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2,3,7-Triazabicyclo[3.3.0]octenes Prepared by Tandem Cascade Reaction of Allyl Azides and Olefinic Dipolarophiles

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Tandem cascade reactions of allyl azides and olefinic dipolarophiles to give cis-fused 2,3,7-triazabicyclo[3.3.0]octenes (**5**, **6** or **7**) are reported. Therein, an intermolecular dipolar cycloaddition of azide and alkene gave a triazoline which was followed by isomerization of the triazoline to a diazo ester (**4**) and then an intramolecular dipolar cycloaddition from the diazo functional group and the double bond in **4** to give **5**. Compound **5** may furthermore undergo a Michael addition to give 7-substituted-2,3,7-triazabicyclo[3.3.0]oct-2-ene (**6**) or a tautomerization to give 2,3,7-triazabicyclo[3.3.0]oct-3-ene (**7**). The reaction may be manipulated to stop at a particular stage by adopting a suitable solvent or an appropriate temperature.

INTRODUCTION

Tandem cascade reactions, also known as domino reactions, are efficient processes to prepare organic compounds. Many syntheses based on this consideration have been developed.[1-6]

The reaction of acrylate with alkyl or aryl azide was found to be a tandem cascade reaction.[7] Therein, a sequence of intermolecular dipolar cycloaddition, isomerization and another intermolecular dipolar cycloaddition gave a Δ^2-pyrazoline. Replacing alkyl azide with allyl azide, we have found that 2,3,7-triazabicyclo[3.3.0]oct-2-enes (**5** and **6**) were obtained by a different tandem cascade reaction sequence; intermolecular dipolar cycloaddition, isomerization, followed by an intramolecular dipolar cycloaddition. This paper describes the full details of our investigation on this tandem cascade reaction and the possibilities to prepare more derivatives of **5** and **6**. Some of these results have been reported as a preliminary communication.[8]

RESULTS AND DISCUSSION

A mixture of one equivalent of allyl azide (**1a**) and 2 equivalents of methyl acrylate (**2u**) dissolved in THF at room temperature was stirred for two days to give a 7-substituted-2,3,7-triazabicyclo[3.3.0]oct-2-ene (**6au**) as the sole product in an isolated yield of 84%. This is a very efficient one pot reaction to prepare a compound having a skeleton like **6** from simple reactants.

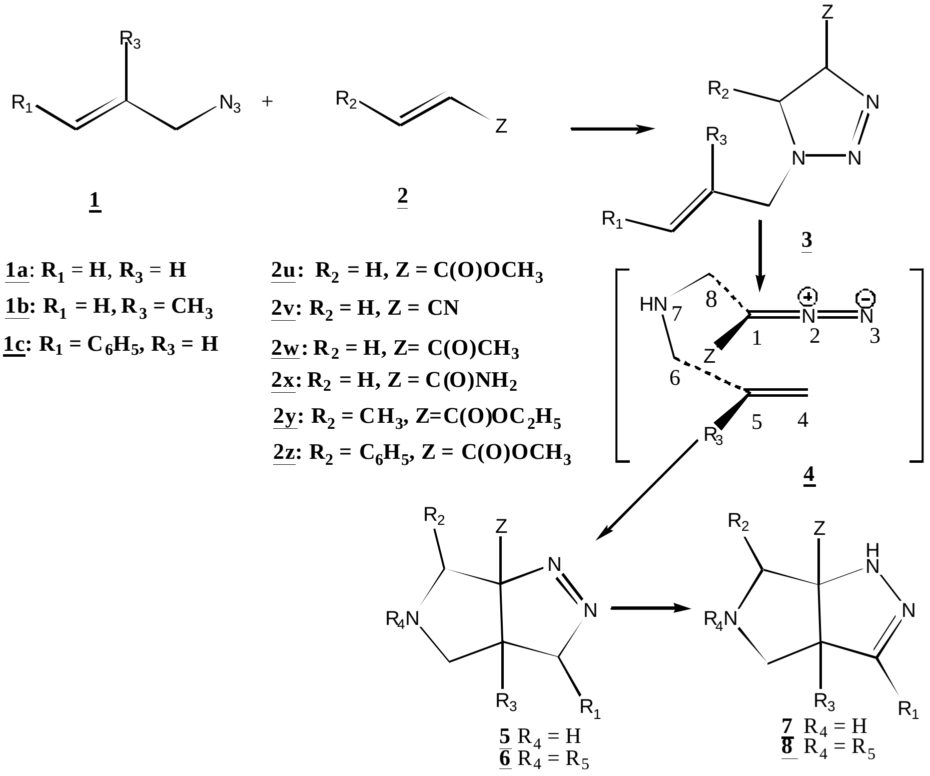
For the purpose of studying the generality of the reaction, more experiments were carried out with various olefinic dipolarophiles, several substituted allyl azides and different solvents. The product obtained could be **3**, a Δ^2-triazoline (entries 1 and 5), **5**, an 7-unsubstituted 2,3,7-triazabicyclo[3.3.0]oct-2-ene (for example, entries 2, 6 and 11), **6**, a 7-substituted-2,3,7-triazabicyclo[3.3.0]oct-2-ene (for example, entries 4 and 7) or a 7-unsubstituted 2,3,7-triazabicyclo[3.3.0]oct-3-ene (**7**), a tautomer of **5** (entry 12). The results are given in Table 1.

All these results could be accounted for by Scheme I. Therein, an intermolecular dipolar cycloaddition of allyl azide and acrylate gave a Δ^2-triazoline (**3**). **3** underwent an isomerization to give a diazo ester (**4**)[9] which subsequently gave **5** by an intramolecular dipolar cycloaddition.[10] In addi-

Table 1. Reaction of Allyl Azides and Olefinic Dipolarophiles

Entry	Reactants	Solvent	Product (yield)
1	**1a** + **2u**	$CHCl_3$ (7 h)	**3au** (53)
2		$CHCl_3$ (4 days)	**5au** (70)
3		DMSO/n-hexane	**5au** (75)
4		THF	**6au** (84)
5	**1a** + **2v**	$CHCl_3$	**3av** (85)
6		THF	**5av** (91)
7		DMSO	**6av** (88)
8	**1a** + **2w**	$CHCl_3$	**6aw** (81)
9		THF	**6aw** (87)
10	**1a** + **2x**	THF	**6ax** (66)
11	**1b** + **2v**	THF	**5bv** (40)
12	**1c** + **2u**	THF	**7cu** (82)
13	**1d** + **2u**	THF	**6du** (51)

Scheme I



1a: $R_1 = H, R_3 = H$
1b: $R_1 = H, R_3 = CH_3$
1c: $R_1 = C_6H_5, R_3 = H$

2u: $R_2 = H, Z = C(O)OCH_3$
2v: $R_2 = H, Z = CN$
2w: $R_2 = H, Z = C(O)CH_3$
2x: $R_2 = H, Z = C(O)NH_2$
2y: $R_2 = CH_3, Z = C(O)OC_2H_5$
2z: $R_2 = C_6H_5, Z = C(O)OCH_3$

**R_1,R_3,R_4 subsituents are omitted in 4 for clarity

tion, Michael addition of acrylate to **5** would give **6**. **5** may give **7** by tautomerization of N=N-CH to NH-N=C.

In an appropriate condition, some of these intermediates could be isolated and the reaction could be controlled to be stepwise. For instance, in chloroform, the reaction of allyl azide and acrylonitrile stopped at the Δ^2-triazoline (**3**) stage to give **3av**. Isolated **3av** in a more polar solvent or at a higher temperature was converted to **5av**. Similarly, isolated **5av**, in an even more polar solvent, DMSO, and the presence of more acrylonitrile underwent Michael addition to give **6av**.

At a higher temperature or in the presence of acid or base, compound **5** could be converted to its tautomer **7**. For instance, **5au** and **5av** were tautomerized to **7au** and **7av**, respectively, in the presence of acid or base.

The assignment of the structures of **3**, **5**, **6** and **7** were based on NMR spectra. To further substantiate these assignments and to study the stereochemistry of the reaction, a single crystal X-ray diffraction study on compound **7av** was carried out. The result confirms our assignment of the structure of **7av** (Fig. 1) and supports our assignment of structures of **5**, **6** and **7**. In addition, it is known that **7av** is cis-fused 2,3,7-triazabicyclo[3.3.0]oct-3-ene. Since tautomerization of **5av** to **7av** involving only N_2, N_3 and C_4, no change in configurations of ring fusion carbons, C_1 and C_5, was supposed to occur, therefore compounds **5** and **6** should be cis-fused 2,3,7-triazabicyclo[3.3.0]oct-2-enes. Husigen[11] pointed out

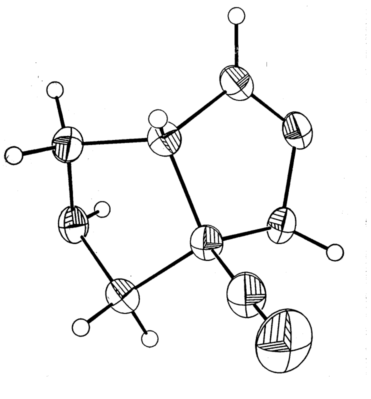
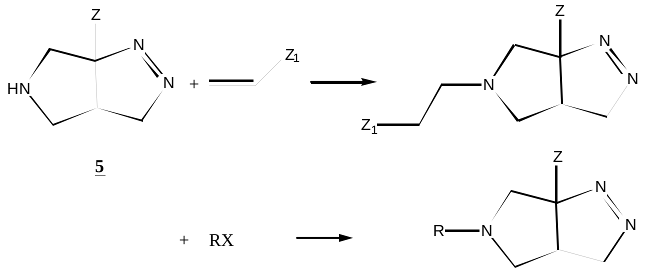


Fig. 1. ORTEP of **7av**.

that there was an orientation complex preceding the transition state for dipolar cycloaddition. In order to fulfill this requirement intramolecularly, C_6-N_7-C_8 linkage must be in one side of the plane formed by C_1, N_3, C_4 and C_5 (**4** in Scheme I), therefore both Z and R_3 must be in the other side. Consequently, the reaction gives a cis-fused bicyclo[3.3.0]oct-2-ene as the product in this intramolecular cycloaddition step.

Since **5au** and **5av**, 2,3,7-triazabicyclo[3.3.0]oct-2-enes without substituent at 7-position are available, it is possible to prepare the corresponding 7-substituted 2,3,7-triazabicyclo[3.3.0]oct-2-enes (**6**) by Michael addition or nucleophilic substitution (Scheme II). Several 7-unsubstituted or 7-substituted 2,3,7-triaza-bicyclo[3.3.0]oct-3-enes (**7**) were also prepared by tautomerization of **5** and **6**. The results are given in Table 2. The yields of these reactions are generally good to excellent.

Scheme II



In conclusion, allyl azides and olefinic dipolarophiles undergo a tandem cascade reaction to give cis-fused 2,3,7-triazabicyclo[3.3.0]octenes in good yields. The reaction can be stopped at different stages by selecting a suitable solvent.

Table 2. Preparations of Derivatives

Product	Z	R	procedure	yield
6au-1	$COOCH_3$	$CH_2CH_2COCH_3$	M*	93
6au-2	$COOCH_3$	$CH_2CH_2COCH_2CH_3$	M	85
6au-3	$COOCH_3$	$CH_2CH_2CH_2CH_3$	S*	88
6au-4	$COOCH_3$	$C_6H_5CH_2$	S	71
6av-1	CN	$CH_2CH_2CH_3$	S	74
6av-2	CN	$CH_2CH{=}CH_2$	S	77
6av-3	CN	propagyl	S	61
7au	$COOCH_3$	$CH_2CH_2CO_2CH_3$	I*	90
7au-1	$COOCH_3$	$CH_2CH_2COCH_3$	I	85
7au-2	$COOCH_3$	$C_6H_5CH_2$	I	87
7av	CN	H	I	81

* M: Michael addition, S: substitution, I: isomerization.

By Michael addition, nucleophilic substitution or tautomerization, many 2,3,7-triazabicyclo[3.3.0]octene derivatives can be prepared.

EXPERIMENTAL SECTION

Reagents and General Procedure

Melting points were determined on a Yanagimoto micromelting point apparatus and are reported uncorrected. The ^1H, ^{13}C and 2D NMR spectra were obtained by an Ace-300 MHz FT-NMR spectrometer. The mass spectra were obtained on a JEOL JMS-SX/SX 102A spectrometer operating at 12 eV. The elemental compositions of compounds were determined by a JOEL JMS-SX/Sx 102A high resolution mass spectrometer. Infrared spectra were obtained on a BIORAD-FTS FT-IR spectrometer.

Allyl azides [12] (**1a**) were prepared by the following procedure; to 1 equivalent of allyl bromide dissolved in a mixture of DMSO and water, 1.2 equivalents of sodium azide were added. After stirring for 3 hours, 50 mL saturated brine was added to the mixture. The organic layer after drying with magnesium sulfate was separated and the solvent was evaporated to obtain allyl azide.

2-Methyl-2-propenyl azide (**1b**) was obtained in a yield of 75%. ^1H NMR ($CDCl_3$) 1.76 (s, 3H), 3.76 (s, 2H), 4.95 (s, 2H). ^{13}C NMR ($CDCl_3$): 20.1 (CH_3), 57.1 (CH_2), 114.1 (CH_2), 139.5 (C), IR: λ_{max} (cm^{-1}) 2100.

E-3-Phenyl-2-propenyl azide (**1c**) was obtained in a yield of 83%. ^1H NMR ($CDCl_3$) 3.82 (d, 2H, $J = 6.6$ Hz), 6.14 (td, 1H, $J = 15.8$, 6.6 Hz), 6.55 (d, 1H, $J = 15.8$ Hz), 7.1-7.4 (m, 5H). ^{13}C NMR ($CDCl_3$): 48.1 (CH_2), 127.1 (CH), 128.1 (CH), 128.5 (CH), 129.1 (CH), 132.3 (CH), 144.1 (C), IR: λ_{max} (cm^{-1}) 2120.

E-2-Butenyl azide (**1d**) was obtained in a yield of 70%. ^1H NMR ($CDCl_3$) 1.71 (d, 3H, $J = 6.2$ Hz), 3.65 (d, 2H, $J = 6.4$ Hz), 5.2-5.6 (m, 1H), 5.7-5.8 (m, 1H). ^{13}C NMR ($CDCl_3$): 18.1 (CH_3), 54.1 (CH_2), 122.1 (CH), 124.5 (CH), IR: λ_{max} (cm^{-1}) 2110.

Procedure A: General procedure for the reaction of allyl azide and alkene carrying electron-withdrawing group

To allyl azide (50 mmol) in 40 mL solvent, olefinic dipolarophile (51 mmol or 102 mmol) dissolved in 10 mL solvent was added dropwise at room temperature. The mixture was stirred for several hours or a few days. The solvent and the unreacted starting materials were removed by rotatory evaporator to give the crude product. The product could be further purified by column chromatography.

1-Allyl-4-methoxycarbonyl-Δ^2-1,2,3-triazaoline (3au)

Following procedure A using chloroform as the solvent, the reaction of allyl azide and methyl acrylate at 0 °C gave **3au** in a reaction time of 7 hours. **3au** is a yellow oil (53%). ^{1}H NMR ($CDCl_3$) 3.23 (d, 2H, J = 12 Hz), 3.72 (s, 3H), 4.07, 4.21 (d of AB, 2H, J = 21.0, 15.0, 6.4 Hz), 4.87 (t, 1H, J = 12 Hz), 5.1-5.3 (m, 2H), 5.6-5.9 (m, 1H). ^{13}C NMR ($CDCl_3$): 46.8 (CH), 52.9 (CH_3), 53.1 (CH_2), 78.2 (CH_2), 119.3 (CH_2), 132.2 (CH), 168.9 (CO); CIMS *m/z* (%) 170 (M+1, 20), 142 (20), 110 (4), 55 (100).

1-Allyl-4-cyano-Δ^2-1,2,3-triazaoline (3av)

The reaction of allyl azide and acrylonitrile using chloroform as the solvent gave **3av** in 2 days. **3av** was obtained as a yellow oil in a yield of 85%. ^{1}H NMR ($CDCl_3$): 3.9-4.15 (m, 2H), 4.2-4.4 (m, 1H), 4.5-4.7 (m, 2H), 5.2-5.4 (m, 2H), 5.7-6.0 (m, 1H). ^{13}C NMR ($CDCl_3$): 45.8 (CH), 52.0 (CH_2), 70.1 (CH_2), 118.5 (CN), 120.2 (CH_2), 131.2 (CH); EIMS *m/z* (%) 136 (M, 12), 108 (32).

1-Methoxycarbonyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (5au)

5au (in a yield of 70%) was prepared from the reaction of allyl azide and methyl acrylate in 4 days by procedure A using chloroform as the solvent. In addition, a mixed solvent of dimethyl sulfoxide (DMSO) and n-hexane (1:1) also give **5au** in a yield of 75%. **5au** is a yellow oil. ^{1}H NMR ($CDCl_3$): 2.67-2.76 (m, 2H), 3.01 (dd, 1H, J = 12.2, 7.1 Hz), 3.31, 3.58 (AB, 2H, J = 12.7 Hz), 3.75 (s, 3H), 4.44, 4.69 (AB part of ABX, 2H, J_{AB} = 18.6 Hz, J_{AX} = 8.7 Hz, J_{BX} = 3.0 Hz). ^{13}C NMR ($CDCl_3$): 40.5 (CH), 52.8 (CH_3), 54.9 (CH_2), 55.7 (CH_2), 85.4 (CH_2), 108.1 (C), 169.6 (CO); CIMS *m/z* (%) 170 (M+1, 28), 141 (2), 110 (11), 82 (100). HRMS: Calcd for $C_7H_{11}N_3O_2$: 169.0849, Found: 169.0860.

1-Cyano-2,3,7-triazabicyclo[3.3.0]oct-2-ene (5av)

Using THF as the solvent, **5av** was prepared in a yield of 91% following procedure A in 14 days. **5av** is a yellow oil. ^{1}H NMR ($CDCl_3$): 2.85-2.95 (m, 2H), 3.07 (m, X part of ABX, 1H), 3.27, 3.78 (AB, 2H, J = 12.0 Hz), 4.59, 4.91 (AB part of ABX, 2H, J_{AB} = 19 Hz, J_{AX} = 9.0 Hz, J_{BX} = 2.8 Hz), ^{13}C NMR ($CDCl_3$): 41.8 (CH), 55.4 (CH_2), 56.9 (CH_2), 86.8 (CH_2), 94.1 (C), 116.7 (CN); EIMS *m/z* (%) 136 (M, 1), 107 (64), 93 (100), 80 (42). HRMS: Calcd. for $C_6H_8N_4$: 136.0748, Found: 136.0750.

7-(2-Methoxycarbonylethyl)-1-Methoxycarbonyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6au)

6au was prepared in a yield of 84% by the reaction of allyl azide and methyl acrylate (molar ratio = 1:2) following procedure A using THF as the solvent. **6au** is a yellow oil. ^{1}H NMR ($CDCl_3$): 2.38 (dd, 1H, J = 9.5, 6.5 Hz), 2.39 (t, 2H, J = 7.5 Hz), 2.66 (t, 2H, J = 7.5 Hz), 2.63-2.70 (m, 2H), 2.73, 3.43 (AX, 2H, J = 10.0 Hz), 3.60 (s, 3H), 3.75 (s, 3H), 4.45, 4.75 (AB part of ABX, 2H, J_{AB} = 18.5 Hz, J_{AX} = 9.0 Hz, J_{BX} = 3.5 Hz). ^{13}C NMR ($CDCl_3$): 33.2 (CH_2), 37.8 (CH), 49.1 (CH_2), 51.3 (CH_3), 52.6 (CH_3), 58.7 (CH_2), 60.0 (CH_2), 85.9 (CH_2), 104.9 (C), 169.0 (CO), 172.2 (CO); EIMS *m/z* (%) 255 (M, 15), 227 (10), 196 (12), 168 (21), 154 (100). HRMS: Calcd. for $C_{11}H_{17}N_3O_4$: 255.1215, Found: 255.1214.

7-(2-Cyanoethyl)-1-Cyano-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6av)

The reaction of allyl azide and acrylonitrile (molar ratio = 1:2) using DMSO as the solvent gave **6av** in a yield of 88% yield in 2 days. **6av** is a yellow oil. ^{1}H NMR ($CDCl_3$): 2.42 (t, 2H, J = 6.6 Hz), 2.56 (dd, 1H, J = 10.0, 6.0 Hz), 2.64-2.80 (m, 2H), 2.76 (d, 1H, J = 10.4 Hz), 2.81 (d, 1H, J = 10.0 Hz), 2.8-2.9 (m, 1H), 3.62 (d, 1H, J = 10.4 Hz), 4.59 (dd, 1H, J = 19.0, J = 3.6 Hz), 4.91 (dd, 1H, J = 19.0 Hz, J = 9.0 Hz). ^{13}C NMR ($CDCl_3$): 17.0 (CH_2), 39.6 (CH), 48.2 (CH_2), 59.4 (CH_2), 60.3 (CH_2), 87.3 (CH_2), 90.9 (C), 116.4 (CN), 117.9 (CN).

7-(3-Oxo-n-butyl)-1-acetyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6aw)

The reaction of allyl azide and methyl vinyl ketone (molar ratio = 1:2) using chloroform or THF as the solvent following procedure A gave **6aw** in a yield of 81% and 87%, respectively, in 2 days. **6aw** is a yellow oil. ^{1}H NMR ($CDCl_3$): 2.03 (s, 3H), 2.28 (dd, 1H, J = 9.6, 6.0 Hz), 2.31 (s, 3H), 2.41 (d, 1H, J = 10 Hz), 2.43-2.47 (m, 2H), 2.58 (t, 2H, J = 6.8 HZ), 2.62 (d, 1H, J = 9.6 Hz), 2.66 (m, 1H), 3.40 (d, 1H, J = 10.0 Hz), 4.34, 4.66 (AB part of ABX, 2H, J_{AB} = 18.6. Hz, J_{AX} = 9.4 Hz, J_{BX} = 3.8 Hz). ^{13}C NMR ($CDCl_3$): 28.3 (CH_3), 29.8 (CH_3), 35.4 (CH), 42.3 (CH_2), 48.3 (CH_2), 59.6 (CH_2), 60.6 (CH_2), 85.6 (CH_2), 112.5 (C), 202.4 (C=O), 207.2 (C=O); EIMS *m/z* (%) 223 (M, 17), 195 (54), 180 (56), 152 (42), 138

(62).

1-Aminocarbonyl-7-(2-aminocarbonylethyl)-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6ax)

The reaction of allyl azide and acrylamide (molar ratio = 1:2) in THF gave **6ax** in a yield of 66% in 2 days following procedure A. **6ax** is a white solid, mp.: 172-174 °C. ^{1}H NMR (CDCl$_3$): 1.84 (t, 2H, J = 6.8 Hz), 1.99 (dd, 1H, J = 8.8, 6.4 Hz), 2.19 (dd, 1H, J = 8.8, 5.2 Hz), 2.22 (t, 2H, J = 6.8 Hz), 2.30-2.37 (m, 1H), 2.35 (d, 1H, J = 10.0 Hz), 3.07 (d, 1H, J = 10.0 Hz), 3.94 (dd, 1H, J = 18.8, 3.6 Hz), 4.32 (dd, 1H, J = 18.8, 9.6 Hz), 5.87 (s, 1H), 6.57 (s, 1H), 6.76 (s, 2H). ^{13}C NMR (CDCl$_3$): 34.6 (CH$_2$), 36.8 (CH), 50.2 (CH$_2$), 60.4 (CH$_2$), 60.7 (CH$_2$), 85.5 (CH$_2$), 106.3 (C), 170.1 (C=O), 173.3 (C=O); EIMS *m/z* (%) 197 (M-28, 30), 182 (9), 114 (100).

1-Methoxycarbonyl-4-phenyl-2,3,7-triazabicyclo[3.3.0]oct-3-ene (7cu)

7cu was prepared by the reaction of *E*-3-phenylallyl azide and methyl acrylate following procedure A in a yield of 82%. **7cu** is a white solid, mp. 180-182 °C; ^{1}H NMR (CDCl$_3$): 3.17 (d, 1H, J = 12.0 Hz), 3.2-3.40 (m, 2H), 3.31 (d, 1H, J = 12.0 Hz), 3.80 (s, 3H), 4.8 (dd, 1H, J = 5.4, 3.4 Hz), 6.54 (b, 1H), 7.30-7.37 (m, 3H), 7.56-7.61 (m, 2H). ^{13}C NMR (CDCl$_3$): 52.9 (CH$_3$), 54.3 (CH$_2$), 58.2 (CH$_2$), 61.1 (CH$_2$), 81.1 (C), 126.1 (CH), 128.1 (CH), 129.0 (CH), 131.2 (C), 153.2 (C), 173.9 (C=O). EIMS *m/z* (%) 245 (M, 8), 203 (74), 186 (5), 171 (100). HRMS: Calcd. for $C_{13}H_{15}N_3O_2$: 245.1161, Found: 245.1160.

1-Methoxycarbonyl-7-(2-methoxycarbonylethyl)-4-methyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6du)

6du was prepared by the reaction of 2-butenyl azide and methyl acrylate following procedure A in a yield of 51%. **6du** is a yellow liquid; ^{1}H NMR (CDCl$_3$): 1.34 (d, 3H, J = 7.2 Hz), 2.27 (dd, 1H, J = 6.3, 3.3 Hz), 2.39 (dd, 1H, J = 9.0, 6.6 Hz), 2.42 (t, 2H, J = 6.9 Hz), 2.69 (t, 2H, J = 6.9 Hz), 2.70 (d, 1H, J = 10.2 Hz), 2.77 (d, 1H, J = 9.0 Hz), 3.47 (d, 1H, J = 10.2 Hz), 3.64 (s, 3H), 3.78 (s, 3H), 4.60 (dq, 1H, J = 7.2, 3.9 Hz). ^{13}C NMR (CDCl$_3$): 18.7 (CH$_3$), 33.4 (CH$_2$), 45.4 (CH$_2$), 49.3 (CH$_2$), 51.6 (CH$_3$), 52.9 (CH$_3$), 58.8 (CH), 59.7 (CH$_2$), 94.4 (CH), 105.0 (C), 169.4 (C=O), 172.4 (C=O). MS (EIMS) *m/z* (%) 269 (M, 3), 241 (8), 226 (29), 168 (100). HRMS: Calcd. for $C_{12}H_{19}N_3O_4$: 269.1371, Found: 269.1374.

1-Cyano-5-methyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (5bv)

5bv was prepared in a yield of 40% by the reaction of 2-methyl-2-propenyl azide and acrylotrile following procedure A using THF as the solvent. **5bv** is a yellow solid, mp. 108-109 °C. ^{1}H NMR (CDCl$_3$): 1.37 (s, 3H), 2.70 (d, 1H, J = 11.8 Hz), 3.00 (d, 1H, J = 11.8 Hz), 3.25 (d, 1H, J = 12.4 Hz), 3.75 (d, 1H, J = 12.4 Hz), 4.51, 4.68 (AB, 2H, J = 19.0 Hz). ^{13}C NMR (CDCl$_3$): 20.5 (CH$_3$), 47.7 (C), 57.3 (CH$_2$), 62.3 (CH$_2$), 92.9 (CH$_2$), 97.8 (C), 115.1 (CN). EIMS *m/z* (%) 15 (M, 1), 121 (31), 93 (100).

1-Cyano-2,3,7-triazabicyclo[3.3.0]oct-3-ene (7av)

5av dissolved in THF is heated to 50 °C for 4 hours; after evaporation of the solvent, **7av** was obtained quantitatively. **7av** is a white solid, m.p. 120-121 °C. ^{1}H NMR (CDCl$_3$): 2.08 (s, 1H), 3.04 (d, 1H, J = 12.5 Hz), 3.09 (dd, 1H, J = 12.6, 7.6 Hz), 3.23 (dd, 1H, J = 12.6, 2.0 Hz), 3.42 (d, 1H, J = 12.5 Hz), 3.99 (ddd, 1H, J = 7.6, 2.2, 2.0 HZ), 6.14 (s, 1H), 6.66 (d, 1H, J = 2.2 Hz), ^{13}C NMR (CDCl$_3$): 53.1 (CH$_2$), 61.2 (CH$_2$), 62.0 (CH), 65.4 (C), 119.5 (C), 144.0 (CH); EIMS *m/z* (%) 137 (M+1, 17), 93 (80). HRMS: Calcd. for $C_6H_8N_4$: 136.0748, Found: 136.0757.

Crystal data for **7av**: Colorless single crystal, 0.3 × 0.3 × 0.4 mm, rhombohedral, space group $P3_221$, unit cell dimensions: a = 6.0988(5) Å, c = 31.485(4) Å; V = 1014.2(3) Å^3; d_{calcd} = 1.338 g/cm^3 (Z 6); radiation Mo-Kα; limits(max) 23.3°, total reflection scanned 3907, 976 unique reflections, 968 observed reflections with $F > 2\sigma(F)$; R = 0.045; R_w = 0.052; 123 refined parameters. List of positional and anisotropic thermal parameters of non-hydrogen atoms, positional and thermal parameters of hydrogen atoms, bond distances and bond angles are available upon request.

Procedure B: General procedure for the Michael addition of 5 to alkenes

To a solution of one equivalent of **5** dissolved in THF, one equivalent of alkene is added slowly. The solution is stirred for one day. The crude is obtained after the solvent is rotatory evaporated. A yellow oil is obtained by column chromatography using silica gel as the packing material and the mixed solvent of ethyl acetate and n-hexane (3:1) as the eluent.

7-(3-Oxo-n-butyl)-1-Methoxycarbonyl-2,3,7-triazabicyclo-[3.3.0]oct-2-ene (6au-1)

6au-1 was prepared in a yield of 93% by the reaction of **5au** and methyl vinyl ketone following procedure B. **6au-1** is a yellow liquid, ^{1}H NMR (CDCl$_3$): 2.01 (s, 3H), 2.32, 2.64 (AM part of AMX, 2H, J_{AM} = 9.2 Hz, J_{AX} =6.5 Hz, J_{MX} = 0 Hz), 2.45 (t, 2H, J = 6.3 Hz), 2.58 (t, 2H, J = 6.3 Hz), 2.57 (d, 1H, J = 10.4 Hz), 2.67 (m, 1H), 3.35 (d, 1H, J = 10,4 Hz), 3.68 (s, 3H), 4.39, 4.65 (AB part of ABX, 2H, J_{AB} = 18.4 Hz, J_{AX} = 9.1 Hz, J_{BX} = 3.5 Hz). ^{13}C NMR ($CDCl_3$): 29.8 (CH_3), 37.9 (CH), 42.2 (CH_2), 48.4 (CH_2), 52.7 (CH_3), 59.0 (CH_2), 60.4 (CH_2), 86.0 (CH_2), 104.8 (C), 170.0 (CO), 207.1 (CO); CIMS *m/z* (%) 240 (M+1, 100), 239 (63), 212 (22). HRMS: Calcd. for $C_{11}H_{17}N_3O_3$: 239.1266, Found: 239.1270.

7-(2-Ethoxycarbonylethyl)-1-Methoxycarbonyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6au-2)

6au-2 was prepared in a yield of 83% by the reaction of **5au** and ethyl acrylate following procedure B. **6au-2** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 1.14 (t, 3H, J = 7.1 Hz), 2.33 (t, 2H, J = 7.1 Hz), 2.35, 2.67 (AM part of AMX, 2H, J_{AM} = 9.4 Hz, J_{AX} = 6.2 Hz, J_{MX} = 0 Hz), 2.62 (t, 2H, J = 7.1 Hz), 2.63 (d, 1H, J = 10.3 Hz), 2.68 (m, 1H), 3.42 (d, 1H, J = 10.3 Hz), 3.73 (s, 3H), 4.04 (q, 2H, J = 7.1 Hz), 4.40, 4.74 (AB part of ABX, 2H, J_{AB} = 18.3 Hz, J_{AX} = 9.1 Hz, J_{BX} = 3.5 Hz). ^{13}C NMR ($CDCl_3$): 14.1 (CH_3), 33.6 (CH_2), 38.0 (CH), 49.4 (CH_2), 52.8 (CH_3), 59.0 (CH_2), 60.2 (CH_2), 60.4 (CH_2), 86.0 (CH_2), 104.9 (C), 169.1 (CO), 171.9 (CO); EIMS *m/z* (%) 269 (M, 63), 241 (40), 153 (100). HRMS: Calcd. for $C_{12}H_{19}N_3O_2$: 269.1371, Found: 269.1378.

Procedure C: General procedure for the substitution reaction of 5 to alkyl halide

A precipitate is obtained from the mixture of equal moles of **5** and alkyl halide dissolved in THF stirring for three days. The precipitate is separated from the solvent and neutralized using a 5% $NaHCO_3$ solution. The crude product is obtained after extraction with chloroform and the removal of the solvent by rotatory evaporation. A brown oil is obtained by column chromatography using silica gel as the stationary phase and the mixture of chloroform and n-hexane (3:1) as the eluent.

7-Butyl-1-Methoxycarbonyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6au-3)

6au-3 was prepared in a yield of 88% by the reaction of **5au** and butyl bromide following procedure C. **6au-3** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 0.82 (t, J = 7.4Hz, 3H), 1.16-1.37 (m, 4H) 2.30 (t, J = 6.9 Hz, 2H), 2.27, 2.66 (AM part of AMX, 2H, J_{AM} = 9.4 Hz, J_{AX} = 6.3 Hz, J_{MX} = 0 Hz), 2.60 (d, 1H, J = 10.2 Hz), 2.65 (dddd, 1H, J = 10.6, 6.2, 3.7, 0.1 Hz), 3.40 (d, 1H, J = 10.2 Hz), 3.73 (s, 3H), 3.46, 4.74 (AB part of ABX, 2H, J_{AB} = 18.3 Hz, J_{AX} = 9.0 Hz, J_{BX} = 3.5 Hz). ^{13}C NMR ($CDCl_3$): 13.9 (CH_3), 20.4 (CH_2), 30.4 (CH_2), 38.0 (CH), 52.7 (CH_3), 54.2 (CH_2), 59.4 (CH_2), 60.7 (CH_2), 86.0 (CH_2), 105.2 (C), 169.4 (CO); EIMS *m/z* (%) 225 (M^+, 19), 196 (5), 154 (100). HRMS: Calcd. for $C_{11}H_{19}N_3O_2$: 225.1373, Found: 225.1483.

7-Benzyl-1-Methoxycarbonyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6au-4)

6au-4 was prepared in a yield of 71% by the reaction of **5au** and benzyl chloride following procedure C. **6au-4** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 2.38, 2.59 (AM part of AMX, 2H, J_{AM} = 9.2 Hz, J_{AX} = 6.40 Hz, J_{MX} = 0 Hz), 2.75 (d, 1H, J = 10.4 Hz), 2.70-2.80 (m, 1H), 3.44 (d, 1H, J = 10.4 Hz), 3.51, 3.55 (AB, 2H, J = 13.1 Hz), 3.74 (s, 3H), 4.48, 4.76 (AB part of ABX, 2H, J_{AB} = 18.3 Hz, J_{AX} = 9.0 Hz, J_{BX} = 3.6 Hz), 7.17-7.28 (m, 5H). ^{13}C NMR ($CDCl_3$): 38.1 (CH), 52.7 (CH_3), 58.2 (CH_2), 59.0 (CH_2), 60.1 (CH_2), 86.0 (CH_2), 105.2 (C), 127.1 (CH), 128.2 (CH), 128.3 (CH), 138.0 (C), 169.3 (CO); EIMS *m/z* (%) 259 (M+, 5), 232 (2), 91 (100). HRMS: Calcd. for $C_{14}H_{17}N_3O_2$: 259.1317, Found: 259.1318.

1-Cyano-7-propyl-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6av-1)

6av-1 was prepared in a yield of 74% by the reaction of **5av** and propyl bromide following procedure C. **6av-1** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 0.75 (t, J = 7.5 Hz, 3H), 1.32 (q, J = 7.5 Hz, 2H), 2.25 (t, J = 7.5 Hz, 2H), 2.34, 3.49 (AM part of AMX, 2H, J_{AM} = 10.3 Hz, J_{AX} =5.9 Hz, J_{MX} = 0 Hz), 2.53 (d, 1H, J = 10.3 Hz), 2.71-2.78 (dddd, 1H, J = 9.3, 5.9, 3.4, 0 Hz), 3.49 (d, 1H, J = 10.3 Hz), 4.50, 4.86 (AB part of ABX, 2H, J_{AB} = 18.7 Hz, J_{AX} = 9.3 Hz, J_{BX} = 3.4 Hz). ^{13}C NMR ($CDCl_3$): 11.4 (CH_3), 21.1 (CH_2), 39.5 (CH), 55.2 (CH_2), 59.7 (CH_2), 60.7 (CH_2), 87.1 (CH_2), 91.1 (C), 116.8 (CN); EIMS *m/z* (%) 179 (M+1, 100), 151 (74), 121 (43). HRMS: Calcd for $C_9H_{14}N_4$: 178.1216, Found: 178.1219.

7-Allyl-1-cyano-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6av-2)

6av-2 was prepared in a yield of 77% by the reaction of **5av** and allyl bromide following procedure C. **6av-2** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 2.40, 2.68 (AM part of AMX, 2H, J_{AM} = 9.6 Hz, J_{AX} =5.9 Hz, J_{MX} = 0 Hz), 2.59 (d, 1H, J = 10.3 Hz), 2.77 (dddd, 1H, J = 9.3, 5.9, 3.4, 0 Hz), 2.97 (d, J = 6.4 Hz, 2H), 3.52 (d, 1H, J = 10.3 Hz), 4.55, 4.93 (AB part of ABX, 2H, J_{AB} = 18.7 Hz, J_{AX} = 9.3 Hz, J_{BX} = 3.4 Hz). 5.07-5.15 (m, 2H), 5.62-5.74 (m, 1H). ^{13}C NMR ($CDCl_3$): 39.7 (CH), 56.2 (CH_2), 59.6 (CH_2), 60.5 (CH_2), 87.2 (CH_2), 91.3 (C), 116.8 (CN), 117.9 (CH), 134.0 (CH_2); CIMS *m/z* (%) 177

(M+1, 100), 149 (61), 99 (65), 84 (70). HRMS: Calcd. for $C_9H_{12}N_4$: 176.1060, Found: 176.1068.

1-Cyano-7-(2-propynyl)-2,3,7-triazabicyclo[3.3.0]oct-2-ene (6av-3)

6av-3 was prepared in a yield of 71% by the reaction of **5av** and 2-propynyl bromide following procedure C. **6av-3** is a yellow liquid, ^{1}H NMR ($CDCl_3$): δ 2.24 (t, J = 2.3 Hz, 1H), 2.51, 2.65 (AM part of AMX, 2H, J_{AM} = 9.6 Hz, J_{AX} =5.8 Hz, J_{MX} = 0 Hz), 2.76 (dddd, 1H, J = 9.3, 5.9, 3.4, 0 Hz), 2.86, 3.36 (AB, 2H, J = 10.8 Hz), 3.28 (d, J = 2.4 Hz, 2H), 4.51, 4.85 (AB part of ABX, 2H, J_{AB} = 18.7 Hz, J_{AX} = 9.0 Hz, J_{BX} = 3.3 Hz). ^{13}C NMR ($CDCl_3$): 39.3 (CH), 40.2 (CH_2), 57.6 (CH_2), 58.4 (CH_2), 74.2 (CH), 76.3 (C), 87.0 (CH_2), 91.0 (C), 116.4 (CN); CIMS m/z (%) 175 (M+1, 100), 147 (76), 82 (95). HRMS: Calcd. for $C_9H_{10}N_4$: 174.0904, Found: 174.0914.

1-Methoxycarbonyl-7-(2-methoxycarbonylethyl)-2,3,7-triazabicyclo[3.3.0]oct-3-ene (7au)

To 1 g of **6au** dissolved in 5 mL of methanol kept at 0 °C, a solution of 2 mL concentrated hydrochloric acid in 15 mL methanol was added dropwise. The mixture was stirred for one hour. The solvent was rotatory evaporated and the residue was neutralized by a 5% $NaHCO_3$ solution. The aqueous solution was then extracted with THF. After evaporation of THF, **7au** could be obtained as an orange oil in a yield of 90%. **7au** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 2.64 (t, 2H, J = 7.4 Hz), 2.66 (d, 1H, J = 8.2 Hz), 2.78 (d, 1H, J = 9.4 Hz), 2.80 (t, 2H, J = 7.4 Hz), 2.88 (m, 1H), 3.04 (dd, 1H, J = 9.4, 2.1 Hz), 3.10 (δ, 1H, J = 9.5 Hz), 3.67 (s, 3H), 3.78 (s, 3H), 6.15 (bs. 1H), 6.61 (d, 1H, J = 1.2 Hz), ^{13}C NMR ($CDCl_3$): 33.2 (CH_2), 49.7 (CH_2), 51.5 (CH_3), 55.8 (CH_3), 56.6 (CH), 57.3 (CH_2), 65.1 (CH_2), 74.2 (C), 144.2 (CH), 172.3 (C=O), 172.9 (C=O); MS (EIMS) m/z (%) 255 (M, 4), 240 (6), 224 (33), 196 (100). HRMS: Calcd. for $C_{11}H_{17}N_3O_4$: 255.1223, Found: 255.1215.

1-(Methoxycarbonyl)-7-(3-oxo-1-butyl)-2,3,7-triazabicyclo-[3.3.0]oct-3-ene (7au-1)

The isomerization of **6au-1** to **7au-1** followed the same procedure as that for the preparation of **7au**. **7au-1** could be obtained as a yellow oil in a yield of 85%, ^{1}H NMR ($CDCl_3$): δ 2.11 (s, 3H), 2.51, 2.80 (AM part of AMX, 2H, J_{AM} = 9.2 Hz, J_{AX} = 6.4 Hz, J_{MX} = 0 Hz), 2.65 (t, J = 7.4 Hz, 2H), 2.68, 3.02 (AB, 2H, J = 9.6 Hz), 2.76 (t, J = 7.4 Hz, 2H), 2.96 (m, 1H), 3.76 (s, 3H), 6.22 (s, 1H), 6.25 (s, 1H). ^{13}C NMR ($CDCl_3$): 30.1 (CH_3), 42.6 (CH_2), 48.9 (CH_2), 52.9 (CH_3), 56.8 (CH_2), 57.7 (CH_2), 65.5 (CH_2), 74.4 (C), 144.5 (CH), 173.1 (C=O), 207.4 (C=O); CIMS m/z (%) 240 (M+1, 77), 182 (35), 113 (100). HRMS: Calcd. for $C_{11}H_{17}N_3O_3$: 239.1266, Found: 239.1260.

1-(Methoxycarbonyl)-7-benzyl-2,3,7-triazabicyclo[3.3.0]-oct-3-ene (7au-2)

The isomerization of **6au-4** to **7au-2** followed the same procedure as that for the preparation of **7au-1**. The yield was 87%. **7au-2** is a yellow liquid, ^{1}H NMR ($CDCl_3$): 2.54, 2.90 (AM part of AMX, 2H, J_{AM} = 9.1 Hz, J_{AX} = 7.5 Hz, J_{MX} = 0 Hz), 2.70, 3.02 (AB, 2H, J = 9.6 Hz), 3.53, 3.65 (AB, 2H, J = 13.1 Hz), 3.71 (s, 3H, OCH_3), 3.78 (m, 1H), 6.16 (s, 1H), 6.17 (s, 1H), 7.14-7.26 (m, 5H). ^{13}C NMR ($CDCl_3$): 52.7 (CH_3), 56.7 (CH_2), 57.0 (CH_2), 58.5 (CH), 65.1 (CH_2), 74.2 (C), 126.9 (CH), 128.1 (CH), 128.4 (CH), 137.8 (C), 144.4 (CH), 173.0 (C=O); EIMS m/z (%) 260 (M+1, 100), 91 (25). HRMS: Calcd. for $C_{14}H_{17}N_3O_2$: 259.1317, Found: 259.1302.

Supplementary Materials

Tables of crystal data for **7av** including tables of hydrogen coordinates, U values, bond lengths, bond angles, anisotropic parameters, and data collection parameters.

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Key Words

Allyl azide; Cycloaddition; Diazo compounds; Isomerization; Bicyclic heterocyclic compounds; Tandem cascade reaction; One-pot reaction.

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