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Concise Assembly of Highly Substituted Furan-Fused 1,4-Thiazepines and Their Diels−Alder Reactions with Benzynes

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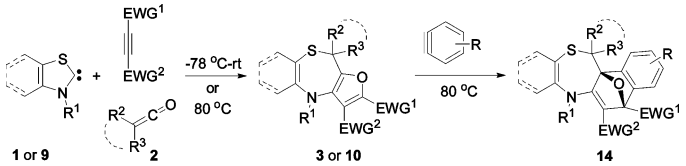

A facile and highly efficient three-component reaction of thiazole or benzothiazole carbenes, disubstituted ketenes, and activated alkynes is disclosed. With this methodology, a polysubstituted ring system containing furo[2,3-*c*]thiazepine core can be constructed from simple and readily accessible starting materials in good yields. The scope and limitation of this transformation were investigated in detail by using various thiazole carbene, ketene, and alkyne components. Furthermore, the synthetic utilities of these unique polyheterocyclic compounds were demonstrated via their Diels−Alder reactions with benzynes to furnish thiazepine-fused 7-oxanorbornadiene derivatives in excellent yields.

Introduction

The aryl- and heteroaryl-fused 1,4-thiazepines[1] are an important group of compounds with interesting pharmacological properties,[2] such as antiarrhythmic, antispasmodic, angiogenic, and CNS activities,[3] and therefore represent promising synthetic targets. The development of efficient synthetic strategies to the related scaffolds may provide a valuable access to novel physiologically active agents. On the other hand, polysubstituted furan has been found as a key structural unit in many bioactive natural products and pharmaceuticals,[4] accordingly, various annulated derivatives such as benzo-, thieno-, isoxazolo-, furo-, pyridino-, pyridazino-, and indolofurans have been synthesized and their properties investigated.[5] However, to the best of our knowledge, the furan-fused 1,4-thiazepine that combines furan and thiazepine fragments in one molecule has scarcely been demonstrated previously.

On the basis of the nucleophilicity of thiazole carbenes,[6,7] in a preliminary communication, we described a highly efficient multicomponent domino synthesis of furo[2,3-*c*]thiazepine

SCHEME 1. Synthesis of Polysubstituted Furan-Fused 1,4-Thiazepine Derivatives

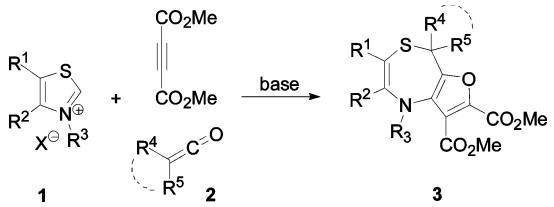

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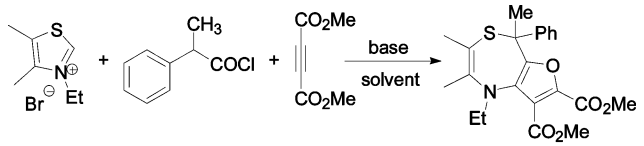
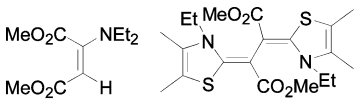
TABLE 1. Effects of Reaction Conditions[a]



1a **2a** **3a**

entry	base	solvent	*T* (°C)	*t* (h)[b]	yield (%)[c]
1	*i*-Pr_2NEt	CH_2Cl_2	−20 to 25	8	64
2	*i*-Pr_2NEt	CH_2Cl_2	−78 to 25	4	83
3	*i*-Pr_2NEt + NaH[d]	CH_2Cl_2	−78 to 25	7	62
4	NaH	CH_2Cl_2	−78 to 25	4	67[e]
5	NEt_3	CH_2Cl_2	−78 to 25	7	25
6	DBU	CH_2Cl_2	−78 to 25	8	<5[d]
7	*i*-Pr_2NEt	CH_2Cl_2	−78 to 0	3	<5
8	*i*-Pr_2NEt	THF	−78 to 25	8	<5
9	*i*-Pr_2NEt	toluene	−25 to 25	8	0
10	*i*-Pr_2NEt	CH_3CN	−40 to 25	8	45
11	*i*-Pr_2NEt	DME	−65 to 25	9	0
12[f]	*i*-Pr_2NEt	CH_2Cl_2	−78 to 25	4	84

[a] General conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), DMAD (1.5 mmol), and base (2.5 mmol). [b] Reaction time for consuming all of the starting materials. [c] Isolated yields. [d] *i*-Pr_2NEt (1.2 mmol), NaH (1.3 mmol). [e] NaH (1.2 mmol), phenyl(methyl)ketene was used instead of **2a**. [f] Reaction conditions: **1a** (2.5 mmol), **2a** (1.0 mmol), DMAD (2.5 mmol), and *i*-Pr_2NEt (4.0 mmol).

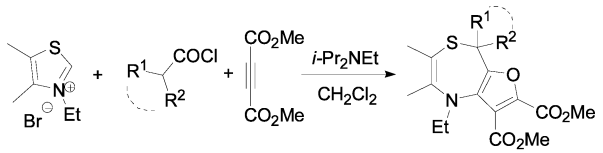


4a **4b**

FIGURE 1. Structures of compounds **4a** and **4b**.

derivatives (**3**) from thiazolium salts (**1**), disubstituted ketenes (**2**), and activated alkynes (Scheme 1).[8] It is noteworthy that, contrary to the typical reactivity of ketene,[9−11] both of the double bonds (C═C and C═O) in disubstituted ketene are used in the assembly of the polysubstituted bicyclic compound **3**. Although this approach performed with high efficiency in constructing the furo[2,3-*c*]thiazepine core, the implications from the experimental results are not fully apparent. Moreover, the scope and limitation of this reaction such as the structures of each component as well as the synthetic utilities of the unique bicyclic product **3** clearly warranted further research. Herein, we report the results of our detailed investigations on the multicomponent reaction involving thiazole carbenes, ketenes, and activated alkynes for the convergent synthesis of highly substituted furan-fused 1,4-thiazepines and their Diels−Alder reactions with benzynes resulting in 7-oxanorbornadienes derivatives.[12]

TABLE 2. Reactions of Thiazolium Salt 1a, Acetyl Chlorides 2, and DMAD for the Synthesis of Furan-Fused 1,4-Thiazepines 3a−r

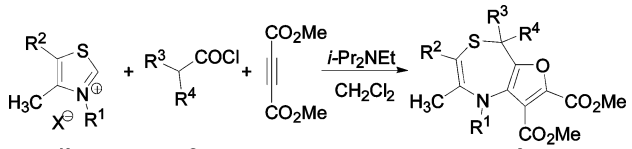


1a **2a-r** **3a-r**

entry	R^1	R^2	**2**	*t* (h)[a]	yield of **3** (%)[b]
1	Me	Ph	**2a**	4	**3a**, 83
2	Me	4-$MeOC_6H_4$	**2b**	5.5	**3b**, 85
3	Me	4-MeC_6H_4	**2c**	7	**3c**, 84
4	Me	1-naphthyl	**2d**	9.5	**3d**, 59
5	Me	4-ClC_6H_4	**2e**	8	**3e**, 74
6	Me	4-BrC_6H_4	**2f**	7	**3f**, 72
7	Me	2-ClC_6H_4	**2g**	3.5	**3g**, 81
8	Me	2-BrC_6H_4	**2h**	4.5	**3h**, 77
9	Me	3-ClC_6H_4	**2i**	7	**3i**, 83
10	Me	4-$NO_2C_6H_4$	**2j**	17	**3j**, 28
11	Et	Ph	**2k**	2.5	**3k**, 91
12	*i*-Pr	4-ClC_6H_4	**2*l***	6	**3*l***, Nd[c]
13	Ph	Ph	**2m**	4	**3m**, 76
14	Me	Me	**2n**	7	**3n**, 84
15	Me	Et	**2o**	7	**3o**, 88
16		$-(CH_2)_4-$	**2p**	6	**3p**, 81
17		$-(CH_2)_5-$	**2q**	7	**3q**, 85

[a] Reaction time for consuming all of the starting materials. [b] Isolated yields. [c] No product was detected.

TABLE 3. Formations of Products 3s−z by the Reactions of Thiazolium Salts 1b−g, Acetyl Chloride 2, and DMAD



1b-g **2** **3s-z**

1b, **1g**: X = I
1c-f: X = Br

entry	R^1	R^2	**1**	**2**	*t* (h)[a]	yield of **3** (%)[b]
1	Me	Me	**1b**	**2a**	5.5	**3s**, 78
2	Me	Me	**1b**	**2c**	5	**3t**, 80
3	Me	Me	**1b**	**2e**	7	**3u**, 74
4	Bn	Me	**1c**	**2k**	6	**3v**, 84
5	Et	H	**1d**	**2c**	7	**3w**, 78
6	Bu	H	**1e**	**2k**	4.5	**3x**, 86
7	Bn	H	**1f**	**2k**	3	**3y**, 81
8	Me	$AcO(CH_2)_2-$	**1g**	**2k**	7	**3z**, 71

[a] Reaction time for consuming all of the starting materials. [b] Isolated yields.

Results and Discussion

The three-component reaction was carried out by dropping the mixture of α-methyl phenylacetyl chloride (**2a**) and dimethyl

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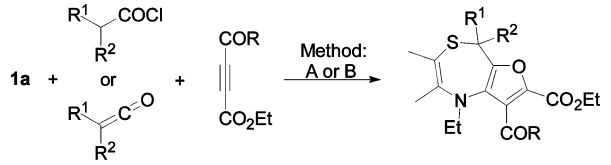
TABLE 4. Reactions of Thiazolium Salt 1a, 2, and Activated Alkynes 5a−e



entry	R^1	R^2	R	5	method[a]	yield of 6 (%)[b]
1	Ph	Ph	OEt	**5a**	A	**6a**, 78
2	Et	Ph	OEt	**5a**	A	**6b**, 83
3	$-(CH_2)_5-$		OEt	**5a**	A	**6c**, 81
4	Ph	Ph	Ph	**5b**	A	**6d**, <5
					B	**6d**, 81
5	Ph	Ph	4-MePh	**5c**	A	**6e**, <5
					B	**6e**, 83
6	Ph	Ph	4-BrPh	**5d**	A	**6f**, <5
					B	**6f**, 87
7	Ph	Ph	*t*-Bu	**5e**	A	**6g**, <5
					B	**6g**, 85
8	Et	Ph	4-BrPh	**5d**	A	**6h**, <5
					B	**6h**, 38
9	Me	Ph	4-BrPh	**5d**	A	**6i**, <5
					B	**6i**, 32
10	$-(CH_2)_5-$		4-BrPh	**5d**	A	**6j**, 55
					B	**6j**, 46
11	Me	Me	4-BrPh	**5d**	A	**6k**, 58
					B	**6k**, <5
12	Me	Et	4-MePh	**5c**	A	**6*l***, 62
					B	**6*l***, 26
13	Me	Et	*t*-Bu	**5e**	A	**6m**, 46
					B	**6m**, 18

[a] Method A: **1a** (1.0 mmol), acetyl chloride (1.2 mmol), alkyne (1.5 mmol), and *i*-Pr_2NEt (2.5 mmol). Method B: **1a** (1.0 mmol), ketene (1.2 mmol), alkyne (1.5 mmol), and NaH (1.2 mmol), then aqueous workup. [b] Isolated yields.

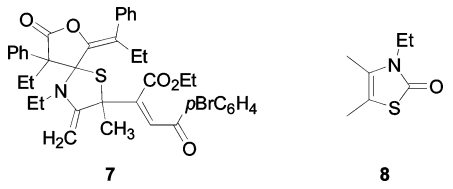


FIGURE 2. Structures of compounds **7** and **8**.

acetylenedicarboxylate (DMAD) to a suspension of thiazolium salt **1a** in CH_2Cl_2 in the presence of a base at −78 °C. Thus, a thiazole carbene and a ketene were assumed to be initially generated in situ from their corresponding precursors (**1a** and **2a**) by the base, respectively. However, as the activated alkyne (DMAD) is sensitive to some nucleophiles, the basicity and nucleophilicity of the base may have critical effects on this transformation. Accordingly, several typical bases including NEt_3, *i*-Pr_2NEt, DBU, and NaH were investigated for this reaction. As disclosed in Table 1, *i*-Pr_2NEt proved to be the optimum base among those tested (entries 1−6). Sodium hydride afforded the desired product **3a** in 67% yield with isolated phenyl(methyl)ketene instead of **2a** (entry 4). In contrast, using NEt_3 as the base, the yield of compound **3a** decreased dramatically due to the formation of dimethyl-(*E*)-2-diethylaminobutenoate **4a** (61% yield, Figure 1) arising from the addition of NEt_3 onto DMAD (entry 5).[13] The survey of solvents demonstrated that CH_2Cl_2 was the choice of solvent, whereas THF, toluene, CH_3CN, or DME decreased the reaction efficiency and resulted in poor yield of **3a** (entries 2, 8−11). Furthermore, it was observed that the temperature has a vital effect on this reaction; only a trace amount of product was obtained when the reaction temperature was maintained below 0 °C (entry 7). Attempts to improve the transformation by using excess amounts of **1a** and DMAD were unsuccessful; a roughly equal yield of **3a** was accessed aligned with a byproduct of **4b** (comparing entry 2 with entry 12).

Under the optimized reaction conditions, a variety of disubstituted acetyl chlorides **2** were submitted to the reaction with thiazolium salt **1a** and DMAD (Table 2). From α-methyl arylacetyl chlorides **2a**−**k**, the corresponding products **3a**−**k** were formed in good to excellent yields. Nevertheless, the substrates with an electron-rich aromatic group (entries 2 and 3) performed better than their electron-poor counterparts (entries 5−9); especially in the case of α-methyl 4-nitrophenylacetyl chloride **2j**, the reaction was significantly sluggish and led to a disappointing yield of the product **3j** under the same conditions (entry 10). The size of alkyl substitutes enclosed in α-alkyl arylacetyl chlorides also played important roles in the tandem reaction. The ethyl-substituted substrate **2k** completed the conversion within 2.5 h to produce **3k** in a higher yield of 91% than that of **2a**, whereas the compound **2*l*** bearing a bulky isopropyl group did not undergo the similar reaction (comparing entries 1, 11, and 12). One explanation for these results is that the increased bulk may assist the ring-expansion step, but a very crowded substitutent (e.g., isopropyl) inhibited the initial formation of a spirocycle intermediate.[14] Next, the transformations of dialkyl acetyl chlorides **2n**−**q** were exploited under the same conditions leading to the synthesis of furo[2,3-*c*]-thiazepines **3n**−**q** in 81−88% yields (entries 14−17). To our delight, the tricyclic products **3p** and **3q** of more skeletal complexity were easily and high efficiently constructed from simple substrates.[15]

We next turned our attention to test a set of thiazolium salts **1b**−**g** from the commercially available thiazoles under previous conditions in order to extend the molecular diversity of furo-[2,3-*c*]thiazepines (Table 3). As a result, a range of furo[2,3-*c*]thiazepines **3s**−**z** with various substituents were obtained in one step by simply mixing thiazolium salts, disubstituted acetyl chlorides **2**, and DMAD.

Encouraged by these results, the range of activated alkynes was then probed to get a better insight into the generality of this reaction (Table 4). In the presence of *i*-Pr_2NEt, diethyl acetylenedicarboxylate (**5a**) conducted the reaction smoothly to provide **6a**−**c** from corresponding substrates (entries 1−3). As for 4-oxo-2-alkynoates **5b**−**e**, two different experimental procedures were established for the transformations in the following studies. The optimized results revealed that both aryl- and *tert*-butyl-substituted alkynes **5b**−**e** reacted with **1a** and diphe-

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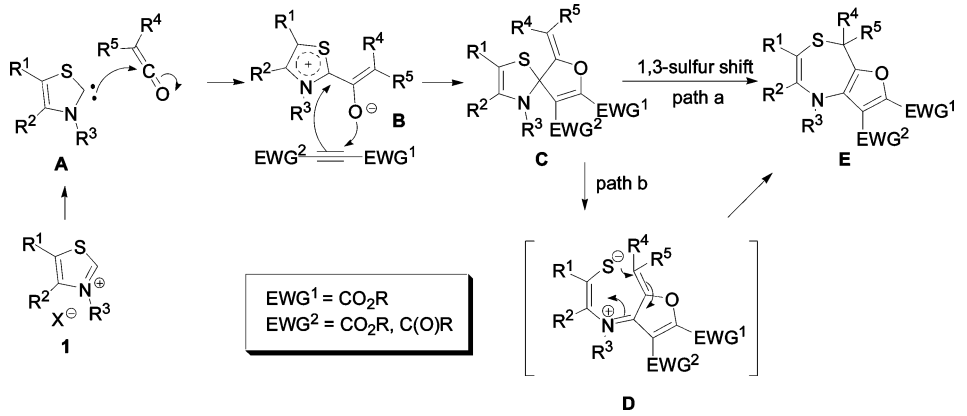
(14) See the proposed mechanism in Scheme 2.

(15) With dichloro acetyl chloride as the ketene precursor, the desired product **3r** was not detected.

SCHEME 2. Proposed Mechanism

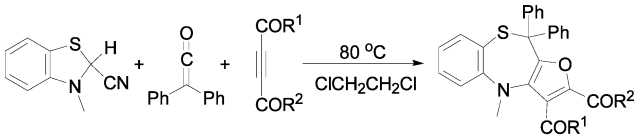


nylketene directly to provide 1,4-thiazepines **6d**−**g** exclusively in good yields via Method B, respectively (entries 4−7). In contrast, only moderate yields of the target products were obtained when R^1 or R^2 involved in the ketene component was an alkyl group no matter by Method A or Method B (entries 8−13), presumably due to the instability of the related ketenes and their reactivity toward 4-oxo-2-alkynoate **5** upon treatment with *i*-Pr_2NEt.[16] In addition, when phenyl(ethyl)ketene was enclosed in the reaction by using Method B, an AB_2C-type byproduct **7**[17] (Figure 2) was isolated in 30% yield along with the product **6h** (entry 8, Table 4), while with phenyl(methyl)-ketene instead, 3-ethyl-4,5-dimethylthiazole-2-one **8** was isolated in 54% yield after aqueous workup, which was derived from the unreacted thiazole carbene (entry 9).[18]

On the basis of the experimental results, a plausible mechanism that accounts for this novel three-component reaction is devised as shown in Scheme 2. The in situ generated thiazole carbene **A** from thiazolium salt **1** initially attacked the disubstituted ketene to give zwitterion **B**, which then underwent an oxa-Michael addition to the activated alkyne and subsequently converted into the spirocycle intermediate **C** through intramolecular annulation. Next, two pathways were proposed for the ring-transformation of spirocycle **C**, a concerted (path A) or a stepwise (path B) pathway. In path A, the ring expansion of **C** would proceed to directly afford the furothiazepine **E**, an aromatic compound, via a [1,3]-sigmatropic sulfur shift.[19] On the other hand (path B), ring opening of **C** produced a reactive thiolate **D**, which could subsequently undergo a 7-endo-trig cyclization to produce thiazepine ring **E**.[20]

As tricyclic heterocycles, especially those azaheterocycles, are important scaffolds in medicinal chemistry,[21] according to the current tentative mechanism, the reactivity of the benzothiazole carbene was further investigated for the synthesis of annulated tricyclic derivatives. To our satisfaction, by using cyano-benzothiazoline **9** as the precursor of carbene instead of thiazolium salt **1**, the corresponding furan-fused 1,4-benzothiazepines **10a**−**d** were successfully formed from diphenylketene, and activated alkynes in 52−65% yields under thermodynamic conditions (Table 5). Similar to the previous results for the thiazolium variant **1a** (entry 12, Table 1), accompanied by the formation of **10a**, the byproduct **11**[22] was isolated in 32% yield (entry 1, Table 5 and Figure 3).

TABLE 5. Reactions of Benzothiazole Carbene, Diphenylketene, and Activated Alkynes[a]



9 **10a-d**

entry	R^1	R^2	yield of **10** (%)[b]
1	MeO	MeO	**10a**, 56
2	Ph	EtO	**10b**, 65
3	Me	EtO	**10c**, 58
4	*t*-Bu	EtO	**10d**, 52

[a] General conditions: **9** (1.0 mmol), diphenylketene (1.2 mmol), alkyne (1.2 mmol), 80 °C for 12 h. [b] Isolated yields.

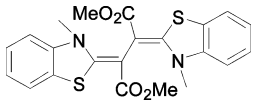


FIGURE 3. Structure of compound **11**.

The unique structure of furan-fused 1,4-thiazepines can be of some potential synthetic utility, for instance, through Diels−Alder reaction with arynes to form 1,4-thiazepine-fused 7-oxanorbornadienes,[23] which may have interesting biological activities and are also quite useful intermediates in the total synthesis of natural products and analogues. As shown in Table 6, selected compounds **3**, **6**, and **10** reacted sufficiently with a

(16) For the examples in entries 4−9, Table 4, ketene was found to react with the activated alkyne to form some volatile unidentified products.

(17) The structure of compound **7** was unambiguously confirmed by single-crystal X-ray diffraction, see the Supporting Information.

(18) Itoh, T.; Nagata, K.; Okada, M.; Ohsawa, A. *Tetrahedron* **1993**, *49*, 4859.

(19) For rearrangements in the thizaole system, see: (a) Abbott, P. J.; Acheson, R. M.; Eisner, U.; Watkin, D. J.; Carruthers, J. R. *Chem. Commun.* **1975**, 155. (b) Potts, K. T.; Choudhury, D. R.; Westby, T. R. *J. Org. Chem.* **1976**, *41*, 187.

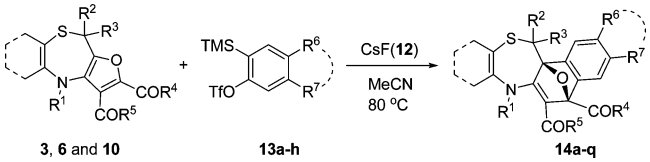
(20) For similar transformations in the convertion of β-lactamase inhibitor, see: (a) Micetich, R. G.; Maiti, S. N.; Tanaka, M.; Yamazaki, T.; Ogawa, K. *J. Org. Chem.* **1986**, *51*, 853. (b) Nukaga, M.; Abe, T.; Venkatesan, A. M.; Mansour, T. S.; Bonomo, R. A.; Knox, J. R. *Biochemistry* **2003**, *42*, 13152.

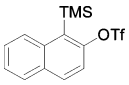
(21) Baldessarini, R. J. In *Goodman and Gilman's the Pharmacological Basis of Therapeutics*, 10th ed.; Hardman, J. G., Limbird, L. E., Eds.; McGraw-Hill: New York, 2001; pp 447−483.

(22) The structure of compound **11** was unambiguously confirmed by single-crystal X-ray diffraction; see the Supporting Information.

(23) For reviews on the Diels−Alder reaction, see: (a) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650. (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogian-nakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668. (c) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701.

TABLE 6. Diels−Alder Reactions of Furan-Fused 1,4-Thiazepines with Benzynes[a]



entry	substrate	R^6	R^7	**13**	yield of **14** (%)[b]
1	**3b**	H	H	**13a**	**14a**, 95
2	**3f**	H	H	**13a**	**14b**, 93
3	**3g**	H	H	**13a**	**14c**, 96
4	**3k**	H	H	**13a**	**14d**, 95
5	**6f**	H	H	**13a**	**14e**, 95
6	**6g**	H	H	**13a**	**14f**, 95
7	**6h**	H	H	**13a**	**14g**, 94
8	**6j**	H	H	**13a**	**14h**, 95
9	**10a**	H	H	**13a**	**14i,** 94
10	**10b**	H	H	**13a**	**14j**, 96
11	**6f**	Ph	H	**13b**	**14k**, 92 (1:1)[c]
12	**6f**			**13c**	**14*l***, 88 + trace
13	**6f**	F	F	**13d**	**14m**, 93
14	**6f**	Me	Me	**13e**	**14n**, 96
15	**6f**	$-(CH_2)_3-$		**13f**	**14o**, 93
16	**6f**	$-CH_2OCH_2-$		**13g**	**14p**, 90
17	**6f**			**13h**	**14q**, 96

[a] General conditions: furan **3**, **6**, or **10** (1.0 mmol), benzyne precursor **13** (1.5 mmol), CsF (3.0 mmol), 80 °C for 100 min. [b] Isolated yields. [c] Ratio of isolated yields.

set of symmetric benzynes, no matter electron-rich, deficient, or bulky ones, to furnish the corresponding 7-oxanorbornadienes **14** in excellent yields (entries 1−10 and 13−17). The structures of compounds **14** were confirmed by NMR spectroscopic analysis and further by single-crystal X-ray diffraction of **14e** (see the Supporting Information). On the other hand, the reactions of **6f** with unsymmetrical benzynes were also explored. A 1:1 mixture of regioisomers of **14k** was obtained in 92% combined yield when 4-phenylbenzyne was employed (entry 11), while 1,2-didehydronaphthalene **13c** gave a highly regioselective product in 88% yield due to the steric hindrance (entry 12, Table 6).

Conclusion

In conclusion, we have discovered a facile and efficient three-component reaction of thiazole or benzothiazole carbenes, disubstituted ketenes, and activated alkynes. A highly substituted ring system containing furo[2,3-*c*]thiazepine core can be generated from simple and readily accessible starting materials via this methodology. Furthermore, the Diels−Alder reactions of the unique furo[2,3-*c*]thiazepines with benzynes were exploited to give thiazepine-fused 7-oxanorbornadienes derivatives in excellent yields. With high atom-economy and considerable potential for synthetic and biological uses, we conceived that this novel multicomponent reaction described herein will find application in the synthesis of heterocyclic compounds and natural products as well as in the exploration of some novel bioactive molecules.

Experimental Section

General Procedure for the Synthesis of Furan-Fused 1,4-Thiazepine Derivatives 3a−z. To a solution of thiazolium salt **1** (1.0 mmol) in anhydrous CH_2Cl_2 (3 mL) was added *i*-Pr_2NEt (2.5 mmol) at −78 °C. After 10−15 min, a solution of acetyl chloride **2** (1.2 mmol) and DMAD (1.5 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min and then stirred at this temperature for 30 min. The reaction temperature was raised slowly to room temperature for an additional several hours. On completion of the reaction, the solvent was removed under vacuum, and the residue was quickly passed through a short pad of neutral Al_2O_3 column with a hexane−ether mixture (5:1) as eluent; the crude obtained was recrystallized from hexane to afford the desired products **3a−z**.

Furan-fused 1,4-thiazepine 3a: white solid; mp 124−126 °C; IR (film) υ 3005, 2970, 1718, 1710, 1437, 1419, 1345, 1296, 828, 767 cm^{-1}; ^1H NMR (500 MHz, d_6-DMSO) δ 7.32 (t, J = 7.5 Hz, 2H), 7.25 (t, J = 7.0 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 3.91 (s, 3H), 3.75 (s, 3H), 3.35−3.22 (m, 2H), 1.98 (s, 3H), 1.88 (s, 3H), 1.48 (s, 3H), 1.05 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, d_6-DMSO) δ 164.5, 157.8, 150.8, 147.2, 144.2, 136.5, 130.9, 128.6, 127.6, 126.7, 122.2, 118.4, 53.5, 52.7, 49.8, 44.3, 27.1, 22.8, 17.0, 14.7; HRMS (ESI) calcd for $C_{22}H_{25}NO_5SNa$ ([M + Na]$^+$) 438.1346, found 438.1325.

Furan-fused 1,4-thiazepine 3d: pale yellow solid; mp 151−153 °C; IR (film) υ 2977, 2956, 1726, 1704, 1545, 1247, 962, 787 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 8.82 (d, J = 8.4 Hz, 1H), 7.91−7.88 (m, 2H), 7.68 (s, 1H), 7.51 (t, J = 8. Hz, 1H), 7.45−7.35 (m, 2H), 3.93 (s, 3H), 3.63 (s, 3H), 3.56−3.41 (m, 2H), 2.18 (s, 3H), 2.06 (s, 3H), 1.97 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 164.3, 157.4, 150.3, 149.7, 136.9, 136.6, 134.9, 131.5, 129.6, 128.9, 128.5, 126.8, 125.4, 125.2, 125.1, 124.9, 122.2, 118.7, 52.4, 51.4, 49.6, 44.2, 22.9, 15.8, 14.5; HRMS (ESI) calcd for $C_{26}H_{27}NO_5SNa$ ([M + Na]$^+$) 488.1502, found 488.1482.

Furan-fused 1,4-thiazepine 3j: pale yellow solid; mp 152−154 °C; IR (film) υ 2977, 1735, 1715, 1654, 1518, 1347, 858, 794 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 8.20 (d, J = 9.2 Hz, 2H), 7.45 (d, J = 9.2 Hz, 2H), 3.95 (s, 3H), 3.80 (s, 3H), 3.50−3.28 (m, 2H), 2.09 (s, 3H), 1.94 (d, J = 1.2 Hz, 3H), 1.47 (d, J = 1.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 165.1, 158.5, 153.1, 152.3, 147.9, 146.3, 138.0, 132.1, 128.6, 124.1, 122.9, 118.8, 53.2, 52.3, 50.2, 44.9, 26.8, 22.5, 17.1, 14.6; HRMS (ESI) calcd for $C_{22}H_{24}N_2O_7SNa$ ([M + Na]$^+$) 483.1196, found 483.1182.

Furan-fused 1,4-thiazepine 3z: white solid; mp 114−115 °C; IR (film) υ 2952, 1738, 1625, 1548, 1440, 1346, 980, 762 cm^{-1}; ^1H NMR (500 MHz, d_6-acetone) δ 7.28−7.21 (m, 3H), 7.08 (d, J = 7.5 Hz, 2H), 3.95 (s, 3H), 3.80 (s, 3H), 3.79−3.71 (m, 3H), 3.04 (s, 3H), 2.54−2.46 (m, 2H), 2.27−2.25 (m, 1H), 1.96 (s, 3H), 1.91 (s, 3H), 1.40−1.38 (m, 1H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, d_6-acetone) δ 169.9, 164.5, 157.7, 154.3, 145.4, 144.2, 136.7, 133.2, 127.9, 127.0, 126.7, 121.6, 115.3, 61.5, 55.6, 52.5, 51.6, 37.4, 34.4, 33.1, 19.9, 16.0, 9.8; HRMS (ESI) calcd for $C_{25}H_{29}NO_7SNa$ ([M + Na]$^+$) 510.1557, found 510.1564.

Dimethyl-(*E*)-2-diethylaminobutenoate 4a: pale yellow oil; IR (film) υ 3095, 2981, 2863, 1744, 1694, 1570, 1446, 1378, 1158, 973, 862, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.61 (s, 1H), 3.93 (s, 3H), 3.63 (s, 3H), 3.19 (q, J = 6.8 Hz, 2H), 1.18 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 166.1, 153.7, 82.8, 52.8, 50.6, 44.8, 12.6; HRMS (ESI) calcd for $C_{10}H_{17}NO_4Na$ ([M + Na]$^+$) 238.1050, found 238.1055.

General Procedure for the Synthesis of Furan-Fused 1,4-Thiazepine Derivatives 6a−m. Method A: To a solution of thiazolium salt **1a** (1.0 mmol) in anhydrous CH_2Cl_2 (3 mL) was added *i*-Pr_2NEt (2.5 mmol) at −78 °C. After 10−15 min, a solution of substituted acetyl chloride (1.2 mmol) and alkynes **5a−e** (1.5 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min and then the mixture was stirred at this temperature for 30 min. The reaction temperature was raised slowly to room temperature for an additional several hours. On completion of the reaction, The solvent was removed under vacuum, and the residue was quickly passed through a short pad of neutral Al_2O_3 column with a hexane−ether mixture (5:1) as eluent; the crude obtained was recrystallized from

hexane to afford the desired products **6a**−**m**. **Method B:** To a solution of thiazolium salt **1a** (1.0 mmol) in anhydrous CH_2Cl_2 (3 mL) was added NaH (1.2 mmol) at −78 °C. After 10−15 min, a solution of disubstituted ketene (1.2 mmol) and alkynes **5a**−**e** (1.5 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min and then the mixture was stirred at this temperature for 30 min. The reaction temperature was then raised slowly to room temperature for an additional several hours. On completion of the reaction, cold water (1.5 mmol) was added with stirring and the solvent was removed under vacuum. The residue was quickly passed through a short pad of neutral Al_2O_3 column with a hexane−ether mixture (5:1) as eluent; the crude obtained was recrystallized from hexane to afford the desired products **6a**−**m**.

Furan-fused 1,4-thiazepine 6a (Method A): white solid; mp 136−138 °C; IR (film) υ 2986, 2936, 1738, 1722, 1548, 1370, 1179, 744, 697 cm^{-1}; ^1H NMR (500 MHz, d_6-acetone) δ 7.35−7.26 (m, 10H), 4.41 (q, J = 7.2 Hz, 2H), 4.18 (q, J = 7.0 Hz, 2H), 3.45 (q, J = 7.0 Hz, 2H), 1.88 (s, 3H), 1.38 (t, J = 7.0 Hz, 2H), 1.23−1.17 (m, 9H); ^{13}C NMR (125 MHz, d_6-acetone) δ 163.9, 157.1, 150.9, 145.3, 143.3, 137.0, 130.7, 129.1, 127.7, 127.3, 122.3, 118.5, 61.7, 60.8, 58.9, 44.4, 21.1, 16.3, 13.8, 13.5, 13.4; HRMS (ESI) calcd for $C_{29}H_{31}NO_5SNa$ ([M + Na]$^+$) 528.1815, found 528.1824.

Furan-fused 1,4-thiazepine 6d (Method B): yellow solid; mp 145−146 °C; IR (film) υ 2980, 2931, 1729, 1705, 1537, 1247, 1185, 954, 698 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.94 (d, J = 6.8 Hz, 2H), 7.66−7.53 (m, 3H), 7.34−7.25 (m, 10H), 3.90 (q, J = 6.8 Hz, 2H), 3.10 (q, J = 7.2 Hz, 2H), 1.68 (s, 3H), 1.19 (s, 3H), 1.01 (t, J = 7.0 Hz, 3H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 191.8, 158.0, 151.7, 146.6, 144.2, 138.2, 137.8, 134.7, 133.0, 130.1, 130.0, 129.7, 128.6, 128.6, 128.1, 119.4, 61.4, 59.7, 46.1, 22.0, 17.1, 14.4, 13.8; HRMS (ESI) calcd for $C_{33}H_{31}NO_4SNa$ ([M + Na]$^+$) 560.1866, found 560.1879.

Furan-fused 1,4-thiazepine 6h (Method B): white solid; mp 138−140 °C; IR (film) υ 2975, 2928, 1736, 1702, 1539, 1188, 898, 699 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.98 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.8 Hz), 7.31 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 4.06 (q, J = 7.2 Hz, 2H), 3.17−3.12 (m, 1H), 3.06−3.01 (m, 1H), 2.59−2.50 (m, 2H), 1.74 (s, 3H), 1.31 (s, 3H), 1.06 (t, J = 7.6 Hz, 3H), 1.01−0.95 (m, 6H); ^{13}C NMR (100 MHz, d_6-acetone) δ 190.0, 157.2, 145.8, 149.5, 145.4, 136.8, 136.2, 133.7, 132.1, 130.9, 128.3, 127.8, 127.0, 126.7, 126.6, 118.4, 60.6, 55.2, 45.1, 32.8, 21.6, 16.3, 13.4, 13.0, 9.7; HRMS (ESI) calcd for $C_{29}H_{30}BrNO_4SNa$ ([M + Na]$^+$) 590.0971, found 590.0978.

Furan-fused 1,4-thiazepine 6j (Method A): Pale yellow oil; IR (film) υ 2935, 2860, 1732, 1546, 1308, 1245, 1186, 856, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 4.08 (q, J = 7.2 Hz, 2H), 2.98 (q, J = 6.8 Hz, 2H), 2.22−2.14 (m, 2H), 2.02 (s, 3H), 1.95−1.91 (m, 2H), 1.79 (d, J = 8.8 Hz, 6H), 1.63−1.60 (m, 2H), 1.40−1.36 (m, 1H), 1.00−0.94 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 157.9, 151.0, 150.2, 136.0, 135.8, 132.0, 131.2, 130.8, 129.0, 127.1, 117.6, 61.0, 49.8, 45.5, 36.0, 25.5, 23.5, 21.5, 16.9, 14.1, 13.7; HRMS (ESI) calcd for $C_{26}H_{30}BrNO_4SNa$ ([M + Na]$^+$) 554.0971, found 554.0980.

Furan-fused 1,4-thiazepine 6l (Method A): pale yellow oil; IR (film) υ 2936, 2869, 1734, 1544, 1307, 1242, 1184, 856, 699 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.85 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 4.05 (q, J = 7.2 Hz, 2H), 3.05 (q, J = 7.2 Hz, 2H), 2.43 (s, 3H), 2.06−2.02 (m, 4H), 1.92−1.86 (m, 1H), 1.80 (s, 3H), 1.60 (s, 3H), 1.02−0.94 (m, 9H); ^{13}C NMR (100 MHz, d_6-acetone) δ 190.3, 157.3, 150.1, 149.5, 144.5, 136.0, 135.0, 131.2, 129.3, 129.2, 128.1, 117.2, 60.3, 48.4, 44.8, 34.1, 27.3, 23.1, 20.8, 16.3, 13.6, 13.1, 8.9; HRMS (ESI) calcd for $C_{25}H_{31}NO_4SNa$ ([M + Na]$^+$) 464.1866, found 464.1874.

Furan-fused 1,4-thiazepine 6m (Method A): pale yellow oil; IR (film) υ 2932, 2863, 1735, 1540, 1308, 1240, 1183, 854, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.30 (q, J = 7.2 Hz, 2H), 3.26 (q, J = 7.2 Hz, 2H), 2.05 (s, 3H), 1.91 (s, 3H), 1.89−1.85 (m, 1H), 1.63 (s, 1H), 1.57 (s, 3H), 1.33 (t, J = 6.8 Hz, 3H), 1.26 (s, 9H), 1.08 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1, 158.3, 149.1, 134.2, 130.6, 118.7, 61.0, 48.4, 46.6, 45.4, 27.0, 24.3, 18.7, 14.2, 13.8, 9.4; HRMS (ESI) calcd for $C_{22}H_{33}NO_4SNa$ ([M + Na]$^+$) 430.2023, found 430.2028.

4-(4-Bromophenyl)-2-[4,9-diethyl-2-methyl-3-methylene-8-oxo-9-phenyl-6-(1-phenylpropylidene)-7-oxa-1-thia-4-aza-spiro-[4.4]non-2-yl]-4-oxo-but-2-enoic acid ethyl ester 7: white solid; mp 188−190 °C; IR (film) υ 2976, 2930, 1738, 1712, 1542, 1125, 899, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 2.0 Hz, 2H), 7.69−7.54 (m, 4H), 7.38−7.29 (m, 6H), 7.21 (d, J = 6.8 Hz, 2H), 7.00 (s, 1H), 4.15−4.09 (m, 2H), 3.51 (d, J = 2.0 Hz, 1H), 3.30 (d, J = 1.6 Hz, 1H), 3.04−2.93 (m, 3H), 2.73−2.68 (m, 1H), 2.32−2.27 (m, 1H), 2.01−1.95 (m, 1H), 1.86 (s, 3H), 1.11−1.05 (m, 6H), 0.88 (t, J = 7.6 Hz, 3H), 0.78 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 173.4, 166.0, 148.4, 146.1, 142.0, 137.8, 135.4, 132.5, 132.0, 129.9, 129.1, 129.0, 128.6, 128.3, 128.2, 127.8, 127.3, 127.1, 85.1, 82.3, 61.7, 61.2, 58.9, 40.2, 31.6, 28.4, 23.9, 13.5, 12.0, 11.9, 8.7; HRMS (ESI) calcd for $C_{39}H_{40}BrNO_5SNa$ ([M + Na]$^+$) 736.1703, found 736.1712.

3-Ethyl-4,5-dimethylthiazole-2-one 8: colorless oil; IR (film) υ 2930, 2862, 1732, 1535, 1305, 1240, 1180, 851, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.73 (t, J_1 = 7.6 Hz, J_2 = 6.4 Hz, 2H), 2.08 (s, 3H), 2.06 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 126.2, 106.3, 38.2, 14.4, 11.9, 11.2; HRMS (ESI) calcd for $C_7H_{11}NOSNa$ ([M + Na]$^+$) 180.0459, found 180.0458.

General Procedure for the Synthesis of Furan-Fused 1,4-Benzothiazepine Derivatives 10a−**d**. At 80 °C, a solution of cyano-benzothiazoline **9** (1.0 mmol) in DCE (3 mL) was added dropwise to a solution of diphenylketene (1.2 mmol) and alkynes (1.2 mmol) in DCE (5 mL) over 45 min; the mixture was then stirred at this temperature overnight. On completion of the reaction, The solvent was removed under vacuum, and the residue was quickly passed through a short pad of neutral Al_2O_3 column with a hexane−ether mixture (5:1) as eluent to afford the desired products **10a**−**d**.

Furan-fused 1,4-benzothiazepine 10a: white solid; mp 174−176 °C; IR (film) υ 2978, 2955, 1736, 1716, 1542, 1446, 740, 699 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.33−7.22 (m, 12H), 7.02 (d, J = 7.6 Hz, 1H), 6.86−6.82 (m, 1H), 3.99 (s, 3H), 3.71 (s, 3H), 3.46 (s, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 164.3, 157.1, 154.5, 144.1, 142.3, 137.1, 135.9, 131.2, 129.9, 128.6, 127.7, 127.3, 126.9, 124.3, 122.5, 121.8, 60.5, 52.3, 51.4, 40.6; HRMS (ESI) calcd for $C_{28}H_{23}NO_5SNa$ ([M + Na]$^+$) 508.1189, found 508.1196.

Furan-fused 1,4-benzothiazepine 10b: white solid; mp 183−185 °C; IR (film) υ 2974, 2952, 1735, 1712, 1540, 1443, 742, 699 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 8.05 (d, J = 7.6 Hz, 2H), 7.72 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 2H), 7.32−7.26 (m, 8H), 7.24−7.20 (m, 3H), 7.06−7.01 (m, 2H), 6.83 (t, J = 7.6 Hz, 1H), 3.94 (q, J = 7.2 Hz, 2H), 3.21 (s, 3H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 191.0, 156.8, 154.7, 142.7, 137.7, 137.2, 136.0, 133.8, 132.7, 130.1, 129.2, 128.9, 127.9, 127.5, 127.5, 127.4, 124.6, 123.0, 60.6, 60.6, 42.3, 12.9; HRMS (ESI) calcd for $C_{34}H_{27}NO_4SNa$ ([M + Na]$^+$) 568.1553, found 568.1562.

Furan-fused 1,4-benzothiazepine 10c: white solid; mp 132−134 °C; IR (film) υ 2977, 2955, 1739, 1720, 1547, 1448, 746, 702 cm^{-1}; ^1H NMR (400 MHz, d_6-acetone) δ 7.34−7.22 (m, 12H), 7.01 (q, J_1 = 1.6 Hz, J_2 = 6.4 Hz, 1H), 6.88−6.86 (m, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.37 (s, 3H), 2.73 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-acetone) δ 198.5, 157.3, 154.7, 145.4, 142.6, 136.0, 136.0, 131.7, 130.9, 130.2, 128.8, 128.0, 127.8, 127.4, 124.9, 123.9, 60.9, 60.5, 42.6, 32.1, 13.4; HRMS (ESI) calcd for $C_{29}H_{25}NO_4SNa$ ([M + Na]$^+$) 506.1397, found 506.1390.

Furan-fused 1,4-benzothiazepine 10d: white solid; mp 137−139 °C; IR (film) υ 2970, 2952, 1734, 1725, 1546, 1445, 744, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 4.4 Hz, 2H), 7.22−7.18 (m, 10H), 6.99 (d, J = 6.8 Hz, 1H), 6.87−6.83 (m, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.29 (s, 3H), 1.38 (s, 9H), 1.21 (t,

J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 157.9, 154.0, 148.9, 142.1, 138.2, 136.7, 135.5, 132.2, 131.2, 130.4, 130.0, 128.9, 128.6, 128.6, 127.8, 127.3, 127.3, 126.7, 126.0, 61.1, 60.4, 45.5, 45.4, 27.2, 14.1; HRMS (ESI) calcd for $C_{32}H_{31}NO_4SNa$ ([M + Na]$^+$) 548.1866, found 548.1870.

2,3-Bis(3-methyl-3*H*-benzothiazol-2-ylidene)succinic acid dimethyl ester 11: white solid; mp 154−156 °C; IR (film) υ 2954, 2935, 1735, 1718, 1540, 1437, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.59 (m, 2H), 7.31−7.27 (m, 2H), 7.15−7.12 (m, 4H), 3.62 (s, 6H), 3.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 159.0, 142.4, 127.0, 125.8, 122.3, 121.3, 109.7, 88.7, 51.6, 35.0; HRMS (ESI) calcd for $C_{22}H_{20}N_2O_4S_2Na$ ([M + Na]$^+$) 463.0757, found 463.0763.

General Procedure for the Diels−Alder Reaction of Furan-Fused 1,4-Thiazepine with Benzynes. To a solution of furan-fused 1,4-thiazpines **3**, **6**, or **10** (0.2 mmol) and benzyne precursors **13a−h** (0.3 mmol) in acetonitrile was added CsF (0.6 mmol). The mixture was heated to reflux for 1.5 h. On completion of the reaction, the solvent was removed under vacuum and diethyl ether was added to precipitate the salt. The solid was filtered off through a short pad of neutral Al_2O_3 column and the filtrate was concentrated. The residue was then recrystallized from CH_2Cl_2/hexane to afford the desired products **14a−q**.

1,4-Thiazepine-fused 7-oxanorbornadiene 14a: pale yellow solid; mp 205−207 °C; IR (KBr) υ 3056, 2976, 2935, 1749, 1618, 1446, 1314, 1184, 1065, 852, 751, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01(d, J = 7.2 Hz, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.51 (d, J = 9.2 Hz, 2H), 7.08−7.02 (m, 2H), 6.82 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.78 (s, 3H), 3.72 (s, 3H), 3.44 (q, J = 6.8 Hz, 1H), 2.90 (q, J = 6.8 Hz, 1H), 1.90 (s, 3H), 1.72 (s, 3H), 1.31 (s, 3H), 0.52 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 167.5, 162.7, 157.8, 148.9, 148.6, 140.1, 134.2, 130.0, 125.8, 124.6, 122.1, 120.6, 119.9, 112.5, 97.1, 87.0, 55.1, 52.4, 50.1, 49.5, 31.4, 24.9, 23.1, 17.5, 14.0; HRMS (ESI) calcd for $C_{29}H_{31}NO_6SNa$ ([M + Na]$^+$) 544.1764, found 544.1772.

1,4-Thiazepine-fused 7-oxanorbornadiene 14b: yellow solid; mp 216−218 °C; IR (KBr) υ 3059, 2978, 2936, 1754, 1619, 1448, 1316, 1186, 1066, 855, 754, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.2 Hz, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.48 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.11−7.00 (m, 2H), 3.90 (s, 3H), 3.72 (s, 3H), 3.47−3.40 (m, 1H), 2.91−2.85 (m, 1H), 1.90 (s, 3H), 1.73 (s, 3H), 1.33 (s, 3H), 0.51 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 167.4, 162.7, 148.7, 148.4, 141.5, 140.5, 130.7, 130.3, 126.0, 124.6, 124.5, 121.4, 120.8, 120.5, 120.4, 96.8, 87.2, 52.6, 51.1, 49.9, 49.6, 24.8, 23.1, 17.6, 12.1; HRMS (ESI) calcd for $C_{28}H_{28}BrNO_5SNa$ ([M + Na]$^+$) 592.0764, found 592.0776.

1,4-Thiazepine-fused 7-oxanorbornadiene 14e: yellow solid; mp 213−215 °C; IR (KBr) υ 3058, 2979, 2932, 1749, 1613, 1444, 1318, 1180, 1067, 850, 749, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.62 (m, 8H), 7.46 (d, J = 8.0 Hz, 2H), 7.25−7.10 (m, 6H), 6.93 (t, J = 7.4 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 4.19−4.13 (m, 2H), 2.85 (q, J = 6.4 Hz, 2H), 2.42 (q, J = 6.8 Hz, 2H), 1.61 (s, 3H), 1.24 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 0.52 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 168.4, 166.6, 148.1, 147.6, 143.1, 142.0, 141.8, 138.7, 131.8, 130.5, 130.4, 130.0, 129.5, 127.2, 127.0, 126.9, 126.8, 126.4, 125.5, 124.9, 124.2, 120.6, 119.4, 96.4, 88.2, 61.7, 58.5, 51.4, 22.9, 16.6, 13.8, 13.1; HRMS (ESI) calcd for $C_{39}H_{34}BrNO_4SNa$ ([M + Na]$^+$) 714.1284, found 714.1269.

1,4-Thiazepine-fused 7-oxanorbornadiene 14f: pale yellow solid; mp 208−211 °C; IR (KBr) υ 3055, 2998, 2948, 1752, 1701, 1561, 1201, 1142, 808, 754, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 6.8 Hz, 1H), 7.19−7.08 (m, 6H), 6.83 (d, J = 7.6 Hz, 1H), 6.74 (t, J = 7.6 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 3.16 (q, J = 6.9 Hz, 1H), 2.62 (q, J = 6.8 Hz, 1H), 1.79 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.28 (s, 9H), 1.21 (s, 3H), 0.51 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5, 167.1, 159.6, 148.8, 147.8, 143.4, 143.3, 142.4, 131.7, 130.8, 130.5, 127.0, 126.8, 126.6, 126.1, 124.8, 124.7, 124.1, 119.8, 118.3, 95.8, 89.0, 61.8, 58.0, 50.0, 45.3, 27.0, 22.8, 17.3, 14.1, 13.7; HRMS (ESI) calcd for $C_{37}H_{39}NO_4SNa$ ([M + Na]$^+$) 616.2492, found 616.2493.

1,4-Thiazepine-fused 7-oxanorbornadiene 14*l*: white solid; mp 221−223 °C; IR (KBr) υ 3052, 2973, 2895, 1745, 1583, 1456, 1270, 1065, 1034, 855, 744, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 7.6 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 8.8 Hz, 3H), 7.54 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.6 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.21−7.11 (m, 6H), 4.39−4.33 (m, 2H), 2.69−2.64 (m, 1H), 2.29−2.24 (m, 1H), 1.56 (s, 3H), 1.22 (t, J = 7.6 Hz, 6H), 0.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.1, 169.0, 166.9, 148.0, 146.8, 143.2, 142.2, 142.0, 138.4, 132.2, 132.0, 130.5, 130.5, 129.8, 128.1, 127.7, 127.3, 127.0, 126.8, 126.5, 126.3, 125.6, 125.5, 125.1, 124.9, 122.8, 119.4, 97.2, 90.8, 62.1, 58.3, 51.5, 22.9, 16.4, 13.9, 13.8; HRMS (ESI) calcd for $C_{43}H_{36}BrNO_4SNa$ ([M + Na]$^+$) 764.1441, found 764.1453.

1,4-Thiazepine-fused 7-oxanorbornadiene 14q: yellow solid; mp 215−217 °C; IR (KBr) υ 3058, 2978, 2928, 1741, 1585, 1445, 1134, 1095, 754, 720, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ =9.21 (d, J = 5.2 Hz, 1H), 8.62 (d, J = 7.6 Hz, 1H), 8.53 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 5.6 Hz, 2H), 7.87 (s, 1H), 7.75 (s, 2H), 7.60 (s, 4H), 7.39−7.32 (m, 4H), 7.23−7.16 (m, 3H), 7.00 (d, J = 7.2 Hz, 2H), 6.95 (d, J = 6.8 Hz, 1H), 4.46−4.23 (m, 2H), 2.77 (br, 1H), 2.36 (q, J = 6.5 Hz, 1H), 1.61 (s, 3H), 1.21 (t, J = 6.8 Hz, 3H), 1.16 (s, 3H), 0.27 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 167.5, 147.5, 143.8, 141.4, 138.1, 132.0, 130.6, 130.2, 130.1, 129.8, 129.3, 128.8, 128.1, 127.3, 127.0, 127.0, 126.6, 126.5, 126.0, 125.8, 125.4, 125.4, 124.7, 124.6, 122.9, 122.5, 102.1, 102.1, 89.8, 62.5, 56.6, 49.1, 22.0, 15.6, 13.8, 13.8; HRMS (ESI) calcd for $C_{47}H_{38}BrNO_4SNa$ ([M + Na]$^+$) 814.1597, found 814.1587.

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Supporting Information Available: Crystallographic information files (CIF) for compound **7**, **11**, and **14e**, experimental procedures and characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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