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Phosphine-mediated annulation of *N*-protected imines with DEAD

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ABSTRACT

In the presence of triphenylphosphine, the reactions of *N*-protected imines or their precursors with DEAD proceeded smoothly to give the corresponding functionalized 1*H*-1,2,4-triazole-1,4(5*H*)-dicarboxylate derivatives in good to high yields under mild conditions. A plausible mechanism has been proposed on the basis of the control experiments.

1. Introduction

The discovery of novel synthetic methodologies to facilitate the construction of heteroatom-containing ring systems in an efficient way from readily available starting materials remains a challenging goal in organic synthesis because these heterocyclic compounds may exhibit antitumor or antibiotic activity or other biological properties, which make them to be attractive synthetic targets in their own right.[1] Recently, the nucleophilic phosphine-catalyzed/mediated reactions for the synthesis of carbo- and heterocycles have attracted much attention.[2] The most interesting examples are the Lu's [3+2] cycloaddition to form cyclopentene and pyrrolidine derivatives[3] and [4+2] process to construct six-membered heterocyclic rings by Kwon[4] and Fu.[5] These phosphine-catalyzed [3+2] or [4+2] cyclization reactions of allenoates have been proven to be powerful synthetic tools in the rapid formation of cyclic molecular complexity. In this paper, we wish to report a novel phosphine-mediated annulation of *N*-protected imines with diethyl azo dicarboxylate (DEAD) to form functionalized 1*H*-1,2,4-triazole-1,4(5*H*)-dicarboxylate derivatives in good yields under mild conditions. To our delight, we found that these nitrogen-containing heterocyclic compounds could be formed in good to excellent yields from the easily available precursors of these *N*-protected imines under mild conditions. In this paper, we wish to report this finding.

2. Results and discussion

The investigation aroused from the reaction of *N*-Boc-protected imine **1** (1.0 equiv) and DEAD in the presence of a stoichiometric amount of triphenylphosphine (1.0 equiv) in tetrahydrofuran (THF) at room temperature (20 °C) (Table 1, entry 1). Two nitrogen-containing five-membered cyclic products 4-*tert*-butyl 1-ethyl 3-ethoxy-5-phenyl-1*H*-1,2,4-triazole-1,4(5*H*)-dicarboxylate **2** and diethyl 3-ethoxy-5-phenyl-1*H*-1,2,4-triazole-1,4(5*H*)-dicarboxylate **3a** were obtained in 49% yield and 18% yield, respectively. The structure of products **2** and **3a** were assigned on the basis of spectroscopic analyses. Their structures were further unambiguously obtained from single-crystal X-ray analysis (Figs. 1 and 2).[6,7] Raising the reaction temperature to 60 °C or increasing the employed amounts of DEAD and triphenylphosphine to 2.0 equiv did not significantly improve the yields of **2** and **3a** (Table 1, entries 2 and 3). When the reaction was carried out using **1**:DEAD:PPh_3=1:1.5:1.5 in THF at room temperature, it was found that the corresponding annulation products **2** and **3a** were obtained in 58% yield and 23% yield, respectively (Table 1, entry 4). Changing the concentration of the reaction system revealed that products **2** and **3a** could be formed in quantitative yields under high concentration (Table 1, entry 7). The examination of solvent effects indicated that THF is the solvent of choice for this reaction and when the reaction was carried out in protic solvent, such as *tert*-amyl-OH, no reaction occurred (Table 1, entries 8–15).

Having identified optimal reaction conditions, we attempted to obtain a single product using N–CO_2Et-protected imine **4** to replace *N*-Boc-protected imine **1** in this interesting annulation reaction under the standard conditions (Scheme 1). As shown in Scheme 1,

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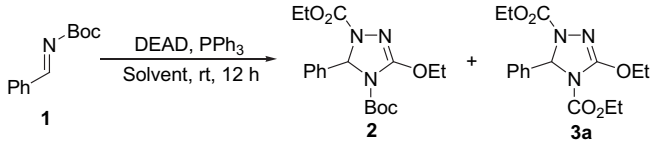
Table 1
Optimization of the reaction conditions[a]



Entry	1:DEAD:PPh3	Solvent	mol/L	Yield (%)[b]	
				2	**3a**
1	1:1:1	THF	0.1	49	18
2[c]	1:1:1	THF	0.1	47	15
3	1:2:2	THF	0.1	44	22
4	1:1.5:1.5	THF	0.1	58	23
5	1:1.5:1.5	THF	0.2	72	25
6	1:1.5:1.5	THF	0.04	60	25
7	1:1.5:1.5	THF	0.4	75	25
8	1:1.5:1.5	DCM	0.4	58	30
9	1:1.5:1.5	Toluene	0.4	69	28
10	1:1.5:1.5	Acetonitrile	0.4	64	22
11	1:1.5:1.5	DMF	0.4	40	28
12	1:1.5:1.5	*t*-Amyl-OH/THF (1:1)	0.4	NR	NR
13	1:1.5:1.5	DMSO	0.4	35	27
14	1:1.5:1.5	Ether	0.4	62	23
15	1:1.5:1.5	Dioxane	0.4	65	22

[a] Compound **1** (0.2 mmol) was dissolved in THF, then PPh_3 (0.2 mmol), and DEAD (0.2 mmol) were added and the reaction mixture was stirred for 12 h.
[b] Isolated yields.
[c] The reaction was carried out at 60 °C.

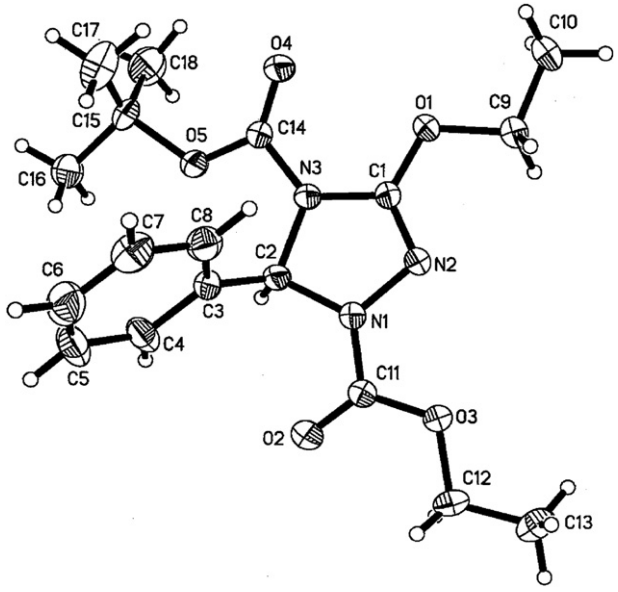


Fig. 1. Single-crystal X-ray structure of **2**.

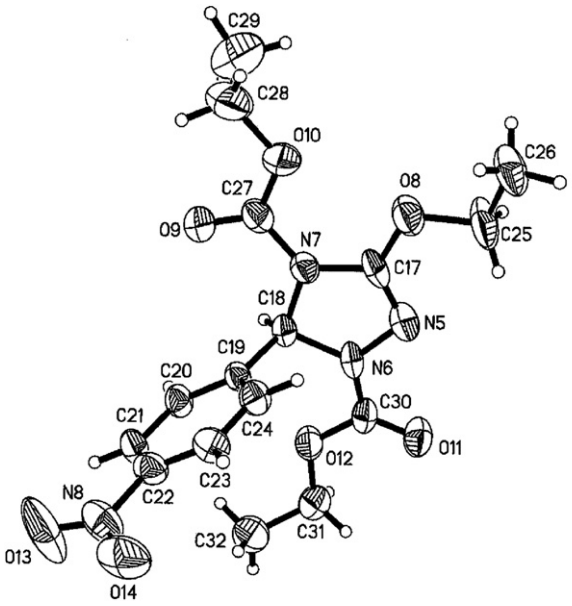


Fig. 2. Single-crystal X-ray structure of **3a**.

we found that the corresponding annulation product **3a** was obtained as a sole product in >99% yield under the optimal conditions. Further examination revealed that using its precursor **5a** as the substrate also afforded the corresponding product **3a** in >99% yield in the presence of DEAD (3.0 equiv) and PPh_3 (3.0 equiv) under otherwise identical conditions (Scheme 1) in which the extra amounts of DEAD and PPh_3 were used to generate the corresponding *N*-protected imine from its precursor. This finding provided a more convenient access to this type of heterocyclic compounds under mild conditions.

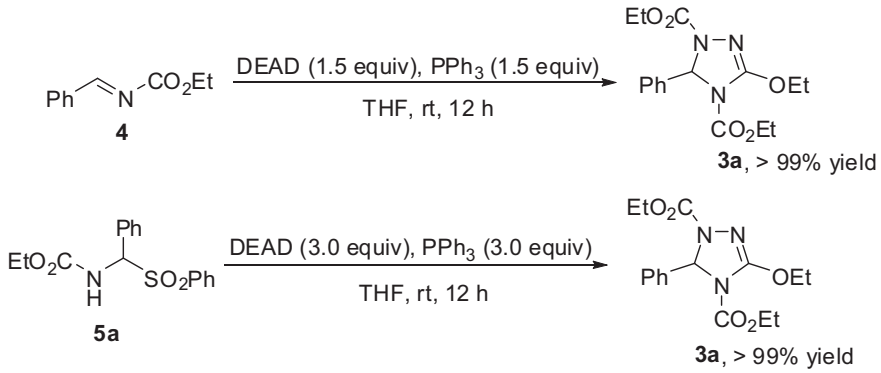
Using other phosphines, such as PPh_2Me, $PPhMe_2$, and PBu_3 did not further improve the yield of **3a** (Table 2, entries 1–3) and nitrogen-containing Lewis bases, such as triethylamine (TEA), 4-*N*,*N*-dimethylpyridine (DMAP) or 1,4-diazabicyclo[2,2,2]octane (DABCO) did not promote the reaction (Table 2, entries 4–6), indicating that PPh_3 is the best promoter for this reaction.

Next, we turned our attention to substrate scope with respect to a variety of precursors **5** (Table 3, entries 1–9). We were pleased to isolate the nitrogen-containing heterocyclic compounds **3** in good to excellent yields. The yields of the corresponding five-membered heterocyclic product **3** were not influenced significantly by the electronic nature of **5**. Interestingly, the aliphatic substrate **5i** with DEAD also proceeded smoothly, furnishing the product **3i** in 76% yield (Table 3, entry 8). Their structures were determined by spectroscopic data, Mass and HRMS.

Using *N*-Boc-protected imine **1**'s precursor **6** as the substrate to react with di-*tert*-butyl azo dicarboxylate (DTAD) produced the corresponding heterocyclic product **7** in 37% yield under the standard conditions (Table 4, entry 1). Using other phosphines, such as PPh_2Me, $PPhMe_2$ or PBu_3 did not improve the yield of **7**, presumably due to the steric hindrance of DTAD (Table 4, entries 2–4). In the presence of other nitrogen-containing Lewis bases, such as DMAP or DABCO, no reaction occurred either (Table 4, entries 5 and 6).

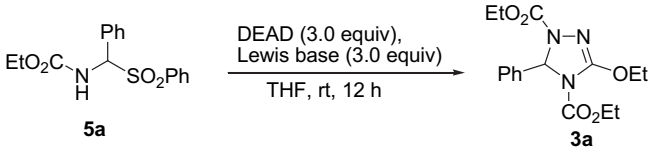
The mechanism suggested in Scheme 2 may be invoked to rationalize the reaction. Initially, the reaction of triphenylphosphine with DEAD **A** generates the zwitterionic intermediate **B**, which undergoes nucleophilic addition to imino group of *N*-Boc-protected imine to form intermediate **C**. The intramolecular addition of Boc-N^- anion to the carbonyl group in intermediate **C** gives intermediate **D**, which subsequently undergoes elimination of triphenylphosphine oxide to generate the product **2** via intermediate **E**. The mechanism for the formation of **3a** is also proposed in Scheme 2. The elimination of $BocO^-$ from intermediate **C** gives intermediate **F** and the released $BocO^-$ anion can attack DEAD to give intermediate **G**, which undergoes the elimination of EtO^- anion to give product **H**. The released EtO^- anion attacks the N=C=O group in intermediate **F** generates intermediate **I**, which can undergo the similar intramolecular nucleophilic attack to produce intermediate **J**. The elimination of triphenylphosphine oxide gives product **3a** via intermediate **K** (Scheme 2).

As shown in Scheme 3, the extra amounts of DEAD and PPh_3 are required to generate the zwitterionic intermediate **B**, which deprotonates *N*-Boc-protected imine's precursor to form the corresponding *N*-Boc-protected imine (Scheme 3).



Scheme 1. Annulation of *N*-protected imine **4** or its precursor **5a** and DEAD in the presence of triphenylphosphine.

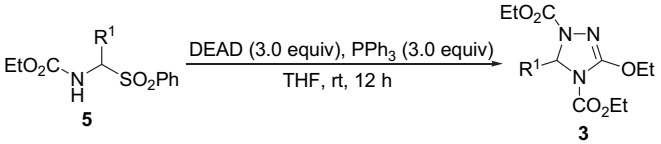
Table 2
Annunation of precursor **5a** with DEAD in the presence of different Lewis bases[a]



Entry	Lewis base	Yield (%)[b]
		3a
1	PPh_2Me	90
2	$PPhMe_2$	81
3	PBu_3	80
4	TEA	NR[c]
5	DMAP	NR[c]
6	DABCO	NR[c]

[a] Compound **5a** (0.2 mmol) was dissolved in THF, then Lewis base (0.6 mmol) and DEAD (0.6 mmol) were added and the reaction mixture was stirred at room temperature for 12 h.
[b] Isolated yields.
[c] No reaction.

Table 3
Scope of the annulation in the presence of triphenylphosphine[a]

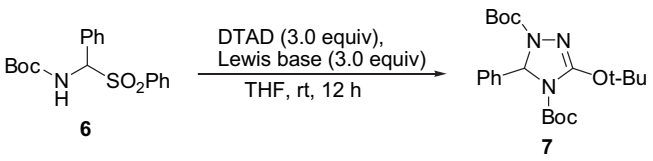


Entry	R^1	Yield (%)[b]
		3
1	*p*-$CF_3C_6H_4$, **5b**	**3b**, 94
2	*p*-$NO_2C_6H_4$, **5c**	**3c**, 97
3	*o*-$NO_2C_6H_4$, **5d**	**3d**, 95
4	*m*-$NO_2C_6H_4$, **5e**	**3e**, 94
5	3,5-$(CF_3)_2C_6H_3$, **5f**	**3f**, 88
6	3,4-$Cl_2C_6H_3$, **5g**	**3g**, 93
7	2-Cl-4-$NO_2C_6H_3$, **5h**	**3h**, 95
8	 , **5i**	**3i**, 76
9	*p*-ClC_6H_4, **5j**	**3j**, 91

[a] Compound **5** (0.3 mmol) was dissolved in THF, then PPh_3 (0.9 mmol) and DEAD (0.9 mmol) were added and the reaction mixture was stirred for 12 h.
[b] Isolated yields.

The further transformation of compound **2** has been shown in Scheme 4. Upon treatment of heterocyclic product **2** with trifluoroacetic acid (TFA) in dichloromethane (DCM) at room temperature produced the corresponding cyclic product **8** in 95% yield.

Table 4
Annunation of precursor **6** with DTAD in the presence of Lewis bases[a]



Entry	Lewis base	Yield (%)[b]
		7
1	PPh_3	37
2	PPh_2Me	33
3	$PPhMe_2$	30
4	PBu_3	Complex
5	DMAP	NR[c]
6	DABCO	NR[c]

[a] Compound **6** (0.3 mmol) was dissolved in THF, then Lewis base (0.9 mmol) and DTAD (0.9 mmol) were added and the reaction mixture was stirred for 12 h.
[b] Isolated yields.
[c] No reaction.

In general, products **2** and **8** are quite stable and they are difficult to be used for the Heck or Suzuki coupling reactions.

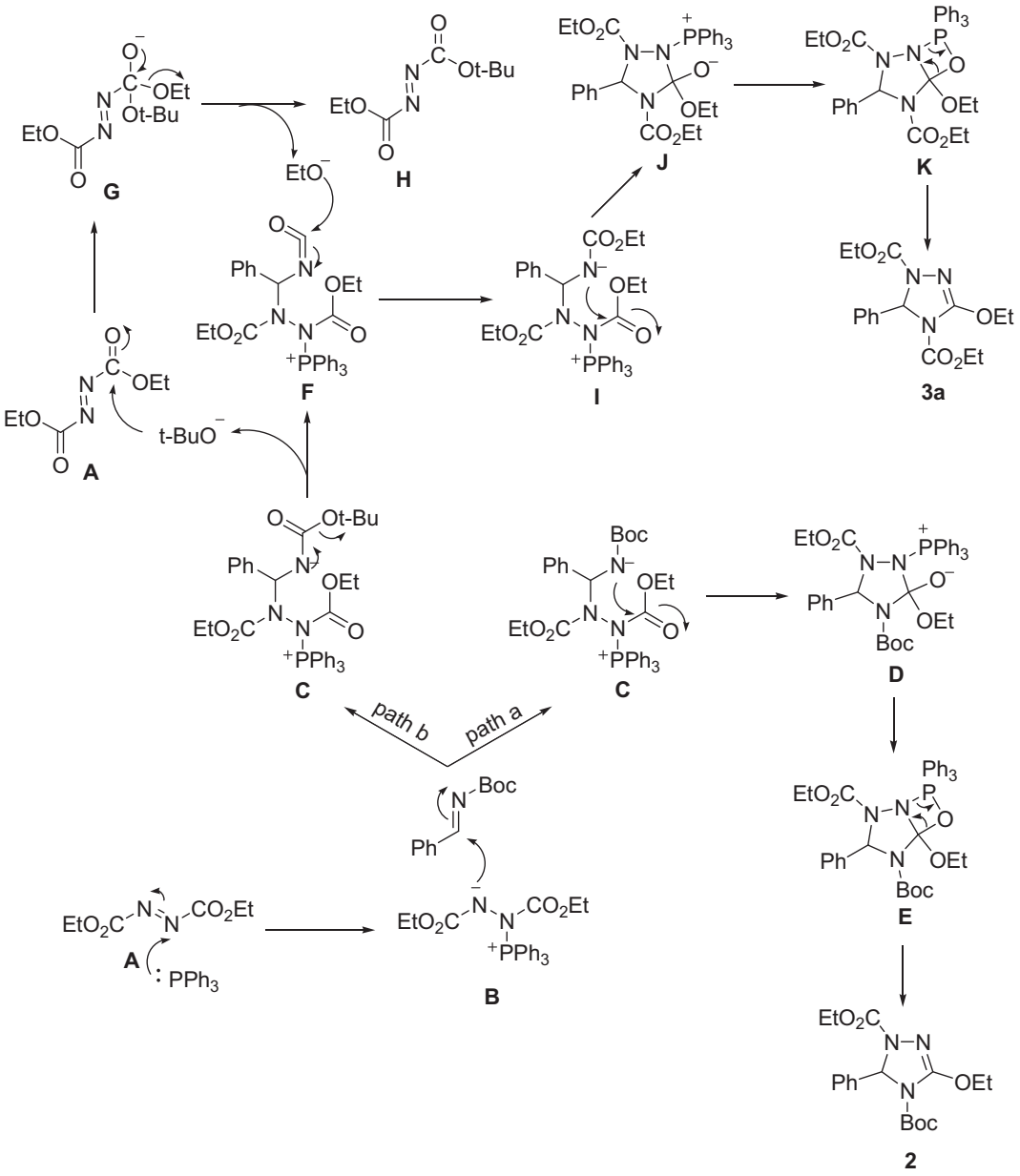
3. Conclusion

In summary, we have disclosed a facile synthesis of functionalized 1*H*-1,2,4-triazole-1,4(5*H*)-dicarboxylate derivatives in good yields by phosphine-mediated annulation reactions of *N*-protected imines or their precursors with DEAD under mild conditions. The electron-withdrawing imino-group is believed to play an important role in these transformations,[2d,8] and a plausible mechanism is proposed. Efforts are underway to elucidate the mechanistic details of this annulation and to extend the scope of substrates in this interesting annulation reaction.

4. Experimental section

4.1. General remarks

Mps were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded for a solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. *J*-values are in 300 M or 400 MHz. Mass spectra were recorded with an HP-5989 instrument and HRMS was measured by a Finnigan MA^+ mass spectrometer. The solid compounds reported in this paper gave satisfactory CHN microanalyses with a Carlo-Erba 1106 analyzer. Commercially obtained reagents were

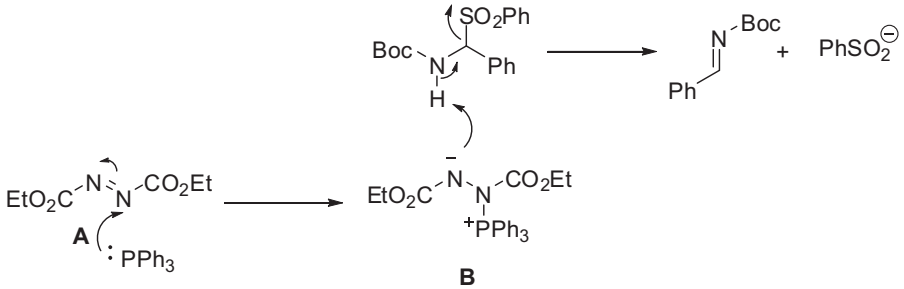


Scheme 2. A plausible mechanism for the formation of **2** and **3**.

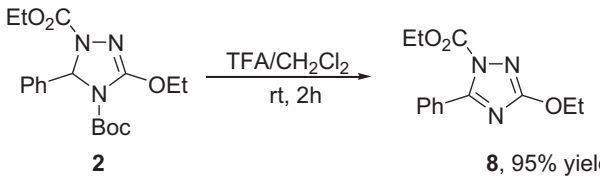
used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure. Reaction experiments were performed under argon condition.

4.2. Typical reaction procedure for the preparation of diethyl 3-ethoxy-5-phenyl-5*H*-1,2,4-triazole-1,4-dicarboxylate 3a

To a mixture of ethyl phenyl(phenylsulfonyl)methylcarbamate **5a** (0.2 mmol) and DEAD (0.6 mmol) in THF (0.6 mL)



Scheme 3. A plausible mechanism for the formation of *N*-Boc-protected imine.



Scheme 4. Transformation of compound **2**.

was added triphenylphosphine (0.6 mmol) under argon atmosphere and the reaction mixture was stirred for 12 h at room temperature. After the reaction solution was concentrated under reduced pressure, the residue was purified by flash chromatography on silica gel (Eluent: EtOAc/petroleum=1/4) to afford pure product **3a**.

*4.2.1. 4-tert-Butyl 1-ethyl 3-ethoxy-5-phenyl-5H-1,2,4-triazole-1,4-dicarboxylate (**2**).* Mp 135–138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.19–1.21 (m, 3H, CH_3), 1.31 (s, 9H, CH_3), 1.47 (t, 3H, J=7.2 Hz, CH_3), 4.15–4.20 (m, 2H, CH_2), 4.49 (q, 2H, J=7.2 Hz, CH_2), 6.62 (s, 1H, CH), 7.34–7.37 (m, 3H, ArH), 7.43–7.45 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.3, 14.5, 27.8, 62.0, 67.7, 76.7, 83.5, 126.8, 128.3, 129.1, 138.3, 147.2, 153.0; IR (CH_2Cl_2): ν 2981, 2933, 1751, 1722, 1700, 1643, 1459, 1408, 1369, 1266, 1218, 1140, 1019, 906, 853, 743, 699 cm^{-1}; MS (ESI) m/z (%): 364.4 $[M+H]^+$ (100); MS (ESI) calcd for $C_{18}H_{25}N_3NaO_5$ $[M+Na]^+$ requires 386.1684, found: 386.1686; Anal. Calcd for $C_{18}H_{25}N_3O_5$ (%) (363.4): C, 59.49; H, 6.93; N, 11.56%. Found: C, 59.55; H, 6.73; N, 11.43%.

*4.2.2. Diethyl 3-ethoxy-5-phenyl-5H-1,2,4-triazole-1,4-dicarboxylate (**3a**).* Mp 137–138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.16 (t, 3H, J=7.2 Hz, CH_3), 1.19–1.28 (m, 3H, CH_3), 1.47 (t, 3H, J=7.2 Hz, CH_3), 4.12 (q, 2H, J=7.2 Hz, CH_2), 4.13–4.21 (m, 2H, CH_2), 4.49 (q, 2H, J=7.2 Hz, CH_2), 6.70 (s, 1H, CH), 7.34–7.37 (m, 3H, ArH), 7.44–7.46 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 14.2, 14.4, 62.0, 62.7, 67.8, 76.5, 126.7, 128.3, 129.2, 137.9, 148.5, 152.5; IR (CH_2Cl_2): ν 2958, 2928, 2855, 1746, 1646, 1458, 1376, 1261, 1094, 1023, 803, 740, 701 cm^{-1}; MS (ESI) m/z (%): 336.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{21}N_3NaO_5$ $[M+Na]^+$ requires 358.1385, found: 358.1373.

*4.2.3. Diethyl 3-ethoxy-5-(4-(trifluoromethyl)phenyl)-5H-1,2,4-triazole-1,4-dicarboxylate (**3b**).* Mp 145–147 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.19 (t, 3H, J=7.2 Hz, CH_3), 1.20–1.32 (m, 3H, CH_3), 1.47 (t, 3H, J=7.2 Hz, CH_3), 4.15 (q, 2H, J=7.2 Hz, CH_2), 4.17–4.23 (m, 2H, CH_2), 4.50 (q, 2H, J=7.2 Hz, CH_2), 6.76 (s, 1H, CH), 7.55–7.66 (m, 4H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 14.1, 14.4, 62.3, 63.1, 68.0, 76.4, 121.9, 125.4, 125.5, 127.2, 128.5, 129.1, 129.4, 131.0, 131.5, 134.1, 137.8, 141.5, 148.5, 151.2, 152.3; ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$) δ −63.1; IR (CH_2Cl_2): ν 2929, 2856, 1752, 1725, 1703, 1643, 1457, 1407, 1370, 1348, 1303, 1269, 1166, 1141, 1021, 927, 905, 847, 779, 738, 700 cm^{-1}; MS (ESI) m/z (%): 404.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{17}H_{20}F_3N_3NaO_5$ $[M+H]^+$ requires 426.1256, found: 426.1247.

*4.2.4. Diethyl 3-ethoxy-5-(4-nitrophenyl)-5H-1,2,4-triazole-1,4-dicarboxylate (**3c**).* Mp 142–144 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.20 (t, 3H, J=7.2 Hz, CH_3), 1.25–1.34 (m, 3H, CH_3), 1.49 (t, 3H, J=7.2 Hz, CH_3), 4.16 (q, 2H, J=7.2 Hz, CH_2), 4.18–4.27 (m, 2H, CH_2), 4.50 (q, 2H, J=7.2 Hz, CH_2), 6.79 (s, 1H, CH), 7.64–7.68 (m, 2H, ArH), 8.22–8.27 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 14.3, 14.6, 62.7, 63.4, 68.4, 76.2, 123.9, 128.1, 144.5, 148.5, 148.6, 152.4; IR (CH_2Cl_2): ν 2931, 2856, 1750, 1733, 1700, 1684, 1558, 1533, 1464, 1373, 1269, 1140, 1019, 909, 852, 784, 739, 700 cm^{-1}; MS (ESI) m/z (%): 381.4 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{21}N_4O_7$ $[M+H]^+$ requires 381.1411, found: 381.1405.

*4.2.5. Diethyl 3-ethoxy-5-(2-nitrophenyl)-5H-1,2,4-triazole-1,4-dicarboxylate (**3d**).* Mp 143–145 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.13 (t, 3H, J=7.2 Hz, CH_3), 1.25–1.30 (m, 3H, CH_3), 1.48 (t, 3H, J=7.2 Hz, CH_3), 4.10 (q, 2H, J=7.2 Hz, CH_2), 4.10–4.24 (m, 2H, CH_2), 4.52 (q, 2H, J=7.2 Hz, CH_2), 6.64 (s, 1H, CH), 7.49–7.55 (m, 1H, ArH), 7.64–7.68 (m, 2H, ArH), 7.90–7.93 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.9, 14.2, 14.3, 62.1, 63.3, 68.3, 71.2, 124.3, 128.0, 130.0, 132.9, 133.5, 148.1, 148.5, 152.3; IR (CH_2Cl_2): ν 2982, 2930, 1761, 1730, 1648, 1609, 1534, 1449, 1375, 1344, 1270, 1123, 1016, 916, 853, 819, 788, 753, 711 cm^{-1}; MS (ESI) m/z (%): 403.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{18}H_{19}N_4O_7$ $[M+H]^+$ requires 403.1248, found: 403.1228.

*4.2.6. Diethyl 3-ethoxy-5-(3-nitrophenyl)-5H-1,2,4-triazole-1,4-dicarboxylate (**3e**).* Mp 141–143 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.22 (t, 3H, J=7.2 Hz, CH_3), 1.31–1.36 (m, 3H, CH_3), 1.48 (t, 3H, J=7.2 Hz, CH_3), 4.17 (q, 2H, J=7.2 Hz, CH_2), 4.28–4.36 (m, 2H, CH_2), 4.50 (q, 2H, J=7.2 Hz, CH_2), 6.80 (s, 1H, CH), 7.58 (t, 1H, J=7.8 Hz, ArH), 7.83 (d, 1H, J=7.8 Hz, ArH), 8.22–8.26 (m, 1H, ArH), 8.32–8.34 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.9, 14.2, 14.4, 62.5, 63.3, 68.2, 76.2, 122.3, 124.2, 129.6, 133.0, 139.9, 148.2, 148.5, 152.2; IR (CH_2Cl_2): ν 2961, 1731, 1648, 1536, 1457, 1376, 1351, 1262, 1098, 1022, 805, 732, 706 cm^{-1}; MS (ESI) m/z (%): 381.4 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{21}N_4O_7$ $[M+H]^+$ requires 381.1405, found: 381.1416.

*4.2.7. Diethyl 5-(3,5-bis(trifluoromethyl)phenyl)-3-ethoxy-5H-1,2,4-triazole-1,4-dicarboxylate (**3f**).* Mp 152–155 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.22 (t, 3H, J=7.2 Hz, CH_3), 1.27–1.31 (m, 3H, CH_3), 1.48 (t, 3H, J=7.2 Hz, CH_3), 4.18 (q, 2H, J=7.2 Hz, CH_2), 4.16–4.23 (m, 2H, CH_2), 4.52 (q, 2H, J=7.2 Hz, CH_2), 6.80 (s, 1H, CH), 7.89 (s, 1H, ArH), 7.91 (s, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 14.2, 14.4, 62.7, 63.5, 68.4, 76.2, 117.6, 121.2, 123.2, 123.29, 123.34, 124.8, 127.1, 127.5, 128.4, 131.3, 131.8, 132.2, 132.7, 140.0, 140.6, 148.4, 152.3; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ −62.9; IR (CH_2Cl_2): ν 2927, 2855, 1750, 1725, 1642, 1510, 1460, 1407, 1370, 1348, 1267, 1171, 1140, 1023, 929, 905, 834, 781, 737, 701 cm^{-1}; MS (ESI) m/z (%): 472.5 $[M+H]^+$ (100); MS (ESI) calcd for $C_{18}H_{19}F_6N_3NaO_5$ $[M+Na]^+$ requires 494.1121, found: 494.1136.

*4.2.8. Diethyl 5-(3,4-dichlorophenyl)-3-ethoxy-5H-1,2,4-triazole-1,4-dicarboxylate (**3g**).* Mp 149–151 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.22 (t, 3H, J=7.2 Hz, CH_3), 1.24–1.28 (m, 3H, CH_3), 1.47 (t, 3H, J=7.2 Hz, CH_3), 4.17 (q, 2H, J=7.2 Hz, CH_2), 4.18–4.20 (m, 2H, CH_2), 4.48 (q, 2H, J=7.2 Hz, CH_2), 6.65 (s, 1H, CH), 7.31 (dd, 1H, J_1=2.0 Hz, J_2=8.0 Hz ArH), 7.44 (d, 1H, J=8.0 Hz, ArH), 7.55 (d, 1H, J=2.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 14.2, 14.5, 62.5, 63.3, 68.1, 76.1, 126.3, 129.0, 130.6, 132.7, 133.5, 138.1, 148.5, 152.3; IR (CH_2Cl_2): ν 2956, 2926, 2855, 1731, 1648, 1536, 1459, 1375, 1350, 1266, 1170, 1018, 742 cm^{-1}; MS (ESI) m/z (%): 404.2 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{19}Cl_2N_3NaO_5$ $[M+Na]^+$ requires 426.0594, found: 426.0600.

*4.2.9. Diethyl 5-(2-chloro-4-nitrophenyl)-3-ethoxy-5H-1,2,4-triazole-1,4-dicarboxylate (**3h**).* Mp 145–146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.18 (t, 3H, J=6.8 Hz, CH_3), 1.24–1.28 (m, 3H, CH_3), 1.50 (t, 3H, J=6.8 Hz, CH_3), 4.14 (q, 2H, J=6.8 Hz, CH_2), 4.13–4.19 (m, 2H, CH_2), 4.53 (q, 2H, J=6.8 Hz, CH_2), 7.12 (s, 1H, CH), 7.57 (d, 1H, J=8.8 Hz, ArH), 8.15 (dd, 2H, J_1=2.8 Hz, J_2=8.8 Hz ArH), 8.34 (d, 1H, J=2.8 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 14.2, 14.4, 62.6, 63.3, 68.3, 74.2, 124.3, 124.9, 130.8, 137.5, 140.2, 146.9, 148.2, 152.1; IR (CH_2Cl_2): ν 2982, 2957, 2928, 2856, 1730, 1650, 1530, 1449, 1376, 1271, 1147, 1055, 901, 858, 741 cm^{-1}; MS (ESI) m/z (%): 415.3

$[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{19}ClN_4NaO_7$ $[M+Na]^+$ requires 437.0835, found: 437.0841.

*4.2.10. Diethyl 5-cyclohexyl-3-ethoxy-5H-1,2,4-triazole-1,4-dicarboxylate (**3i**).* Mp 132–135 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.09–1.15 (m, 5H, CH_2), 1.31 (t, 3H, J=7.2 Hz, CH_3), 1.30–1.35 (m, 3H, CH_3), 1.42 (t, 3H, J=7.2 Hz, CH_3), 1.67–1.78 (m, 5H, CH_2), 4.24 (q, 2H, J=7.2 Hz, CH_2), 4.22–4.29 (m, 2H, CH_2), 4.40 (q, 2H, J=7.2 Hz, CH_2), 5.90 (d, 1H, J=3.3 Hz, CH); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 14.6, 25.8, 26.0, 26.2, 26.9, 43.0, 62.2, 62.8, 67.6, 76.6, 149.8, 154.0; IR (CH_2Cl_2): ν 2982, 2931, 2855, 1753, 1728, 1642, 1449, 1399, 1375, 1302, 1231, 1134, 1062, 1019, 964, 912, 890, 760 cm^{-1}; MS (ESI) m/z (%): 342.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{28}N_3O_5$ $[M+H]^+$ requires 342.2024, found: 342.2031.

*4.2.11. Diethyl 5-(4-chlorophenyl)-3-ethoxy-5H-1,2,4-triazole-1,4-dicarboxylate (**3j**).* Mp 147–148 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.19 (t, 3H, J=7.2 Hz, CH_3), 1.17–1.22 (m, 3H, CH_3), 1.46 (t, 3H, J=7.2 Hz, CH_3), 4.14 (q, 2H, J=7.2 Hz, CH_2), 4.13–4.19 (m, 2H, CH_2), 4.48 (q, 2H, J=7.2 Hz, CH_2), 6.68 (s, 1H, CH), 7.32–7.41 (m, 3H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 14.3, 14.5, 62.3, 63.0, 68.0, 76.6, 128.3, 128.7, 135.2, 136.5, 148.6, 152.4; IR (CH_2Cl_2): ν 2984, 2935, 1756, 1726, 1645, 1448, 1400, 1341, 1263, 1127, 1014, 914, 832, 751 cm^{-1}; MS (ESI) m/z (%): 370.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{16}H_{20}ClN_3NaO_5$ $[M+Na]^+$ requires 392.0984, found: 392.0993.

*4.2.12. Di-tert-butyl 3-tert-butoxy-5-phenyl-5H-1,2,4-triazole-1,4-dicarboxylate (**7**).* Mp 140–142 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.32 (s, 9H, *tert*-$(CH_3)_3$), 1.36 (s, 9H, *tert*-$(CH_3)_3$), 1.64 (s, 9H, *tert*-$(CH_3)_3$), 6.47 (s, 1H, CH), 7.32–7.34 (m, 3H, ArH), 7.40–7.42 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 27.8, 28.0, 28.2, 75.8, 81.0, 82.8, 85.9, 126.9, 128.2, 128.8, 139.2, 147.7, 150.0; IR (CH_2Cl_2): ν 2979, 2932, 1715, 1636, 1478, 1427, 1367, 1342, 1254, 1134, 929, 907, 850, 791, 750, 698 cm^{-1}; MS (ESI) m/z (%): 418.3 $[M+H]^+$ (100); MS (ESI) calcd for $C_{22}H_{33}N_3NaO_5$ $[M+Na]^+$ requires 442.2312, found: 442.2317.

4.3. Typical reaction procedure for the preparation of ethyl phenyl(phenylsulfonyl)methylcarbamate 5a

To a mixture of benzaldehyde (10.8 mmol) and ethyl carbamate (10.0 mmol) in THF (4.0 mL) was added water (10 mL), sodium benzenesulfinate dihydrate (10.0 mmol) and formic acid (2.4 mL). After the reaction mixture was stirred for 12–24 h, the reaction solution was treated with water (20 mL), and filtrated. The solid product was washed with ether (10 mL×3) to afford pure product **5a**.

*4.3.1. Ethyl (2-nitrophenyl)(phenylsulfonyl)methylcarbamate (**5d**).* Mp 130–132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.14 (t, 3H, J=7.2 Hz, CH_3), 3.99 (q, 2H, J=7.2 Hz, CH_2), 6.30 (d, 1H, J=6.8 Hz, CH), 7.45 (d, 1H, J=6.8 Hz, NH), 7.57–7.66 (m, 3H, ArH), 7.69–7.75 (m, 3H, ArH), 7.97 (d, 2H, J=7.6 Hz, ArH), 8.15 (d, 1H, J=7.6 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.3, 62.2, 69.0, 125.3, 125.8, 129.1, 129.3, 129.4, 130.6, 133.6, 134.6, 136.6, 149.1, 154.6; IR (CH_2Cl_2): ν 3349, 3003, 1735, 1582, 1534, 1480, 1351, 1309, 1279, 1149, 1083, 859, 788, 757, 707 cm^{-1}.

*4.3.2. Ethyl (3-nitrophenyl)(phenylsulfonyl)methylcarbamate (**5e**).* Mp 129–131 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.13 (t, 3H, J=6.9 Hz, CH_3), 3.96 (q, 2H, J=6.9 Hz, CH_2), 6.09 (d, 1H, J=10.8 Hz, CH), 6.24 (br s, 1H, NH), 7.56–7.62 (m, 3H, ArH), 7.65–7.74 (m, 1H, ArH), 7.85 (d, 1H, J=7.8 Hz, ArH), 7.91–7.94 (m, 2H, ArH), 8.30 (d, 2H, J=7.8 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.3, 62.3, 73.4, 76.7, 123.7, 124.6, 129.3, 129.5, 129.7, 132.1, 134.6, 135.1, 135.9, 148.2, 154.8; IR (CH_2Cl_2): ν 3321, 3097, 3062, 2975, 2931, 1697, 1532, 1448, 1350, 1309, 1282, 1253, 1175, 1082, 1047, 819, 736, 724 cm^{-1}.

*4.3.3. Ethyl (3,4-dichlorophenyl)(phenylsulfonyl)methylcarbamate (**5g**).* Mp 133–135 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.12 (t, 3H, J=6.9 Hz, CH_3), 3.95 (q, 2H, J=6.9 Hz, CH_2), 5.91 (d, 1H, J=9.6 Hz, CH), 6.04 (d, 1H, J=9.6 Hz, NH), 7.29–7.32 (m, 1H, ArH), 7.47–7.59 (m, 4H, ArH), 7.70 (t, 1H, J=7.5 Hz, ArH), 7.89 (d, 2H, J=7.5 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.3, 62.2, 73.2, 128.1, 129.2, 129.4, 130.0, 130.6, 130.7, 133.0, 134.3, 134.4, 136.0, 154.8; IR (CH_2Cl_2): ν 3317, 3066, 2981, 2960, 2932, 1710, 1563, 1528, 1471, 1447, 1375, 1320, 1241, 1146, 1083, 1047, 772, 742, 720 cm^{-1}.

*4.3.4. Ethyl (2-chloro-4-nitrophenyl)(phenylsulfonyl)methylcarbamate (**5h**).* Mp 132–134 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.15 (t, 3H, J=6.9 Hz, CH_3), 3.99 (q, 2H, J=6.9 Hz, CH_2), 6.49 (d, 1H, J=10.5 Hz, CH), 6.65 (d, 1H, J=10.5 Hz, NH), 7.57–7.64 (m, 3H, ArH), 7.70–7.75 (m, 1H, ArH), 7.96 (d, 2H, J=7.5 Hz, ArH), 8.21–8.25 (m, 1H, ArH), 8.51 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.3, 62.3, 70.2, 124.7, 125.4, 129.4, 130.7, 130.8, 131.1, 134.7, 136.2, 142.1, 146.8, 154.8; IR (CH_2Cl_2): ν 3327, 3254, 3102, 2982, 2931, 1714, 1525, 1469, 1447, 1345, 1323, 1277, 1241, 1082, 1055, 828, 773, 741, 687 cm^{-1}.

*4.3.5. Ethyl 3-ethoxy-5-phenyl-1H-1,2,4-triazole-1-carboxylate (**8**).* Mp 120–122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.32 (t, 3H, J=6.8 Hz, CH_3), 1.46 (t, 3H, J=6.8 Hz, CH_3), 4.40 (q, 2H, J=6.8 Hz, CH_2), 4.45 (q, 2H, J=6.8 Hz, CH_2), 7.43–7.53 (m, 3H, ArH), 7.63–7.66 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.9, 14.6, 64.9, 66.1, 127.9, 128.4, 129.5, 130.7, 148.4, 159.2, 167.2; IR (CH_2Cl_2): ν 2957, 2927, 2855, 1767, 1730, 1555, 1530, 1448, 1379, 1351, 1323, 1268, 1083, 829, 742, 701 cm^{-1}; MS (ESI) m/z (%): 262.1 $[M+H]^+$ (100); MS (ESI) calcd for $C_{13}H_{15}N_3NaO_3$ $[M+Na]^+$ requires 284.1006, found: 284.1012.

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Supplementary data

The spectroscopic charts (^{1}H, ^{13}C NMR spectra data) of the compounds shown in Tables 1–3 and X-ray of **2** and **3a** are included in the Supplementary data. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.01.072.

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6. The crystal data of **2** have been deposited in CCDC with number 798642. Empirical Formula: $C_{16}H_{20}N_4O_7$; Formula Weight: 380.36; Crystal size: 0.269×0.225×0.137; Crystal Color, Habit: colorless; Crystal System: Orthorhombic; Lattice Type: Primitive; Lattice Parameters: a=26.476(4) Å, b=8.5138(12) Å, c=16.707(2) Å, α=90°, β=90°, γ=90°, V=3766.0(9) Å^3; Space group: Pca2(1); Z=8; D_{calcd}=1.342 g/cm3; F_{000}=1600; $R1$=0.0667, $wR2$=0.1760. Diffractometer: Rigaku AFC7R
7. The crystal data of **3a** have been deposited in CCDC with number 798091. Empirical Formula: $C_{18}H_{25}N_3O_5$; Formula Weight: 363.41; Crystal size: 0.369×0.303×0.217; Crystal Color, Habit: colorless; Crystal System: Orthorhombic; Lattice Type: Primitive; Lattice Parameters: a=7.1904(5) Å, b=11.3451(8) Å, c=24.3590(17) Å, α=90°, β=90°, γ=90°, V=1987.1(2) Å^3; Space group: P2(1)2(1)2(1); Z=4; D_{calcd}=1.215 g/cm3; F_{000}=776; $R1$=0.0693, $wR2$=0.2227. Diffractometer: Rigaku AFC7R
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