.42 mmol) under N_2 was added KOBu-*t* (159 mg, 1.42 mmol). The resulting mixture was allowed to stir at r.t. for 1 h at which time the solution was cooled in a dry ice/acetone bath to –78 °C. Phosgene (2.2 M in EtOAc, 0.75 mL, 1.62 mmol) was then added in one portion and the resulting mixture was allowed to stir at –78 °C for 0.5 h. The solution was then concentrated in vacuo, redissolved into CH_2Cl_2 (30 mL), washed with H_2O (2 × 20 mL) and then with brine (20 mL). The CH_2Cl_2 layer was dried ($MgSO_4$), filtered, and concentrated in vacuo to afford 434 mg (95%) of **4a** as a white solid, which was recrystallized from EtOAc–hexanes.

5-(3,5-Dimethylphenyl)-3-(3-methoxy-2-methylbenzoyl)-3*H*-[1,3,4]-oxadiazol-2-one (4b)

Compound **4b** was prepared according to the typical procedure above except for the substitution of hydrazide **1b** for **1a**.

3-(4-Chlorobenzoyl)-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one (4c)

Compound **4c** was prepared according to the typical procedure above except for the substitution of hydrazide **1c** for **1a**.

3-*iso*-Butyryl-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one (4d)

Compound **4d** was prepared according to the typical procedure above except for the substitution of hydrazide **1d** for **1a**.

3-Benzoyl-5-*iso*-propyl-3*H*-[1,3,4]-oxadiazol-2-one (4e)

Compound **4e** was prepared according to the typical procedure above except for the substitution of hydrazide **1e** for **1a**.

3-Benzoyl-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-one (4f)

Compound **4f** was prepared according to the typical procedure above except for the substitution of hydrazide **1f** for **1a**.

3-*iso*-Butyryl-5-*iso*-propyl-3*H*-[1,3,4]-oxadiazol-2-one (4g)

Compound **4g** was prepared according to the typical procedure above except for the substitution of hydrazide **1g** for **1a**.

3-(4-Ethylbenzoyl)-5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-thione (5a)

Compound **5a** was prepared according to the typical procedure above except for the substitution of thiophosgene for phosgene.

3-(3-Methoxy-2-methylbenzoyl)-5-(3,5-dimethylphenyl)- 3*H*-[1,3,4]-oxadiazol-2-thione (5b)

Compound **5b** was prepared according to the typical procedure above except for the substitution of hydrazide **1b** for **1a** and the substitution of thiophosgene for phosgene.

3-Benzoyl-5-phenyl-3*H*-[1,3,4]-oxadiazol-2-thione (5f)

Compound **5f** was prepared according to the typical procedure above except for the substitution of hydrazide **1f** for **1a** and the substitution of thiophosgene for phosgene.

4-Ethyl-*N*-phenylbenzamide (6) and 5-(3,5-Dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (7)

A solution of **4a** (500 mg, 1.55 mmol) in THF (8 mL) was charged with aniline (144 mg, 1.55 mmol) and stirred for 4 h, upon which time the reaction was deemed complete by TLC analysis. The THF was removed in vacuo, and the crude product was purified by silica gel column chromatography (EtOAc–hexanes, 1:1) to afford 300 mg (85%) of **6** and 250 mg (85%) of **7**. The analytical data of compound **7** was identical to that of **7** prepared via the Gogoi method.[8]

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(8) We decided to further chemically validate the structure of **4a** utilizing Gogoi's method[7] for the synthesis of 3,5-disubstituted-3*H*-[1,3,4]-oxadiazol-2-ones. We synthesized *N'*-(3,5-dimethylbenzoyl)hydrazinecarboxylic acid ethyl ester from the reaction of a CH_2Cl_2 solution of ethyl carbazate with 3,5-dimethylbenzoyl chloride in the presence of *i*-Pr_2NEt. Reaction of *N'*-(3,5-dimethylbenzoyl)hydrazinecarboxylic acid ethyl ester with $POCl_3$ afforded 5-(3,5-dimethylphenyl)-3*H*-[1,3,4]-oxadiazol-2-one (**7**), which was analytically identical to compound **7** synthesized via Scheme 2 (Table 2). Benzoylation of **7** with 4-ethylbenzoyl chloride afforded 5-(3,5-dimethylphenyl)-3-(4-ethylbenozyl)-3*H*-[1,3,4]-oxadiazol-2-one (**4a**), which was identical in all respects to **4a** synthesized via our phosgene/*N*-*tert*-butyldiacylhydrazine route.
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