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Expeditious synthesis of *N*-bridged heterocycles via dipolar cycloaddition of pentafulvenes with 3-oxidopyridinium betaines

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ABSTRACT

A new and highly versatile approach towards the synthesis of bicyclo[6.3.0]undecanes and bicyclo[5.3.0]decanes was accomplished. The methodology adopted involved [6+3] and [3+2] cycloaddition reactions of pentafulvenes with 3-oxidopyridinium betaines generated either by the action of a base on the pyridinium salt or thermally from pyridinium betaine dimer. These well-functionalized bicyclo[6.3.0]undecanes and bicyclo[5.3.0]decanes offer a wide range of synthetic options, which can be expected to translate into a variety of rapid and efficient synthesis of natural products.

1. Introduction

Fulvenes have intrigued chemists for more than a century due to their theoretical, mechanistic and synthetic importance.[1] Among the various fulvenes, pentafulvenes embody an attractive structural unit as a valuable building block to access polycyclic cyclopentanoids through a diverse array of cycloadditions.[2] Cycloadditions of pentafulvenes (e.g., [4+3],[3] [2+2],[4] [4+2],[5] [2+4],[6] [6+4],[7] [6+2][8]) offer rapid generation of molecular complexity in a relatively easy manner.

Recently, we have reported a novel and efficient dipolar cycloaddition of pentafulvenes with 3-oxidopyrylium betaines, leading to oxabridged bicyclo[6.3.0]undecanes.[9] 3-Oxidopyridinium betaines, derived from 3-hydroxy pyridinium salts are versatile cycloaddition components capable of demonstrating various cycloaddition profiles. They can act as 4π,[10] 2π/6π[11] or as 8π[12] component providing access to a large number of new systems. The participation of pyridinium betaines in 1,3-dipolar cycloaddition was extensively studied by Katritzky et al.[10–13] for the synthesis of core fragments of tropone alkaloids and related natural products. Apart from few reports on the cycloadditions of 3-oxidopyridinium betaines with certain 6π-addends,[13] its reactivity in cycloaddition with pentafulvenes have not been investigated in detail. As part of our interest[9,14] in the chemistry of pentafulvenes aimed at the construction of complex and structurally interesting polycyclic systems, we undertook a detailed study of the reactivity of a variety of pentafulvenes towards 3-oxidopyridinium betaines. The 3-oxidopyridinium betaines used in the study was generated either from pyridinium salt by adding a base at room temperature or by heating pyridinium betaine dimer at elevated temperatures. The details of our investigations are presented in the following sections.

2. Results and discussion

2.1. Base catalyzed generation of betaines

Pentafulvenes selected for our studies were synthesized from the corresponding ketone following Little's procedure.[15] The pyridinium salts,[16] precursors for 3-oxidopyridinium betaines, were synthesized by heating 3-hydroxypyridine with corresponding aryl halides in THF under reflux.

Our initial studies were focused on the reaction of 1-(2-pyrimidyl)-3-oxidopyridinium betaine **2**, generated from 3-hydroxy-1-(2-pyrimidyl)pyridinium bromide **1**, with 6,6-diphenyl fulvene **3**. The reaction proceeded through a [6+3] cycloaddition mode and afforded the adduct **4**, which then rearranged to the more stable adduct **3a** through a 1,5-H shift (Scheme 1).

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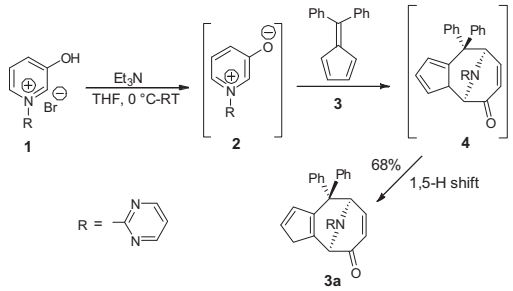


Scheme 1.

The product **3a** was characterized on the basis of spectroscopic data and its structure and stereochemistry was unambiguously confirmed by single crystal X-ray analysis[17] (Fig. 1).

Similar reactivity was observed with other pentafulvenes and bicyclo[6.3.0]undecanes were obtained in moderate to good yields. We also carried out the cycloaddition of various pentafulvenes with 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine derived from 3-hydroxy-1-(5-nitro-2-pyridyl)pyridinium bromide **10**. The results obtained by the reaction of various pentafulvenes with 1-(2-pyrimidyl)-3-oxidopyridinium and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaines are summarized in Table 1.

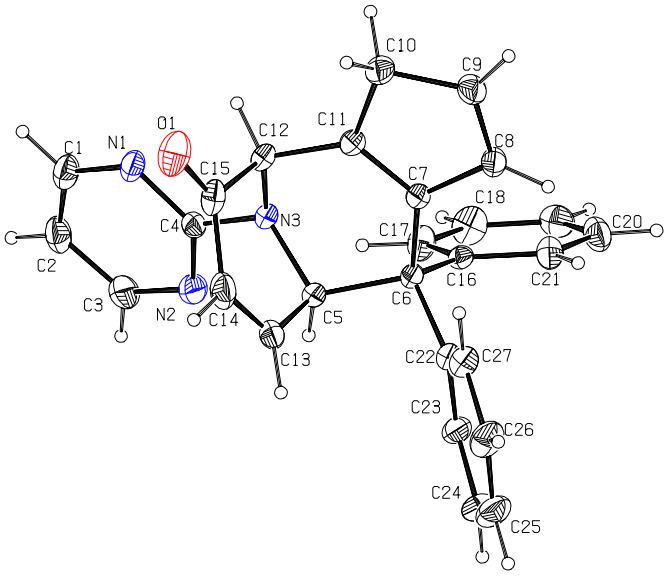
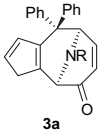
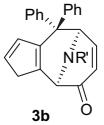
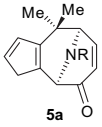
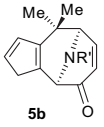
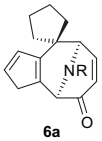
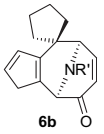
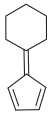
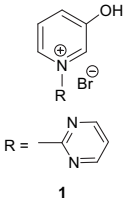
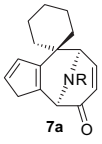
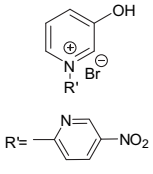
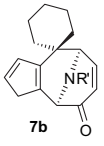
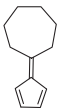
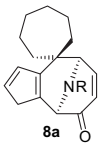
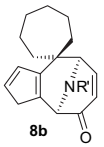
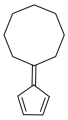
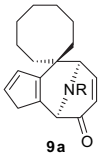
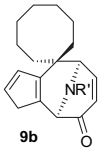


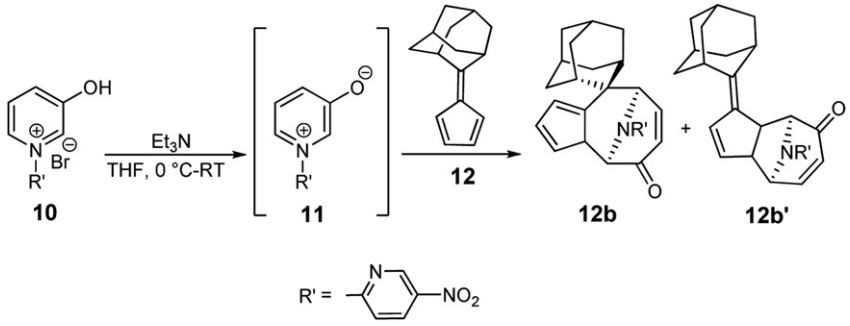
Fig. 1. ORTEP plot for X-ray crystal structure of **3a**.

Table 1
[6+3] Cycloaddition of pentafulvenes with 1-(2-pyrimidyl)-3-oxidopyridinium betaine and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine

Entry	Fulvene	Pyridinium salt	Product	Yield(%)	Entry	Pyridinium salt	Product	Yield(%)
1	 **3**		 **3a**	68	7		 **3b**	66
2	 **5**		 **5a**	72	8		 **5b**	70
3	 **6**		 **6a**	65	9		 **6b**	66
4	 **7**	 **1**	 **7a**	66	10	 **10**	 **7b**	63
5	 **8**		 **8a**	64	11		 **8b**	65
6	 **9**		 **9a**	68	12		 **9b**	63

Reaction conditions: pentafulvene (1.0 equiv), pyridinium salt (1.2 equiv), Et_3N (1.2 equiv), THF, 0 °C-RT, 6 h.

As reported in our earlier studies with 3-oxidopyrylium betaines, the adamantylidenefulvene **12** on reaction with 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine **11** afforded a mixture of [6+3] and [3+2] adducts **12b** and **12b′** in 62% yield. Interestingly, compared to other fulvenes studied, 1,5-H shift was not observed in the [6+3] adduct **12b**. This could be due to the sensitivity of the cycloaddition reaction to the steric bulk of the adamantyl substituent. The reaction is shown in Scheme 2.



Scheme 2.

The structure of [6+3] adduct **12b** was established by various spectroscopic techniques and confirmed using single crystal X-ray analysis[18] (Fig. 2).

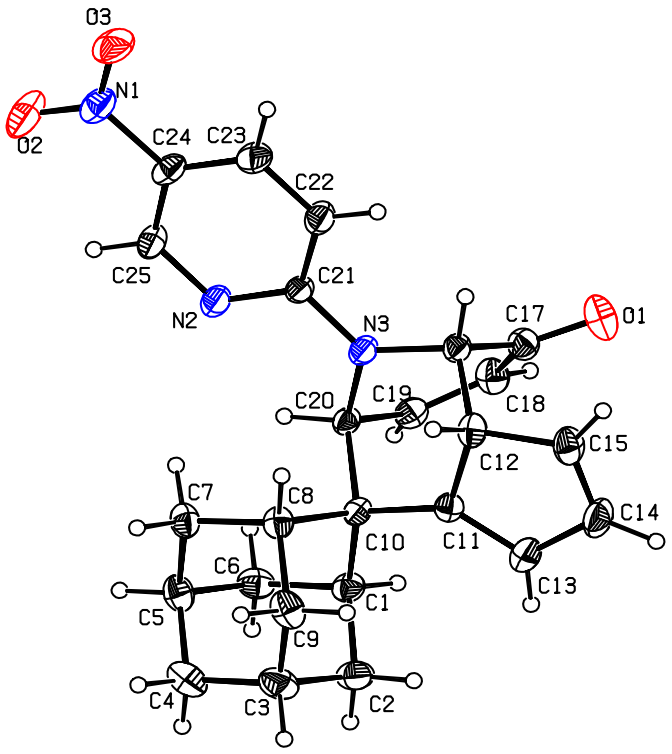


Fig. 2. ORTEP plot for X-ray crystal structure of **12b**.

The 6,6-dithiodimethylenefulvene underwent smooth reaction with betaines **1** and **10** at room temperature, which resulted in the formation of [6+3] adducts [**13a** and **13b**] and an inseparable regioisomeric mixture (1:1) of [3+2] adducts [**13a′** and **13b′**] (Table 2). This could be attributed to the decrease in the electron density of 6,6-dithiodimethylenefulvene caused by the hyperconjugation of empty d orbitals of sulfur and olefin π-electrons.[19] The results obtained for the cycloaddition of adamantylidenefulvene and 6,6-dithiodimethylenefulvene with 3-oxidopyridinium betaines are summarized in Table 2.

2.2. Thermal generation of betaines

The generation of betaines can also be carried out in a slow and controlled manner by heating the 3-oxidopyridinium betaine dimer above 100 °C.[13a,20] The controlled generation of betaines has an important role in cycloaddition reactions, since side reaction pathways, such as dimerizations and consecutive additions, which compete with the desired process can be minimized. Hence, we decided to investigate the cycloaddition profile of pentafulvenes with 3-oxidopyridinium betaines, produced at higher temperatures.

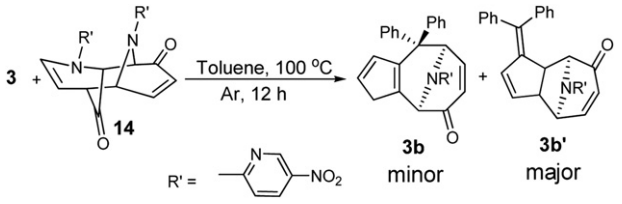
Table 2
Cycloaddition of adamantylidenefulvene and 6,6-dithiodimethylenefulvene with 3-oxidopyridinium betaines

Entry	Fulvene	Pyridinium salt	Products	Yield	
				6+3	3+2
1	12	10	12b, 12b′	36	26
2	13		13b, 13b′	38	31
3	12	1	12a, 12a′	38	26
4	13		13a, 13a′	40	32

Reaction conditions: pentafulvene (1.0 equiv), pyridinium salt (1.2 equiv), Et_3N (1.2 equiv), THF, 0 °C-RT, 6 h.

2.2.1. Thermal generation of betaines at 100 °C. Our studies were initiated by the reaction of 6,6-diphenyl fulvene **3** with 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine **11**, generated from 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer **14** by heating up to 100 °C, in dry toluene under argon atmosphere for 12 h. The reaction afforded a mixture of [6+3], **3b** and [3+2] adduct, **3b′**, with the latter as the major product (Scheme 3).

The structures of both the products were assigned using the usual spectroscopic techniques and that of the [3+2] adduct **3b′** was confirmed by single crystal X-ray analysis[21] (Fig. 3).



Scheme 3.

phenyl substituents and alkyl substituents at the exocyclic position of pentafulvenes, which greatly influences the periselectivity of pentafulvenes towards cycloaddition reactions. The results are shown in Table 3.

The cycloaddition of pentafulvenes with 1-(2-pyrimidyl)-3-oxidopyridinium betaine dimer was also investigated and the reactions resulted in the formation of the corresponding [6+3] and [3+2] adducts in moderate to good yields and the results obtained are summarized in Table 4.

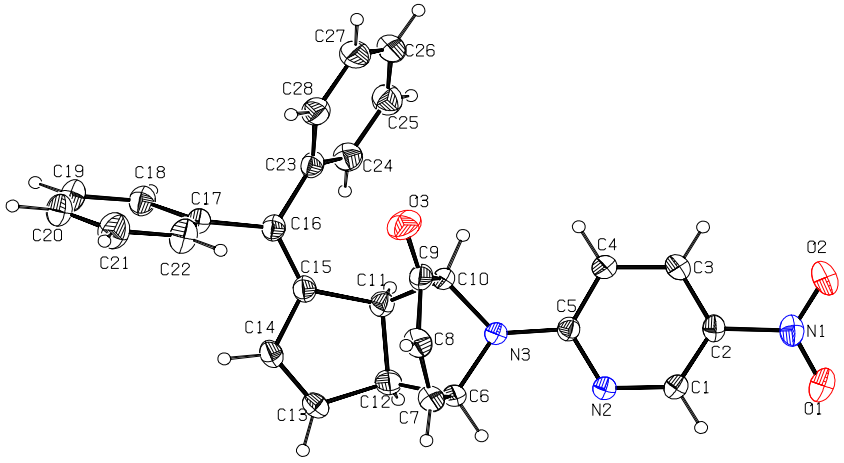
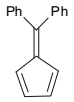
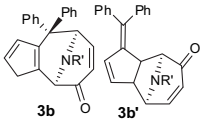
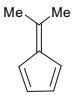
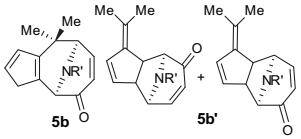
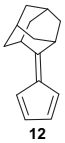
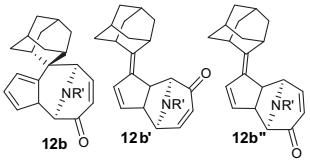
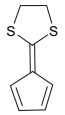
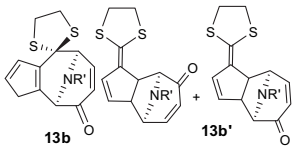


Fig. 3. ORTEP plot for X-ray crystal structure of **3b'**.

The cycloaddition of dimethyl fulvene and 6,6-dithiodimethylenefulvene with 3-oxidopyridinium betaine **11** resulted in the formation of [6+3] adduct along with an inseparable 1:1 regioisomeric mixture of [3+2] adducts. In the case of adamantylidenefulvene, we were able to separate the isomers. This may be due to the difference in the electronic nature between

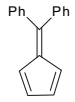
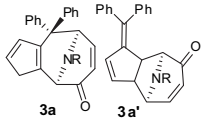
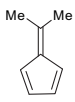
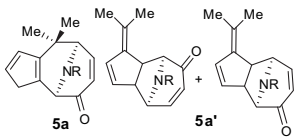
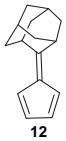
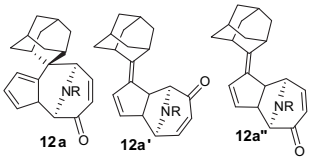
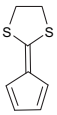
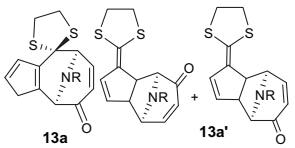
2.2.2. Thermal generation of betaines at 140 °C. Interestingly, when we conducted the cycloaddition reaction of 6,6-diphenyl fulvene with 3-oxidopyridinium betaines generated at 140 °C from their corresponding pyridinium betaine dimer, the reaction afforded exclusively the [3+2] adduct, the product of thermodynamic control. The cycloaddition of diphenyl fulvene **3** with 1-(5-nitro-2-

Table 3
Cycloaddition of pentafulvenes and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer **14** at 100 °C

Entry	Fulvene	Products	Yield	
			6+3	3+2
1	 **3**	 **3b** **3b'**	28	44
2	 **5**	 **5b** **5b'**	20	52
3	 **12**	 **12b** **12b'** **12b"**	24	37
4	 **13**	 **13b** **13b'**	26	42

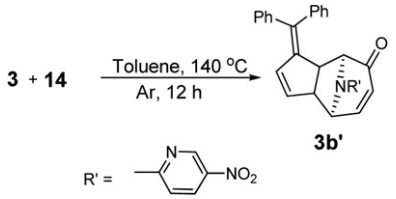
Reaction conditions: pentafulvene (1.0 equiv), 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer (1.2 equiv), toluene, 100 °C, 12 h.

Table 4
Cycloaddition of pentafulvenes with 1-(2-pyrimidyl)-3-oxidopyridinium betaine dimer at 100 °C

Entry	Fulvene	Products	Yield	
			6+3	3+2
1	 **3**	 **3a** **3a'**	30	46
2	 **5**	 **5a** **5a'**	23	54
3	 **12**	 **12a** **12a'** **12a"**	27	42
4	 **13**	 **13a** **13a'**	23	45

Reaction conditions: pentafulvene (1.0 equiv), 1-(2-pyrimidyl)-3-oxidopyridinium betaine dimer (1.2 equiv), toluene, 100 °C, 12 h.

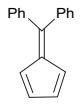
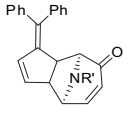
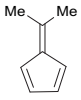
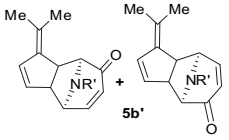
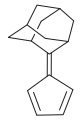
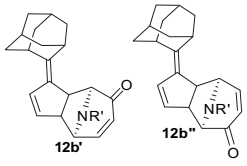
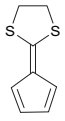
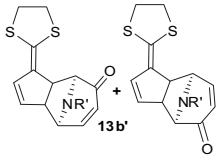
pyridyl)-3-oxidopyridinium betaine dimer **14** is depicted in the Scheme 4.



Scheme 4.

The cycloaddition of dimethyl fulvene and 6,6-dithiodimethylenefulvene with 3-oxidopyridinium betaine **11** resulted in the formation of an inseparable 1:1 regioisomeric mixture of [3+2] adducts. The results obtained with various pentafulvenes and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer **14** are shown in Table 5.

Table 5
Cycloaddition of pentafulvenes and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer **14** at 140 °C

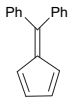
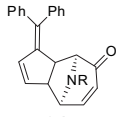
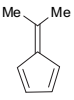
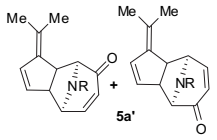
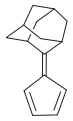
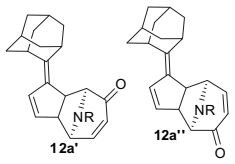
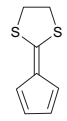
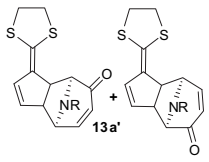
Entry	Fulvene	Products	Yield (%)
1	 **3**	 **3b'**	68
2	 **5**	 **5b'**	78
3	 **12**	 **12b'** **12b''**	60
4	 **13**	 **13b'**	66

Reaction conditions: pentafulvene (1.0 equiv), 1-(5-nitro-2-pyridyl)-3-oxidopyridinium betaine dimer (1.2 equiv), toluene, 140 °C, 12 h.

(1-Pyrimidyl)-3-oxidopyridinium betaine dimer also reacted in a similar manner and the results obtained for the reaction with various pentafulvenes are summarized in Table 6. It is presumed that by using appropriately functionalized pentafulvenes and oxidopyridinium betaines, the present methodology may be useful in the synthesis of a number of cycloheptanoid natural products. The presence of an α,β-unsaturated ketone, a nitrogen bridge and the cyclopentane functionality makes these adducts amenable to a number of synthetic transformations.

The synthesized bicyclo[6.3.0]undecane and bicyclo[5.3.0]decane ring systems are prevalent in nature and have been identified as the key structural units in a number of biologically active compounds (Fig. 4).[22,23] The construction of compounds, incorporating bicyclo[6.3.0]undecane and bicyclo[5.3.0]decane ring systems have thus elicited considerable synthetic efforts over the past several decades.[24–28] Here we were successful in accomplishing the synthesis of 5–7 fused and 5–8 fused bridged frameworks in a simple and efficient manner.

Table 6
Cycloaddition of pentafulvenes and 1-(2-pyrimidyl)-3-oxidopyridinium betaine dimer at 140 °C

Entry	Fulvene	Products	Yield (%)
1	 **3**	 **3a'**	72
2	 **5**	 **5a'**	78
3	 **12**	 **12a'** **12a''**	64
4	 **13**	 **13a'**	69

Reaction conditions: pentafulvene (1.0 equiv), 1-(2-pyrimidyl)-3-oxidopyridinium betaine dimer (1.2 equiv), toluene, 140 °C, 12 h.

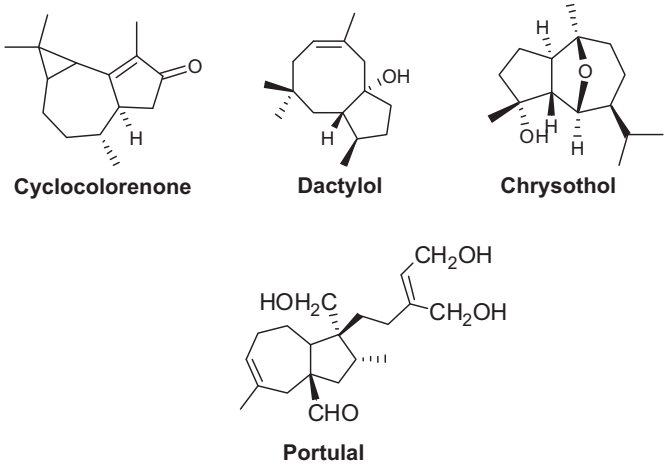


Fig. 4. Some biologically active bicyclo[6.3.0]undecane and bicyclo[5.3.0]decane ring systems.

3. Conclusion

In conclusion, we have explored, in detail, the cycloaddition profile of pentafulvenes with 3-oxidopyridinium betaines, generated under base catalyzed condition and at elevated temperatures. A careful manipulation of the reaction conditions have paved the way for the efficient synthesis of bicyclo[6.3.0]undecane as the kinetic adduct and bicyclo[5.3.0]decanes as the thermodynamic adduct. The methodology assumes significance as bicyclo[6.3.0]undecane and bicyclo[5.3.0]decane frameworks are important synthetic intermediates for a variety of natural products. Application of these compounds in the synthesis of natural products is ongoing and will be reported in due course.

4. Experimental section

4.1. General

All reactions were carried out in oven-dried glasswares under an atmosphere of argon. Progress of reactions were monitored by Thin Layer Chromatography (Silica gel 60 F_{254}, 0.25 mm, Merck), and purification was effected using silica gel column chromatography. NMR spectra were recorded at 300 (^{1}H) and 125 (^{13}C) MHz, respectively, on a Bruker DPX-300 MHz and Bruker AMX-500 spectrometers. Chemical shifts δ were reported relative to TMS (^{1}H) and $CDCl_3$ (^{13}C) as the internal standards. Coupling constants (J) are reported in Hertz (Hz). IR spectra were recorded on a Shimadzu FT-IR spectrophotometer. Mass spectra were recorded under EI/HRMS or FAB/LRMS using JEOL JMS 600H mass spectrometer. Melting points were recorded on a Buchi melting point apparatus and are uncorrected. Pentafulvenes were prepared according to the literature procedure.[15] The pyridinium salts,[16] precursors for 3-oxidopyridinium betaines, were synthesized by heating 3-hydroxypyridine with the corresponding aryl halides in THF under reflux and the pyridinium betaine dimers were synthesized from the corresponding pyridinium salts by treating with Et_3N in CH_3CN at room temperature. Commercial grade solvents were distilled prior to use. Triethylamine, THF and toluene were dried as per the standard procedures.

4.1.1. General experimental procedure for base catalyzed reaction. The pentafulvene (1 mmol) and pyridinium salt (1.2 mmol) were taken in an R.B. and dry THF was added and cooled to 0 °C in an ice bath and dry triethylamine (1.2 mmol) was added and stirred for 6 h under argon atmosphere. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel (60–120 mesh) using 15% ethyl acetate/hexane mixture as eluent to afford the product as a pale yellow crystalline solid. The product was recrystallized from ethyl acetate/hexane mixture.

4.1.2. General experimental procedure for temperature assisted reaction. The pentafulvene (1 mmol) and pyridinium salt dimer (1.2 mmol) were taken in an R.B. and 3 ml dry toluene is added and refluxed for 12 h under argon atmosphere at 100/140 °C. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel (60–120 mesh) using 15% ethyl acetate/hexane mixture as eluent to afford the products as pale yellow crystalline solids. The products were recrystallized from ethyl acetate/hexane mixture.

4.2. Spectroscopic data for new compounds

Compound **3a**. Yield: 68% as pale yellow solid. R_f: 0.53 (7:3 hexane/EtOAc). Mp=206 °C. IR (KBr) ν_{max}: 3005, 2956, 2926, 1689, 1581, 1556, 1492, 1442, 1431, 1425, 1392, 1373, 1238, 1221, 1184 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.44 (d, 2H, J=4.44 Hz), 7.59–7.56 (m, 2H), 7.29–7.16 (m, 6H), 7.07–7.04 (m, 2H), 6.71–6.67 (m, 2H), 6.49–6.43 (m, 2H), 6.06–6.01 (m, 1H), 5.85 (s, 1H), 5.67 (d, 1H, J=10.20 Hz), 3.29–3.08 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.8, 161.5, 157.9, 143.1, 142.6, 134.3, 133.4, 133.1, 132.7, 130.5, 129.7, 128.5, 128.4, 128.1, 128.0, 127.1, 126.2, 112.2, 60.1, 59.4, 41.2, 36.7. HRMS (EI): m/z calcd for $C_{27}H_{21}N_3O$: 403.1685. Found: (M^+) 403.1694.

Compound **5a**. Yield: 72% as pale yellow solid. R_f: 0.54 (7:3 hexane/EtOAc). Mp=176 °C. IR (KBr) ν_{max}: 3010, 2924, 2848, 1690, 1574, 1548, 1472, 1448, 1383, 1214, 1193, 1085 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, 2H, J=4.71 Hz), 7.01–6.96 (m, 1H), 6.54–6.47 (m, 1H), 6.41–6.38 (m, 2H), 5.88–5.80 (m, 2H), 5.50 (d, 1H, J=5.04 Hz), 3.03–2.85 (m, 2H), 1.35 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8, 160.9, 157.5, 147.2, 145.9, 131.6, 129.3, 125.6, 110.6, 59.2, 56.7, 40.8, 38.2, 29.0, 23.4. HRMS (EI): m/z calcd for $C_{17}H_{17}N_3O$: 279.1372. Found: (M^+) 279.1375.

Compound **6a**. Yield: 65% as pale yellow solid. R_f: 0.51 (7:3 hexane/EtOAc). Mp=184 °C. IR (KBr) ν_{max}: 3013, 2920, 2841, 1693, 1565, 1551, 1476, 1441, 1380, 1215, 1190, 1076 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, 2H, J=4.50 Hz), 7.03–6.98 (m, 1H), 6.56–6.53 (m, 1H), 6.43–6.41 (m, 2H), 5.89–5.86 (m, 2H), 5.60 (d, 1H, J=4.82 Hz), 3.08–2.91 (m, 2H), 1.93–1.70 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.4, 161.1, 157.6, 147.4, 145.7, 131.6, 130.7, 125.5, 125.3, 110.9, 59.3, 58.6, 41.0, 39.3, 33.5, 25.8, 25.5, 24.3. HRMS (EI): m/z calcd for $C_{19}H_{19}N_3O$: 305.1528. Found: (M^+) 305.1530.

Compound **7a**. Yield: 66% as pale yellow solid. R_f: 0.56 (7:3 hexane/EtOAc). Mp=189 °C. IR (KBr) ν_{max}: 3018, 2927, 2856, 1701, 1583, 1554, 1469, 1394, 1377, 1242, 1182, 1016 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (d, 2H, J=4.65 Hz), 7.00–6.93 (m, 1H), 6.46–6.42 (m, 2H), 6.33–6.32 (m, 1H), 6.03–6.00 (m, 1H), 5.83–5.77 (m, 2H), 2.99–2.82 (m, 2H), 1.94–1.56 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.0, 161.0, 157.8, 147.6, 146.5, 133.4, 132.4, 130.5, 125.9, 110.7, 59.2, 58.5, 42.2, 41.2, 34.8, 31.8, 25.7, 22.3, 21.5. HRMS (EI): m/z calcd for $C_{20}H_{21}N_3O$: 319.1685. Found: (M^+) 319.1691.

Compound **8a**. Yield: 64% as pale yellow solid. R_f: 0.54 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3015, 2921, 2840, 1695, 1571, 1542, 1471, 1445, 1380, 1212, 1183, 1089 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (d, 2H, J=4.80 Hz), 7.06–7.01 (m, 1H), 6.54–6.51 (m, 2H), 6.43–6.40 (m, 1H), 5.88–5.84 (m, 2H), 5.73 (d, 1H, J=4.56 Hz), 3.10–2.84 (m, 2H), 1.89–1.61 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.6, 161.2, 157.7, 147.7, 133.6, 131.2, 130.3, 125.8, 110.98, 61.7, 59.4, 40.5, 39.8, 34.5, 31.3, 30.5, 23.9, 23.6. HRMS (EI): m/z calcd for $C_{21}H_{23}N_3O$: 333.1841. Found: (M^+) 333.1843.

Compound **9a**. Yield: 68% as pale yellow solid. R_f: 0.53 (7:3 hexane/EtOAc). Mp=192 °C. IR (KBr) ν_{max}: 3016, 2931, 2840, 1692, 1571, 1540, 1472, 1448, 1383, 1214, 1193, 1085 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (d, 2H, J=4.88 Hz), 7.01–6.96 (m, 1H), 6.54–6.50 (m, 2H), 6.46–6.38 (m, 1H), 5.90–5.84 (m, 2H), 5.77–5.73 (m, 1H), 3.13–2.86 (m, 2H), 1.97–1.59 (m, 14H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.8, 161.1, 157.6, 147.9, 132.9, 131.8, 130.4, 110.8, 65.7, 59.5, 45.0, 40.9, 34.6, 29.8, 29.4, 27.7, 25.4, 22.7, 22.1. HRMS (EI): m/z calcd for $C_{22}H_{25}N_3O$: 347.1998. Found: (M^+) 347.2006.

Compound **3b**. Yield: 66% as pale yellow solid. R_f: 0.57 (7:3 hexane/EtOAc). Mp=216 °C. IR (KBr) ν_{max}: 3010, 2956, 2926, 2856, 1734, 1589, 1506, 1463, 1408, 1375, 1340, 1296, 1211, 1170 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.20 (d, 1H, J=2.61 Hz), 8.31 (dd, 1H, J_1=2.67 Hz, J_2=9.36 Hz), 7.52–7.49 (m, 2H), 7.29–7.19 (m, 6H), 7.07–7.04 (m, 2H), 6.79 (d, 1H, J=9.42 Hz), 6.77–6.48 (m, 3H), 6.13–6.08 (m, 1H), 5.71 (d, 1H, J=9.92 Hz), 5.26 (s, 1H), 3.41–3.18 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.9, 159.8, 143.4, 142.1, 133.5, 133.1, 132.5, 132.0, 129.2, 128.5, 128.3, 128.2, 127.7, 127.6, 126.7, 106.5, 62.0, 57.3, 41.1, 38.5. HRMS (EI): m/z calcd for $C_{28}H_{21}N_3O_3$: 447.1583. Found: (M^+) 447.1585.

Compound **5b**. Yield: 70% as pale yellow solid. R_f: 0.55 (7:3 hexane/EtOAc). Mp=185 °C. IR (KBr) ν_{max}: 3012, 2970, 1695, 1589, 1494, 1334, 1296, 1122, 1080 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95 (d, 1H, J=2.58 Hz), 8.16 (dd, 1H, J_1=2.71 Hz, J_2=9.42 Hz), 7.04–6.94 (m, 1H), 6.68–6.59 (m, 1H), 6.40–6.28 (m, 2H), 5.90–5.83 (m, 1H), 5.37 (br s, 2H), 3.00–2.84 (m, 2H), 1.30 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.2, 159.6, 136.0, 134.3, 133.4, 132.3, 130.1, 130.0, 125.5, 125.3, 104.9, 61.1, 60.3, 41.0, 38.8, 29.0, 23.3. HRMS (EI): m/z calcd for $C_{18}H_{17}N_3O_3$: 323.1270. Found: (M^+) 323.1272.

Compound **6b**. Yield: 66% as pale yellow solid. R_f: 0.53 (7:3 hexane/EtOAc). Mp=190 °C. IR (KBr) ν_{max}: 3010, 2960, 1697, 1568, 1486, 1351, 1293, 1121, 1080 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (d, 1H, J=2.74 Hz), 8.25 (dd, 1H, J_1=2.70 Hz, J_2=9.30 Hz), 7.04–6.99 (m, 1H), 6.68–6.64 (m, 1H), 6.49–6.38 (m, 2H), 5.93 (d 1H,

J=10.27 Hz), 5.63 (br s, 1H), 5.38 (br s, 1H), 3.07–2.95 (m, 2H), 1.91–1.70 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.0, 159.4, 135.8, 134.5, 133.2, 132.1, 130.5, 130.0, 125.4, 125.1, 104.9, 61.1, 60.4, 41.0, 39.4, 35.2, 33.4, 25.7, 24.2. HRMS (EI): *m*/*z* calcd for $C_{20}H_{19}N_3O_3$: 349.1426. Found: (M^+) 349.1428.

Compound **7b**. Yield: 63% as pale yellow solid. R_f: 0.52 (7:3 hexane/EtOAc). Mp=190 °C. IR (KBr) ν_{max}: 3008, 2964, 1696, 1576, 1497, 1340, 1290, 1125, 1082 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.06 (d, 1H, *J*=2.49 Hz), 8.24 (dd, 1H, J_1=2.64 Hz, J_2=9.42 Hz), 7.10–7.03 (m, 1H), 6.70–6.61 (m, 1H), 6.50–6.43 (m, 2H), 6.18 (br s, 1H), 5.97–5.92 (m, 1H), 5.28 (br s, 1H), 3.08–3.01 (m, 2H), 1.93–1.61 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.9, 159.6, 135.8, 134.1, 133.4, 132.4, 130.8, 130.3, 130.0, 125.5, 104.7, 61.2, 60.4, 41.2, 39.7, 36.5, 31.7, 25.5, 22.4, 21.7. HRMS (EI): *m*/*z* calcd for $C_{21}H_{21}N_3O_3$: 363.1583. Found: (M^+) 363.1587.

Compound **8b**. Yield: 65% as pale yellow solid. R_f: 0.55 (7:3 hexane/EtOAc). Mp=190 °C. IR (KBr) ν_{max}: 3008, 2962, 1697, 1574, 1496, 1342, 1284, 1135, 1086 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (d, 1H, *J*=2.79 Hz), 8.24 (dd, 1H, J_1=2.70 Hz, J_2=9.30 Hz), 7.07–7.00 (m, 1H), 6.65–6.61 (m, 1H), 6.48–6.34 (m, 2H), 5.94–5.90 (m, 1H), 5.71 (br s, 1H), 5.40 (br s, 1H), 3.16–2.96 (m, 2H), 1.82–1.54 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.2, 159.7, 135.8, 134.4, 133.4, 132.1, 130.7, 129.6, 129.3, 125.6, 104.7, 61.0, 59.8, 40.6, 38.9, 34.6, 31.4, 30.7, 23.9, 23.6. HRMS (EI): *m*/*z* calcd for $C_{22}H_{23}N_3O_3$: 377.1739. Found: (M^+) 377.1742.

Compound **9b**. Yield: 63% as pale yellow solid. R_f: 0.55 (7:3 hexane/EtOAc). Mp=190 °C. IR (KBr) ν_{max}: 3008, 2966, 1694, 1571, 1499, 1355, 1282, 1121, 1073 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.03 (d, 1H, *J*=2.41 Hz), 8.24 (dd, 1H, J_1=2.75 Hz, J_2=9.30 Hz), 7.03–6.98 (m, 1H), 6.73–6.63 (m, 1H), 6.45–6.36 (m, 2H), 5.93–5.88 (m, 1H), 5.61 (br s, 1H), 5.43 (br s, 1H), 3.17–2.90 (m, 2H), 1.93–1.68 (m, 14H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.4, 159.7, 135.9, 133.4, 132.3, 131.4, 129.9, 129.2, 125.7, 104.9, 65.9, 61.3, 41.0, 40.9, 34.8, 31.4, 29.6, 29.2, 28.0, 25.4, 25.0. HRMS (EI): *m*/*z* calcd for $C_{23}H_{25}N_3O_3$: 391.1896. Found: (M^+) 391.1898.

Compound **12b**. Yield: 36% as pale yellow solid. R_f: 0.48 (7:3 hexane/EtOAc). Mp=176 °C. IR (KBr) ν_{max}: 3026, 2914, 2856, 1685, 1593, 1504, 1483, 1423, 1338, 1296, 1211, 1124 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95 (d, 1H, *J*=1.20 Hz), 8.17–8.15 (m, 1H), 6.93–6.90 (m, 1H), 6.69 (d, 1H, *J*=5.43 Hz), 6.40–6.39 (m, 2H), 6.24 (m, 2H), 5.81 (d, 1H, *J*=6.00 Hz), 5.09 (br s, 1H), 3.34 (d, 1H, *J*=4.29 Hz), 2.49–2.46 (m, 2H), 2.29–2.26 (m, 1H), 2.00–1.53 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.5, 159.5, 148.0, 147.5, 146.0, 136.1, 133.8, 133.5, 131.2, 131.0, 129.8, 104.8, 64.5, 54.1, 52.8, 49.3, 38.9, 35.5, 34.6, 33.7, 33.7, 33.0, 32.4, 27.8, 27.5. HRMS (EI): *m*/*z* calcd for $C_{25}H_{25}N_3O_3$: 415.1896. Found: (M^+) 415.1897.

Compound **12b′**. Yield: 30% as pale yellow solid. R_f: 0.40 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3026, 2920, 2854, 1691, 1593, 1506, 1483, 1419, 1338, 1296, 1242, 1120, 1002 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.00 (d, 1H, *J*=2.45 Hz), 8.19 (dd, 1H, J_1=2.61 Hz, J_2=9.27 Hz), 6.97–6.92 (m, 1H), 6.60 (d, 1H, *J*=9.27 Hz), 6.45 (d, 1H, *J*=5.52 Hz), 5.89 (d, 1H, *J*=9.69 Hz), 5.65–5.62 (m, 1H), 5.44 (br s, 1H), 4.99 (br s, 1H), 4.14–4.07 (m, 1H), 3.99–3.93 (m, 1H), 2.78–2.64 (m, 3H), 1.97–1.73 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 159.4, 151.5, 146.2, 144.9, 136.7, 135.1, 133.1, 130.1, 129.2, 127.7, 107.2, 69.2, 57.8, 53.7, 45.6, 39.8, 39.6, 38.4, 37.1, 36.4, 34.9, 28.3, 27.9. HRMS (EI): *m*/*z* calcd for $C_{25}H_{25}N_3O_3$: 415.1896. Found: (M^+) 415.1898.

Compound **13b**. Yield: 38% as pale yellow solid. R_f: 0.51 (7:3 hexane/EtOAc). Mp=182 °C. IR (KBr) ν_{max}: 3020, 2956, 2926, 2854, 1734, 1595, 1462, 1377, 1340, 1294, 1118, 1047 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.06 (s, 1H), 8.29–8.26 (m, 1H), 7.22–7.16 (m, 1H), 6.78 (d, 1H, *J*=9.24 Hz), 6.63–6.40 (m, 2H), 5.93 (d, 1H, *J*=10.23 Hz), 5.81 (br s, 1H), 5.55 (br s, 1H), 3.69–3.46 (m, 4H), 3.17–3.15 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.1, 159.2, 159.1, 146.1, 133.6, 133.2, 131.2, 130.1, 125.5, 107.3, 67.5, 65.8, 60.0, 40.7, 39.6. HRMS (EI): *m*/*z* calcd for $C_{18}H_{15}N_3O_3S_2$: 385.0555. Found: (M^+) 385.0560.

Compound **13b′**. Mixture of regioisomers. Yield: 66% as pale yellow solid. R_f: 0.42 (7:3 hexane/EtOAc). IR (KBr) ν_{max}: 3037, 2926, 2856, 1732, 1460, 1375, 1246, 1081, 1047 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95–8.90 (m, 2H), 8.17–8.12 (m, 2H), 7.35–7.31 (m, 1H), 6.96–6.91 (m, 1H), 6.56–6.46 (m, 2H), 6.21–6.17 (m, 2H), 5.91–5.84 (m, 2H), 5.75–5.73 (m, 1H), 5.67–5.66 (m, 1H), 5.46–5.43 (m, 2H), 5.40 (br s, 1H), 5.27 (s, 1H), 5.03 (s, 1H), 4.77 (s, 1H), 3.96–3.94 (m, 2H), 3.58–3.56 (m, 1H), 3.47–3.29 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7, 192.2, 159.6, 151.0, 145.6, 136.2, 134.6, 133.2, 132.1, 131.3, 127.3, 107.4, 68.0, 59.7, 56.0, 49.4, 38.7. HRMS (EI): *m*/*z* calcd for $C_{18}H_{15}N_3O_3S_2$: 385.0555. Found: (M^+) 385.0561.

Compound **12a**. Yield: 38% as pale yellow solid. R_f: 0.49 (7:3 hexane/EtOAc). Mp=182 °C. IR (KBr) ν_{max}: 3003, 2918, 2856, 1681, 1583, 1554, 1469, 1450, 1396, 1224, 1188, 1099 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, 2H, *J*=4.74 Hz), 6.99–6.94 (m, 1H), 6.55–6.52 (m, 1H), 6.48–6.46 (m, 1H), 6.41–6.35 (m, 2H), 6.27 (s, 1H), 5.89–5.85 (m, 2H), 3.40 (d, 1H, *J*=7.11 Hz), 2.73–2.69 (m, 1H), 2.58–2.54 (m, 1H), 2.38–2.34 (m, 1H), 1.99–1.55 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.1, 157.8, 148.8, 148.0, 147.6, 133.1, 132.1, 130.8, 130.3, 128.7, 110.9, 67.8, 57.0, 53.7, 52.2, 38.9, 34.7, 34.4, 33.7, 33.1, 32.8, 32.0, 27.9, 27.6. HRMS (EI): *m*/*z* calcd for $C_{24}H_{25}N_3O$: 371.1998. Found: (M^+) 371.2003.

Compound **12a′**. Yield: 32% as pale yellow solid. R_f: 0.42 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3032, 2997, 2990, 2852, 1691, 1581, 1454, 1382, 1292, 1240, 1180, 1101, 1014 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, 2H, *J*=4.77 Hz), 6.94–6.89 (m, 1H), 6.61–6.58 (m, 1H), 6.43–6.41 (m, 1H), 5.90–5.86 (m, 1H), 5.61–5.60 (m, 1H), 5.39–5.36 (m, 1H), 5.22 (d, 1H, *J*=8.37 Hz), 4.09–4.04 (m, 1H), 3.94–3.89 (m, 1H), 2.77–2.70 (m, 2H), 2.25–2.21 (m, 1H), 1.97–1.69 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.9, 161.4, 157.8, 151.9, 144.3, 134.6, 130.6, 129.4, 128.1, 111.9, 68.4, 57.1, 54.2, 45.5, 39.8, 39.6, 38.5, 37.2, 37.1, 36.1, 34.9, 28.4, 28.0. HRMS (EI): *m*/*z* calcd for $C_{24}H_{25}N_3O$: 371.1998. Found: (M^+) 371.2008.

Compound **13a**. Yield: 40% as pale yellow solid. R_f: 0.53 (7:3 hexane/EtOAc). Mp=184 °C. IR (KBr) ν_{max}: 3001, 2958, 2927, 1691, 1579, 1556, 1448, 1386, 1373, 1242 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.29 (d, 2H, *J*=4.62 Hz), 7.16–7.10 (m, 1H), 6.55–6.52 (m, 2H), 6.35 (s, 1H), 6.00 (d, 1H, *J*=4.95 Hz), 5.82–5.78 (m, 2H), 3.59–3.51 (m, 2H), 3.48–3.41 (m, 2H), 3.18–3.07 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7, 160.7, 157.8, 146.4, 133.9, 133.2, 131.4, 130.3, 125.6, 111.6, 67.4, 65.8, 59.2, 40.7, 39.6. HRMS (EI): *m*/*z* calcd for $C_{17}H_{15}N_3OS_2$: 341.0657. Found: (M^+) 341.0658.

Compound **13a′**. Mixture of regioisomers. Yield: 69% as pale yellow solid. R_f: 0.44 (7:3 hexane/EtOAc). IR (KBr) ν_{max}: 3001, 2958, 2927, 1691, 1579, 1556, 1448, 1386, 1373, 1242, 1016 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25–8.20 (m, 4H), 7.30–7.25 (m, 1H), 6.92–6.87 (m, 1H), 6.55–6.49 (m, 2H), 6.22–6.13 (m, 2H), 5.87–5.82 (m, 2H), 5.77–5.74 (m, 1H), 5.64–5.63 (m, 1H), 5.35–5.30 (m, 2H), 5.07–5.03 (m, 2H), 4.06–4.03 (m, 2H), 3.42–3.16 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.4, 193.6, 174.9, 162.2, 161.5, 158.3, 157.9, 152.8, 151.3, 136.7, 135.8, 132.0, 131.1, 130.8, 130.7, 129.8, 128.5, 127.9, 127.6, 112.1, 112.0, 69.2, 67.1, 58.9, 56.4, 49.4, 49.3, 38.6, 38.5, 38.1, 30.6, 29.7, 29.6. HRMS (EI): *m*/*z* calcd for $C_{17}H_{15}N_3OS_2$: 341.0657. Found: (M^+) 341.0659.

Compound **3b′**. Yield: 68% as pale yellow solid. R_f: 0.41 (7:3 hexane/EtOAc). Mp=184 °C. IR (KBr) ν_{max}: 3008, 2926, 2854, 1695, 1595, 1508, 1485, 1413, 1338, 1332, 1292, 1215, 1120 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.97 (s, 1H), 8.14–8.10 (m, 1H), 7.43–7.23 (m, 10H), 7.03–7.00 (m, 1H), 6.42–6.34 (m, 2H), 6.03 (d, 1H, *J*=9.72 Hz), 5.91–5.89 (m, 1H), 5.49 (br s, 1H), 4.53–4.48 (m, 1H), 4.31–4.30 (m, 1H), 4.07–4.03 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.9, 159.3, 151.4, 146.0, 141.8, 139.4, 138.5, 138.4, 136.8, 134.7, 132.9, 129.6, 129.4, 128.3, 127.9, 127.4, 127.2, 107.3, 68.2, 57.8, 53.3, 47.8. HRMS (EI): *m*/*z* calcd for $C_{28}H_{21}N_3O_3$: 447.1583. Found: (M^+) 447.1595.

Compound **5b′**. Mixture of regioisomers. Yield: 78% as pale yellow solid. R_f: 0.42 (7:3 hexane/EtOAc). IR (KBr) ν_{max}: 3020, 2956, 2926, 2854, 1732, 1593, 1506, 1485, 1462, 1421, 1377, 1336, 1296, 1228, 1213, 1180, 1168, 1120 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 9.03 (d, 1H, J=2.46 Hz), 9.00 (d, 1H, J=2.55 Hz), 8.26–8.22 (m, 2H), 7.05–6.93 (m, 2H), 6.69–6.58 (m, 2H), 6.45–6.37 (m, 2H), 6.09–5.85 (m, 3H), 5.72 (d, 1H, J=5.39 Hz), 5.40–5.03 (m, 4H), 3.99 (s, 1H), 3.06–2.71 (m, 3H), 1.29 (s, 6H), 1.25 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.1, 192.8, 159.9, 159.5, 146.2, 146.2, 139.7, 137.1, 136.7, 136.0, 134.3, 133.4, 133.3, 133.1, 132.2, 130.2, 130.0, 129.9, 129.2, 128.9, 127.6, 125.5, 107.1, 104.9, 68.9, 60.9, 60.3, 59.5, 43.4, 40.9, 38.7, 29.6, 23.3, 22.8, 21.1, 20.9. HRMS (EI): m/z calcd for $C_{18}H_{17}N_3O_3$: 323.1270. Found: (M^+) 323.1278.

Compound **12b″**. Yield: 30% as pale yellow solid. R_f: 0.40 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3025, 2922, 2850, 1693, 1591, 1510, 1488, 1424, 1345, 1291, 1236, 1125, 1006 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.94 (d, 1H, J=2.57 Hz), 8.21 (dd, 1H, J_1=2.60 Hz, J_2=9.40 Hz), 6.92 (q, 1H, J=5.12 Hz), 6.61 (d, 1H, J=9.40 Hz), 6.41 (d, 1H, J=5.72 Hz), 5.82 (d, 1H, J=9.83 Hz), 5.62 (dd, 1H, J_1=2.10 Hz, J_2=5.44 Hz), 5.43 (s, 1H), 4.98 (s, 1H), 4.11–4.04 (m, 1H), 3.98–3.93 (m, 1H), 2.77 (s, 1H), 2.64 (s, 1H), 2.16–1.57 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 159.3, 151.2, 146.4, 143.7, 136.4, 134.3, 133.9, 131.6, 128.5, 127.5, 108.1, 68.1, 57.9, 52.8, 43.6, 38.6, 39.8, 38.9, 37.7, 35.7, 35.1, 28.9, 27.8. HRMS (EI): m/z calcd for $C_{25}H_{25}N_3O_3$: 415.1896. Found: (M^+) 415.2009.

Compound **3a′**. Yield: 72% as pale yellow solid. R_f: 0.41 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3043, 2997, 2924, 2856, 1697, 1579, 1454, 1381, 1249, 1184, 1078, 1010 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.15 (d, 2H, J=4.56 Hz), 7.32–7.10 (m, 8H), 6.96–6.94 (m, 2H), 6.90–6.85 (m, 1H), 6.45 (t, 1H, J=4.83 Hz), 6.29 (d, 1H, J=5.40 Hz), 5.93 (d, 1H, J=9.60 Hz), 5.78–5.75 (m, 1H), 5.30–5.26 (m, 1H), 4.60 (d, 1H, J=8.40 Hz), 4.30 (t, 1H, J=8.16 Hz), 4.01–3.96 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.4, 161.4, 157.8, 151.7, 142.3, 142.0, 140.1, 138.1, 138.0, 135.4, 129.9, 129.8, 129.3, 128.7, 128.3, 127.9, 127.3, 127.2, 126.9, 126.8, 112.1, 67.5, 57.3, 54.0, 47.6. HRMS (EI): m/z calcd for $C_{27}H_{21}N_3O$: 403.1685. Found: (M^+) 403.1698.

Compound **5a′**. Mixture of regioisomers. Yield: 78% as pale yellow solid. R_f: 0.42 (7:3 hexane/EtOAc). IR (KBr) ν_{max}: 3034, 2987, 2930, 2848, 1696, 1580, 1459, 1380, 1255, 1188, 1071, 1016 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.33–8.22 (m, 4H), 7.18–7.13 (m, 1H), 6.96–6.89 (m, 1H), 6.54–6.49 (m, 1H), 6.44 (t, 1H, J=4.70 Hz), 6.04–5.97 (m, 2H), 5.84–5.66 (m, 2H), 5.60–5.50 (m, 2H), 5.34–5.27 (m, 1H), 5.18 (s, 1H), 3.42–3.31 (m, 3H), 3.15–3.14 (m, 1H), 3.07–3.06 (m, 1H), 2.77–2.76 (m, 1H), 1.75 (s, 6H), 1.64 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.5, 196.8, 162.2, 157.5, 153.1, 147.9, 142.2, 137.4, 132.2, 128.6, 115.2, 71.3, 68.6, 68.1, 38.9, 34.2, 32.6, 30.5, 28.5, 26.7. HRMS (EI): m/z calcd for $C_{17}H_{17}N_3O$: 279.1372. Found: (M^+) 279.1381.

Compound **12a″**. Yield: 32% as pale yellow solid. R_f: 0.43 (7:3 hexane/EtOAc). Mp=178 °C. IR (KBr) ν_{max}: 3029, 2990, 2929, 2851, 1692, 1575, 1463, 1389, 1253, 1180, 1073, 1015 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, 2H, J=4.65 Hz), 7.40–7.35 (m, 1H), 6.55 (m, 1H), 6.46 (d, 1H, J=5.49 Hz), 5.91 (d, 1H, J=9.66 Hz), 5.79–5.76 (m, 1H), 5.07(d, 1H, J=4.98 Hz), 4.87 (s, 1H), 3.52–3.50 (m, 1H), 3.24 (d, 1H, J=6.87 Hz), 2.89–2.84 (m, 2H), 2.13–1.76 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.1, 162.2, 157.7, 157.4, 153.1, 142.2, 133.8, 131.7, 131.6, 127.4, 111.8, 72.0, 58.4, 55.1, 44.6, 39.3, 39.0, 38.9, 38.8, 37.1, 34.8, 34.7, 28.2, 28.1. HRMS (EI): m/z calcd for $C_{24}H_{25}N_3O$: 371.1998. Found: (M^+) 371.2006.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.11.084.

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17. X-ray crystal data of compound **3a**: empirical formula $C_{27}H_{21}N_3O$; formula weight 403.47; temperature 293(2) K; wavelength 0.71073 Å; crystal system monoclinic; space group C2/c; unit cell dimensions a=17.004(6), A alpha=90 °, b=12.428(4), A beta=99.692(5) °, c=19.828(7) A gamma=90 °; volume=4130(2) A^3, Z=8, density (calculated) 1.298 Mg/m^3, absorption coefficient=0.080 mm^{-1}; F(000) 1696; crystal size=0.64×0.50×0.46 mm. Theta range for data collection 2.04–28.48 °; index ranges −22<=h<=20, −11<=k<=16, −25<=l<=23; reflections collected 11,618; independent reflections 4774 [R(int)=0.0279]; absorption correction

semi-empirical from equivalents; max. and min transmission 0.9640 and 0.9504; refinement method; full-matrix least-squares on F^2; data/restraints/parameters 4774/0/288; goodness-of-fit on F^2 0.979; final R indices [$I>2\sigma(I)$] $R1$=0.0596, $wR2$=0.1780, R indices (all data) $R1$=0.0773, $wR2$=0.1970; largest diff. peak and hole 0.316 and −0.206 e A^{-3}. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 782679.

18. X-ray crystal data of compound **12b**: empirical formula $C_{50}H_{50}N_6O_{6.5}$; formula weight 838.96; temperature 293(2) K; wavelength 0.71073 Å; crystal system monoclinic; space group $P21/c$; unit cell dimensions a=7.4342(11), A alpha=90 °, b=16.510(2), A beta=91.970(3) °, c=33.736(5) A gamma=90 °; volume=4138.4 (11) A^3, Z=4, density (calculated) 1.347 Mg/m^3, absorption coefficient=0. 090 mm^{-1}; F(000) 1776; crystal size=0.58×0.55×0.18 mm. Theta range for data collection 1.73–26 °; index ranges −7<=h<=9, −20<=k<=20, −40<=l<=41; reflections collected 22,132; independent reflections 8082 [R(int)=0.0305]; absorption correction semi-empirical from equivalents; max. and min transmission 0.9839 and 0.9494; refinement method; full-matrix least-squares on F^2; data/restraints/parameters 8082/0/568; Goodness-of-fit on F^2 1.060; final R indices [$I>2\sigma(I)$] $R1$=0.0737, $wR2$=0.1834, R indices (all data) $R1$=0.0993, $wR2$=0. 1992; largest diff. peak and hole 0.471 and −0.504 e A^{-3}. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 782680.
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21. X-ray crystal data of compound **3b′**: empirical formula $C_{28}H_{21}N_3O_3$; formula weight 447.48; temperature 293(2) K; wavelength 0.71073 Å; crystal system triclinic; space group $P-1$; unit cell dimensions a=10.046(3), A alpha=108.112(4) °, b=10. 586(3), A beta=93.776(4) °, c=11.018(3) A gamma=96.178(4) °; volume=1101.1(5)° A^3, Z=2, density (calculated) 1.350 Mg/m^3, absorption coefficient=0.089 mm^{-1}; F (000) 468; crystal size=0.55×0.45×0.30 mm. Theta range for data collection 1. 96–28.41 °; index ranges −13<=h<=13, −13<=k<=13, −14<=l<=14; reflections collected 9186; independent reflections 4896 [R(int)=0.0232]; absorption correction semi-empirical from equivalents; max. and min transmission 0.9737 and 0.9525; refinement method; full-matrix least-squares on F^2; data/restraints/parameters 4896/0/307; Goodness-of-fit on F^2 1.048; Final R indices [$I>2\sigma(I)$] $R1$=0.0515, $wR2$=0.1455, R indices (all data) $R1$=0.0675, $wR2$=0.1577; largest diff. peak and hole 0.242 and −0.164 e A^{-3}. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 782678.
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