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Facile synthesis of 1,2,4-triazolines via PPh_3-triggered reaction of azodicarboxylate with 2-azidoacrylates

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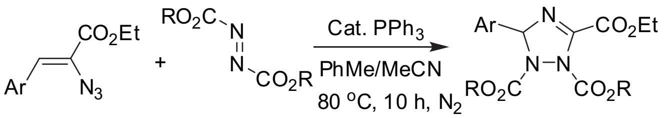
A convenient method for the synthesis of 1,2,4-triazolines by triphenylphosphine-triggered reaction of dialkyl azodicarboxylate with 2-azidoacrylates is described. The cascade reaction procedure is general and efficient.

1. Introduction

1,2,4-Triazolines are an underutilized class of heterocyclic small molecules whose bioactivity remains unexplored. Some work has been devoted to the development of synthetic methods for construction of the 1,2,4-triazoline core, the majority of which involve Mitsunobu reaction of α-amino acids,[1] cycloaddition of oxazoles,[2] addition of imidazopyridine with azodicarboxylates,[3] and reaction of azodicarboxylates with *N*-[(trimethylsilyl) methyl] iminium triflates.[4] Recently, Tepe and Saleem have reported the efficient synthesis of 1,2,4-triazolines utilizing oxazolones.[5] Still, the development of more efficient route to substituted 1,2,4-triazolines is of great interest.

Triphenylphosphine and dialkyl azodicarboxylates were utilized for the formation of Huisgen zwitterion,[6] which plays an important role in Mitsunobu reaction.[7] Nair and co-workers used this zwitterion to synthesize a variety of important compounds.[8] Recently, we have utilized the Huisgen zwitterions to synthesize pyrazolines and triazolinones.[9] Inspired by these works and our recent findings around the reactions of azidoacrylates,[10] we are interested in the cascade reaction of the Huisgen zwitterion with 2-azidoacrylates. Herein, we report the triphenylphosphine-triggered reaction of dialkyl azodicarboxylate with azidoacrylates leading to the formation of 1,2,4-triazolines in good yields under mild conditions (Scheme 1).



Scheme 1. Synthesis 1,2,4-triazolines.

2. Results and discussion

We initially examined the reaction of ethyl 2-azido-3-PMP-acrylate **1a** (1.0 equiv PMP=*p*-methoxyphenyl) with diethyl azodicarboxylate (DEAD) **2a** (2.5 equiv) in the presence of PPh_3 (1.0 equiv) using THF as a solvent under reflux (Table 1, entry 1). The reaction was completed in 24 h to give **3a** in 30% yield. It is noteworthy that solvent system is crucial to the success of this annulation chemistry (Table 1, entries 1–6). By using MeCN/PhMe as the co-solvent, we could improve the yield of product **3a** to 71%. The effect of amount of PPh_3 on this reaction was also evaluated. We found that reducing the amount of PPh_3 from 100 mol % to 20 mol % gave almost the same yield (Table 1, entry 7). When the reaction was catalyzed by 10 mol % PPh_3, the yield was obviously decreased (Table 1, entry 8). Furthermore, we found that using 2.5 equiv DEAD in this reaction gave the best yield (Table 1, entries 7, 9–10). The yield was highly dependent upon the reaction temperature and the time (Table 1, entries 11–13). Thus, the most suitable reaction conditions for the formation of **3a** were established (Table 1, entry 11).

Since ethyl 2-azidoacrylates are readily available from the condensation of aromatic aldehyde and ethyl azidoacetate,[11] we

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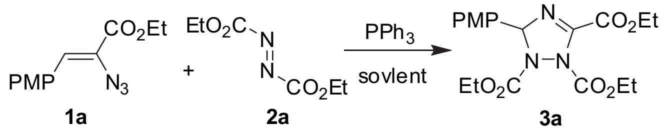
Table 1
Screening for the reaction conditions[a]



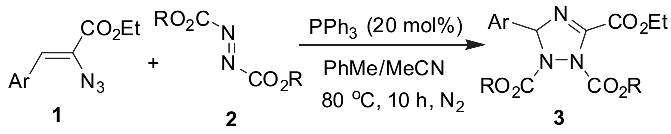
Entry	Solvent	PPh_3 (equiv)	Temp (°C)	Time (h)	Yield[b] (%)
1	THF	1	Reflux	24	30
2	PhMe	1	80	24	0
3	CH_3CN	1	Reflux	24	0
4	DCE	1	Reflux	24	0
5	2,6-dioxane	1	Reflux	24	0
6	PhMe/CH_3CN=1:1	1	80	24	71
7	PhMe/CH_3CN=1:1	0.2	80	24	69
8	PhMe/CH_3CN=1:1	0.1	80	24	58
9	PhMe/CH_3CN=1:1	0.2	80	24	60[c]
10	PhMe/CH_3CN=1:1	0.2	80	24	65[d]
11	PhMe/CH_3CN=1:1	0.2	80	10	68
12	PhMe/CH_3CN=1:1	0.2	80	5	38
13	PhMe/CH_3CN=1:1	0.2	50	24	Trace

[a] Conditions: **1a** (1 mmol), **2a** (2.5 mmol), solvent (10 mL).
[b] Isolated yield.
[c] 2.0 mmol of **2a**.
[d] 3.0 mmol of **2a**.

therefore extended the substrate scope to a variety of reactants under the optimized reaction conditions, and the results are presented in Table 2. From the results of Table 2, the protocol has proven to be useful cascade reaction of 2-azidoacrylates **1a**–**h** with variety of dialkyl azodicarboxylate **2a**–**d**. The reaction could give higher yields when 2-azidoacrylates were bearing electron-deficient groups, such as NO_2 (Table 2, entries 5, 14, and 17). Furthermore, when naphthyl 2-azidoacrylate **1g** was subjected to the cascade reactions, 1,2,4-triazolines (**3g**, **3l**, and **3r**) were obtained in 75–78% yields (Table 2, entries 7, 12, and 18). It should be noted that the reaction with the bulky di-*tert*-butyl azodicarboxylate proceeded smoothly, leading to good yields of triazoline product **3** (Table 2, entries 16–18).

The structures of products **3** (**3a**–**r**) were characterized by ^1H NMR, ^{13}C NMR, IR, MS, and HRMS spectra. The structure of compound **3j** (Table 2, entry 10) was unambiguously confirmed by single-crystal X-ray analysis (Fig. 1).[12]

Table 2
Scope of the reaction[a]



Entry	Ar	R	Product	Yield[b] (%)
1	4-$MeOC_6H_4$ (**1a**)	Et (**2a**)	**3a**	68
2	Ph (**1b**)	Et (**2a**)	**3b**	70
3	4-MeC_6H_4 (**1c**)	Et (**2a**)	**3c**	71
4	4-BrC_6H_4 (**1d**)	Et (**2a**)	**3d**	74
5	3-$NO_2C_6H_4$ (**1e**)	Et (**2a**)	**3e**	83
6	4-PhC_6H_4 (**1f**)	Et (**2a**)	**3f**	77
7	2-*naphthyl* (**1g**)	Et (**2a**)	**3g**	78
8	4-$PhCH_2OC_6H_4$ (**1h**)	Et (**2a**)	**3h**	73
9	4-$MeOC_6H_4$ (**1a**)	$PhCH_2$ (**2b**)	**3i**	73
10	4-BrC_6H_4 (**1d**)	$PhCH_2$ (**2b**)	**3j**	76
11	4-PhC_6H_4 (**1f**)	$PhCH_2$ (**2b**)	**3k**	79
12	2-naphthyl (**1g**)	$PhCH_2$ (**2b**)	**3l**	75
13	4-BrC_6H_4 (**1d**)	$(CH_3)_2CH$ (**2c**)	**3m**	75
14	3-$NO_2C_6H_4$ (**1e**)	$(CH_3)_2CH$ (**2c**)	**3n**	85
15	4-PhC_6H_4 (**1f**)	$(CH_3)_2CH$ (**2c**)	**3o**	77
16	4-$MeOC_6H_4$ (**1a**)	*t*-Bu (**2d**)	**3p**	72
17	3-$NO_2C_6H_4$ (**1e**)	*t*-Bu (**2d**)	**3q**	82
18	2-naphthyl (**1g**)	*t*-Bu (**2d**)	**3r**	76

[a] Reaction conditions: **1** (1 mmol), **2** (2.5 mmol), PPh_3 (0.2 mmol), Toluene/CH_3CN=1:1 (10 mL), 80 °C, 10 h.
[b] Isolated yield.

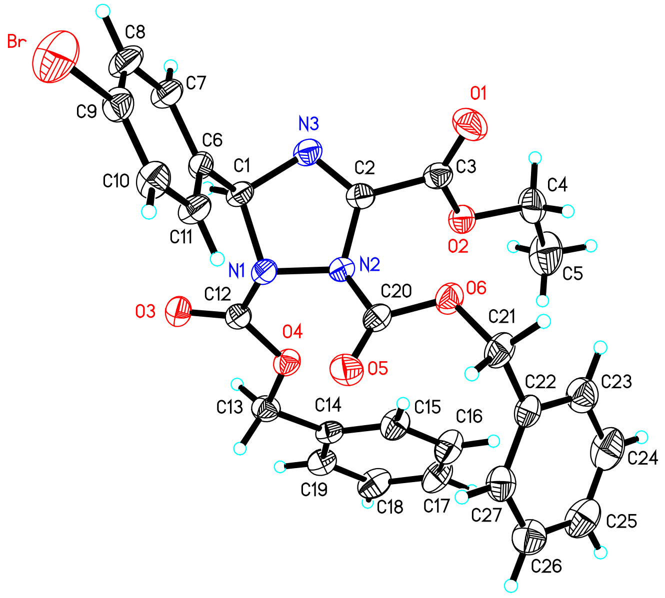
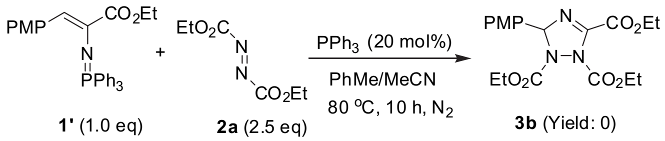


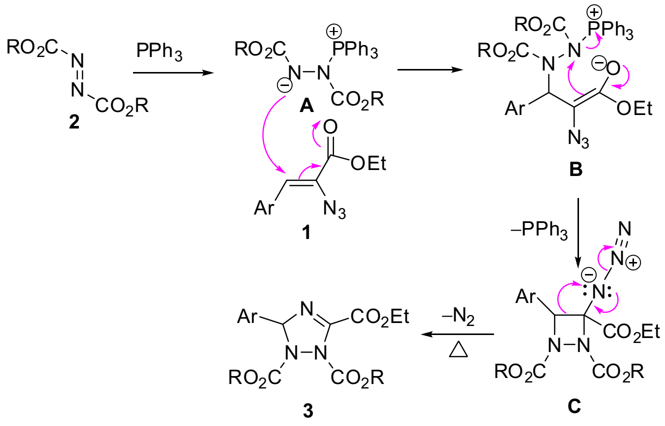
Fig. 1. X-ray crystal structure of **3j**.

To understand the mechanism of the cascade sequence, vinyl iminophosphorane **1′** prepared from 2-azidoacrylate **1a** and PPh_3 via the Staudinger–Meyer reaction was used instead of **1a** to perform the reaction (Scheme 2). We found that it did not follow the same reaction as **1a** and we did not obtain the desired 1,2,4-triazoline product **3a**. These results suggest that the present reaction does not undergo the iminophosphorane intermediate.



Scheme 2. Reaction of iminophosphorane **1′** with DEAD.

On the basis of these results, a tentative mechanism for the cascade reaction is proposed in Scheme 3. The Huisgen zwitterion **A** formed from triphenylphosphine and dialkyl azodicarboxylate **2** adds to 2-azidoacrylate **1** via a Michael-type reaction to give an intermediate **B**, which gives the 1,2-diazetidine **C** and releases PPh_3 via a cyclization reaction. **C** subsequently releases N_2, followed by a Curtius-type rearrangement, to form 1,2,4-triazoline **3**.



Scheme 3. Tentative mechanism for the cascade reaction.

3. Conclusion

In conclusion, we have demonstrated a triphenylphosphine-triggered cascade reaction between dialkyl azodicarboxylate and 2-azidoacrylates, which furnished functionalized 1,2,4-triazolines. The major features of this procedure include: (1) mild conditions, (2) high yields (68–85%), (3) N_2 as the only by-product, (4) the use of catalytic amount of PPh_3, and (5) metal-free.

4. Experimental

4.1. General experimental

NMR spectra were recorded for ^{1}H NMR at 500 MHz and for ^{13}C NMR at 125 MHz. For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ=0) and data are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), and coupling constant in hertz. For ^{13}C NMR, TMS (δ=0) or $CDCl_3$ (δ=77.25) was used as internal standard and spectra were obtained with complete proton decoupling. Low-resolution MS and HRMS data were obtained using ESI ionization. Mp data were measured with micro melting point apparatus. IR spectra were recorded on an FTIR spectrometer (KBr).

4.2. General procedure for the synthesis of 1,2,4-triazolines 3

To a solution of PPh_3 (0.2 mmol) in the mixture solvent of anhydrous toluene/acetonitrile=1:1 (5 mL) was added dropwise a solution of **1** (1 mmol), and **2** (2.5 mmol) in the mixture solvent (5 mL) at 80 °C over 30 min. After the mixture was stirred for 10 h, the solvent was evaporated in vacuum and residual oil was purified by column chromatography on silica gel using hexane/EtOAc (4:1) as the eluent to give pure product **3**.

4.2.1. Triethyl 5-(4-methoxyphenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 1). Light yellow liquid; IR 1755, 1728, 1612, 1513, 1466, 1397, 1305, 1247, 1176, 1031, 831 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, J=8.7 Hz, 2H), 6.89 (d, J=8.7 Hz, 2H), 6.82 (s, 1H), 4.45–4.36 (m, 3H), 4.30–4.25 (m, 3H), 3.79 (s, 3H), 1.39 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 1.27 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.22, 158.63, 157.75, 152.05, 149.04, 128.71, 127.46, 114.34, 87.05, 64.31, 63.77, 63.40, 55.48, 14.54, 14.25, 14.08 ppm; MS (ESI) m/z 416 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{18}H_{23}N_3O_7$+Na): 416.1428; found: 416.1423.

4.2.2. Triethyl 5-phenyl-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 2). Light yellow liquid; IR 1755, 1732, 1645, 1467, 1374, 1321, 1199, 1097, 1056, 1011, 852 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.34 (m, 5H), 6.78 (s, 1H), 4.45–4.37 (m, 3H), 4.31–4.26 (m, 3H), 1.40 (t, J=7.2 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 1.27 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.65, 157.84, 152.01, 149.24, 136.59, 129.13, 129.05, 126.19, 87.37, 64.39, 63.90, 63.48, 14.60, 14.30, 14.13 ppm; MS (ESI) m/z 386 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{17}H_{21}N_3O_6$+Na): 386.1323; found: 386.1318.

4.2.3. Triethyl 5-p-tolyl-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 3). Yellow liquid; IR 1755, 1732, 1645, 1514, 1467, 1397, 1373, 1323, 1200, 1105, 1058, 858 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (t, J=7.4 Hz, 2H), 7.18 (d, J=8.0 Hz, 2H), 6.84(s, 1H), 4.45–4.36 (m, 3H), 4.30–4.25 (m, 3H), 2.34 (s, 3H), 1.39 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 1.28 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.68, 157.83, 152.07, 149.13, 139.01, 133.68, 129.70, 126.09, 87.32, 64.35, 63.83, 63.43, 21.40, 14.59, 14.30, 14.12 ppm; MS (ESI) m/z 400 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{18}H_{23}N_3O_6$+Na): 400.1479; found: 400.1479.

4.2.4. Triethyl 5-(4-bromophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 4). Light yellow liquid; IR 1755, 1732, 1645, 1488, 1467, 1373, 1246, 1201, 1104, 1057, 1011, 858 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, J=8.4 Hz, 2H), 7.30 (d, J=8.4 Hz, 2H), 6.82 (s, 1H), 4.45–4.37 (m, 3H), 4.31–4.26 (m, 3H), 1.40 (t, J=7.1 Hz, 3H), 1.35 (t, J=7.1 Hz, 3H), 1.28 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.53, 157.76, 151.82, 149.49, 135.77, 132.22, 127.97, 123.33, 86.72, 64.55, 64.08, 63.59, 14.60, 14.31, 14.15 ppm; MS (ESI) m/z 464 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{17}H_{20}BrN_3O_6$+Na): 464.0428; found: 464.0432.

4.2.5. Triethyl 5-(3-nitrophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 5). Light yellow liquid; IR 1755, 1643, 1535, 1468, 1374, 1322, 1203, 1095, 1059, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32(s, 1H), 8.22(q, J=9.5 Hz, 1H), 7.81 (d, J=7.8 Hz, 1H), 7.59 (t, J=8.0 Hz, 1H), 6.95 (s, 1H), 4.46–4.41 (m, 3H), 4.35–4.30 (m, 3H), 1.40 (t, J=7.1 Hz, 3H), 1.37 (t, J=7.1 Hz, 3H), 1.32 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.31, 157.64, 151.67, 149.95, 148.80, 138.94, 132.48, 130.20, 124.09, 121.36, 86.29, 64.81, 64.33, 63.73, 14.56, 14.27, 14.10 ppm; MS (ESI) m/z 431 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{17}H_{20}N_4O_8$+Na): 431.1173; found: 431.1181.

4.2.6. Triethyl 5-(biphenyl-4-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 6). Light yellow liquid; IR 1755, 1638, 1489, 1396, 1373, 1322, 1200, 1103, 1057, 1008, 857, 759 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61–7.56 (m, 4H), 7.49–7.42 (m, 4H), 7.36 (d, J=7.3 Hz, H), 6.92 (s, 1H), 4.46–4.38 (m, 3H), 4.33–4.27 (m, 3H), 1.41 (t, J=7.1 Hz, 3H), 1.36 (t, J=7.1 Hz, 3H), 1.29 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.68, 157.88, 152.05, 149.34, 142.18, 140.79, 135.59, 129.07, 127.85, 127.80, 127.40, 126.67, 87.28, 64.46, 63.97, 63.51, 14.63, 14.34, 14.16 ppm; MS (ESI) m/z 462 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{23}H_{25}N_3O_6$+Na): 462.1636; found: 462.1645.

4.2.7. Triethyl 5-(naphthalen-2-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 7). Light yellow liquid; IR 1755, 1643, 1466, 1373, 1319, 1198, 1097, 1057, 858, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88–7.82 (m, 4H), 7.54–7.48 (m, 4H), 7.05 (s, 1H), 4.46–4.40 (m, 3H), 4.34–4.27 (m, 3H), 1.40 (t, J=7.1 Hz, 3H), 1.36 (t, J=7.2 Hz, 3H), 1.28 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.66, 157.93, 152.03, 149.43, 133.93, 133.67, 133.33, 129.05, 128.55, 127.94, 126.83, 126.66, 125.25, 123.89, 87.49, 64.43, 63.99, 63.52, 14.62, 14.33, 14.14 ppm; MS (ESI) m/z 436 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{21}H_{23}N_3O_6$+Na): 436.1479; found: 436.1483.

4.2.8. Triethyl 5-(4-(benzyloxy)phenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 8). Light yellow liquid; IR 1755, 1643, 1611, 1511, 1466, 1373, 1321, 1242, 1106, 1012, 858, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.36 (m, 4H), 7.32 (t, J=8.4 Hz, 3H), 6.97 (d, J=7.3 Hz, 2H), 6.82 (s, 1H), 5.06 (s, 2H), 4.45–4.35 (m, 3H), 4.30–4.26 (m, 3H), 1.40 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 1.27 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.49, 158.69, 157.82, 152.10, 149.12, 136.99, 129.07, 128.84, 128.25, 127.64, 127.57, 115.35, 87.11, 70.27, 64.36, 63.83, 63.45, 14.60, 14.33, 14.14 ppm; MS (ESI) m/z 492 ([M+Na]$^+$); HRMS (ESI): m/z calcd for ($C_{24}H_{27}N_3O_7$+Na): 492.1741; found: 492.1766.

4.2.9. 1,2-Dibenzyl 3-ethyl 5-(4-methoxyphenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 9). Light yellow liquid; IR 1754, 1644, 1611, 1513, 1456, 1386, 1305, 1248, 1176, 1029, 829 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (t, J=7.8 Hz, 8H), 7.25–7.23 (m, 4H), 6.83 (t, J=8.4 Hz, 3H), 5.34 (d, J=12.3 Hz, 1H), 5.25 (q, J=7.7 Hz, 2H), 5.12(d, J=12.1 Hz, 1H), 4.22 (q, J=6.2 Hz, 2H), 3.78 (s, 3H), 1.27 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 160.29, 158.43, 157.69, 152.09, 149.04, 135.39, 134.48, 128.95, 128.85, 128.65, 128.51, 128.42, 128.12, 127.52, 114.42, 87.16, 69.80, 69.13, 63.45, 55.52, 13.96 ppm; MS (ESI) *m*/*z* 540 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{28}H_{27}N_3O_7$+Na): 540.1741; found: 540.1755.

4.2.10. 1,2-Dibenzyl 3-ethyl 5-(4-bromophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 10). White solid, mp 96–97 °C; IR 1759, 1635, 1455, 1396, 1336, 1242, 1155, 983, 871 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.45 (q, J=8.4 Hz, 2H), 7.35 (q, J=6.7 Hz, 8H), 7.25(t, J=10.9 Hz, 4H), 6.86 (s, 1H), 5.36 (d, J=12.3 Hz, 1H), 5.27 (t, J=12.5 Hz, 2H), 5.13(d, J=12.0 Hz, 1H), 4.24 (q, J=6.4 Hz, 2H), 1.26 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.25, 157.62, 151.84, 149.49, 135.39, 134.39, 135.23, 134.32, 132.22, 129.11, 128.91, 128.89, 128.77, 128.60, 128.18, 127.93, 123.37, 86.74, 69.99, 69.35, 63.58, 13.96 ppm; MS (ESI) *m*/*z* 588 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{27}H_{24}BrN_3O_6$+Na): 588.0741; found: 588.0738.

4.2.11. 1,2-Dibenzyl 3-ethyl 5-(biphenyl-4-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 11). Colorless liquid; IR 1754, 1643, 1489, 1456, 1386, 1323, 1195, 1054, 756, 697 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 54 (t, J=8.8 Hz, 4H), 7.46–7.40 (m, 4H), 7.37–7.24 (m, 11H), 6.94 (s, 1H), 5.36 (d, J=12.4 Hz, 1H), 5.27 (t, J=13.1 Hz, 2H), 5.13(d, J=12.1 Hz, 1H), 4.23 (q, J=6.8 Hz, 2H), 1.25 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.41, 157.73, 152.01, 149.23, 142.15, 140.73, 135.35, 135.19, 134.43, 129.06, 129.01, 128.88, 128.79, 128.71, 128.58, 128.18, 127.84, 127.81, 127.37, 126.64, 87.30, 69.92, 69.26, 63.52, 13.97 ppm; MS (ESI) *m*/*z* 586 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{33}H_{29}N_3O_6$+Na): 586.1949; found: 586.1936.

4.2.12. 1,2-Dibenzyl 3-ethyl 5-(naphthalen-2-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 12). Colorless liquid; IR 1755, 1645, 1498, 1456, 1385, 1318, 1195, 1055, 974, 860, 754 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.81 (q, J=5.2 Hz, 4H), 7.49–7.46 (m, 3H), 7.37–7.33 (m, 5H), 7.25–7.19 (m, 5H), 7.09 (s, 1H), 5.37 (d, J=12.4 Hz, 1H), 5.27 (q, J=5.7 Hz, 2H), 5.11(d, J=12.0 Hz, 1H), 4.23 (q, J=6.8 Hz, 2H), 1.25 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.40, 157.73, 151.97, 149.35, 135.32, 134.39, 133.65, 133.58, 133.26, 129.06, 128.84, 128.76, 128.70, 128.62, 128.43, 128.17, 127.89, 126.85, 126.61, 125.29, 123.81, 87.51, 69.87, 69.27, 63.51, 13.95 ppm; MS (ESI) *m*/*z* 560 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{31}H_{27}N_3O_6$+Na): 560.1792; found: 560.1766.

4.2.13. 3-Ethyl 1,2-diisopropyl 5-(4-bromophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 13). Yellow liquid; IR 1756, 1642, 1488, 1467, 1375, 1314, 1182, 1102, 1011, 912, 810 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.50 (d, J=8.4 Hz, 2H), 7.29 (d, J=8.4 Hz, 2H), 6.79 (s, 1H), 5.10–5.01 (m, 2H), 4.42 (q, J=8.5 Hz, 2H), 1.40 (t, J=7.1 Hz, 3H), 1.33 (t, J=7.1 Hz, 6H), 1.27 (q, J=5.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.63, 157.30, 151.45, 149.68, 135.92, 132.16, 127.93, 123.24, 86.54, 73.03, 72.27, 63.51, 22.13, 21.87, 14.13 ppm; MS (ESI) *m*/*z* 492 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{19}H_{24}N_3O_6$+Na): 492.0741; found: 492.0762.

4.2.14. 3-Ethyl 1,2-diisopropyl 5-(3-nitrophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 14). Colorless liquid; IR 1755, 1642, 1536, 1468, 1352, 1312, 1184, 1102, 1056, 736 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.30 (s, 1H), 8.21(d, J=9.6 Hz, 1H), 7.80 (d, J=7.8 Hz, 1H),7.58 (t, J=8.0 Hz, 1H), 6.91 (s, 1H), 5.14–5.04 (m, 2H), 4.40 (q, J=8.5 Hz, 2H), 1.41 (t, J=7.2 Hz, 3H), 1.36 (q, J=5.5 Hz, 6H), 1.32 (t, J=6.8 Hz, 6H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.45, 157.25, 151.28, 150.11, 148.83, 139.15, 132.53, 130.17, 124.07, 121.30, 86.20, 73.43, 72.66, 63.67, 22.13, 21.87, 14.12 ppm; MS (ESI) *m*/*z* 459 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{19}H_{24}N_4O_8$+Na): 459.1486; found: 459.1482.

4.2.15. 3-Ethyl 1,2-diisopropyl 5-(biphenyl-4-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 15). Yellow liquid; IR 1755, 1642, 1488, 1467, 1374, 1313, 1183, 1102, 1052, 1008, 760 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.60–7.56 (m, 4H), 7.48 (d, J=8.2 Hz, 2H), 7.43 (t, J=7.6 Hz, 2H), 7.35 (d, J=7.4 Hz, 1H), 6.90 (s, 1H), 5.12–5.03 (m, 2H), 4.43 (q, J=6.4 Hz, 2H), 1.41 (t, J=7.1 Hz, 3H), 1.35 (t, J=6.8 Hz, 6H), 1.27 (q, J=6.0 Hz, 6H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.74, 157.37, 151.64, 149.49, 142.04, 140.74, 135.70, 129.01, 127.75, 127.35, 126.59, 87.04, 72.87, 72.07, 63.42, 22.13, 21.86, 14.12 ppm; MS (ESI) *m*/*z* 490 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{25}H_{29}N_3O_6$+Na): 490.1949; found: 490.1949.

4.2.16. 1,2-Di-tert-butyl 3-ethyl 5-(4-methoxyphenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 16). Colorless liquid; IR 1755, 1639, 1612, 1514, 1459, 1395, 1332, 1250, 1153, 1032, 962, 832 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.28 (t, J=7.0 Hz, 2H), 6.89 (d, J=8.7 Hz, 2H), 6.71 (s, 1H), 4.40 (q, J=3.8 Hz, 2H), 1.53 (s, 9H), 1.47 (s, 9H), 1.40 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.97, 157.45, 150.42, 149.75, 134.47, 133.65, 133.41, 128.96, 128.50, 127.94, 126.69, 126.57, 125.21, 123.98, 87.03, 85.12, 83.72, 63.28, 28.34, 28.10, 14.15 ppm; MS (ESI) *m*/*z* 472 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{22}H_{31}N_3O_7$+Na): 472.2054; found: 472.2040.

4.2.17. 1,2-Di-tert-butyl 3-ethyl 5-(3-nitrophenyl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 17). White solid, mp 104–105 °C; IR 1756, 1631, 1536, 1369, 1351, 1311, 1247, 1153, 843, 700 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.30 (s, 1H), 8.21(d, J=7.1 Hz, 1H), 7.80 (d, J=7.7 Hz, 1H), 7.58 (t, J=7.9 Hz, 1H), 6.84 (s, 1H), 4.42 (q, J=3.8 Hz, 2H), 1.56 (s, 9H), 1.52 (s, 9H), 1.40 (t, J=7.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.67, 156.18, 150.30, 150.02, 148.86, 139.51, 132.61, 130.16, 123.99, 121.30, 85.86, 85.81, 84.37, 63.51, 28.31, 28.05, 14.13 ppm; MS (ESI) *m*/*z* 487 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{21}H_{28}N_4O_8$+Na): 487.1800; found: 487.1799.

4.2.18. 1,2-Di-tert-butyl 3-ethyl 5-(naphthalen-2-yl)-5H-1,2,4-triazole-1,2,3-tricarboxylate (Table 2, entry 18). Colorless liquid; IR 1755, 1639, 1477, 1371, 1334, 1256, 1152, 1059, 849, 754 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.88–7.84 (m, 4H), 7.53–7.49 (m, 3H), 6.95 (s, 1H), 4.17 (q, J=8.0 Hz, 2H), 1.56 (s, 9H), 1.49 (s, 9H), 1.40 (t, J=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ 160.18, 159.02, 156.37, 150.44, 149.47, 129.40, 127.52, 114.35, 86.61, 85.02, 83.52, 63.21, 55.53, 28.31, 28.07, 14.15 ppm; MS (ESI) *m*/*z* 492 ([M+Na]$^+$); HRMS (ESI): *m*/*z* calcd for ($C_{25}H_{31}N_3O_6$+Na): 492.2105; found: 492.2101.

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Supplementary data

Supplementary data related to this article can be found online version, at doi:10.1016/j.tet.2010.11.043.

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12. CCDC 784753 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.