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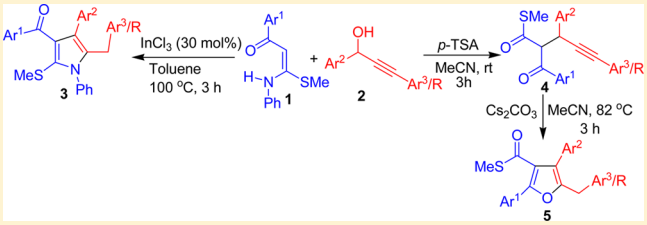
Catalyst-Controlled Straightforward Synthesis of Highly Substituted Pyrroles/Furans via Propargylation/Cycloisomerization of α-Oxoketene-N,S-acetals

Ganesh Chandra Nandi* and Soumini K

Organic Chemistry Section, Chemical Science and Technology Division, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum, Kerala 695019, India

Supporting Information

ABSTRACT: A facile and efficient $InCl_3$ catalyzed one-pot synthesis of highly substituted pyrroles has been developed via a tandem propargylation/cycloisomerization reaction of α-oxoketene-N,S-acetals with propargyl alcohols. Notably, in the presence of Bronsted acid *p*-TSA·H_2O, the reaction afforded the hydrolyzed product propargylated-1,3-dicarbonyl compounds, which upon treatment with Cs_2CO_3 underwent regioselective intramolecular cyclization furnishing tetrasubstituted furan derivatives.



INTRODUCTION

Substituted pyrroles are important synthetic targets for both the academic laboratories and pharmaceutical industry, because of their presence in a wide range of natural products, synthetic materials, and bioactive molecules.[1] Pyrrole is the core structural motif of valuable drugs like Atorvastatin, Tolmetin, Prodigiosin, Obatoclax, and TAK-438 (Figure 1). In addition,

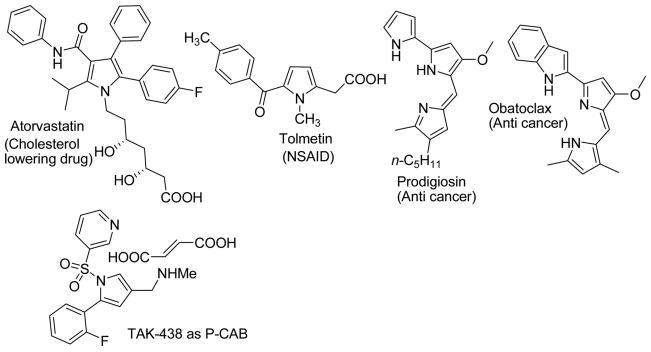


Figure 1. Drug molecules containing pyrrole ring.

pyrroles also show significant functions in supramolecular chemistry as well as in nonlinear optical materials.[2] As a result; much attention has been paid for their preparation by developing new methodologies.

Traditional methods for their preparation include the Hantzsch, Knorr, and Paal-Knorr condensation reactions. But the limitations of the classical methods, such as harsh reaction conditions, regioselectivity, long reaction time, and functional group compatibility, leads to develop numerous new, modified, and efficient strategies employing the multicomponent reactions, cycloaddition reactions, cyclization reactions, reactions of alkynes with enamides, and oxidative cyclization of *N*-allylimines.[3]

α-Oxoketene-N,S-acetals bearing electron-accepting and donating group at both ends of the C−C double bond, considered to be push−pull alkenes, are of immense interest because of their significance in organic synthesis as versatile synthons and/or synthetic intermediates. The moiety has been widely used as important building block for the synthesis of various nitrogen and sulfur heterocycles.[4] In a recent report, we described the synthesis of highly substituted hydro(thiophenes) via propargylation/cyclization of β-ketothioamide.[5a] Subsequently, we envisioned to tune our attention to have *N*-containing heterocycles from the same or related compounds. The long-standing expertise in this area[5b−d] helped us to conclude that the sulfur should be protected to make N−H free for the reaction. Thus, we modified the reactivity of β-ketothioamide through protection of sulfur and transforming it to α-oxoketene-N,S-acetal **1** by treating with base and methyl iodide.[4b] In this context, we developed an efficient and facile $InCl_3$ catalyzed one-pot synthesis of highly substituted pyrroles via a tandem propargylation/cycloisomerization reaction of α-oxoketene-N,S-acetals with propargyl alcohols (Scheme 1). Additionally, the formation of furan ring using *p*-TSA/Cs_2CO_3 has also been described.

RESULTS AND DISCUSSION

The desired α-oxoketene-N,S-acetals (**1**) and propargylic alcohols (**2**) were synthesized according to literature procedures.[4b,6] The synthesis of substituted pyrrole **3a** was first under taken. Consequently, we treated α-oxoketene-N,S-

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Scheme 1. Synthesis of Pyrroles and Furans from α-Oxoketene-N,S-acetals

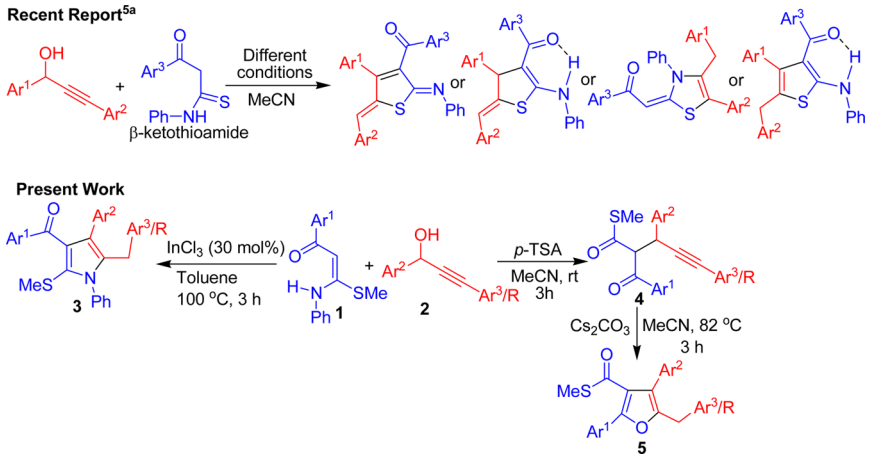
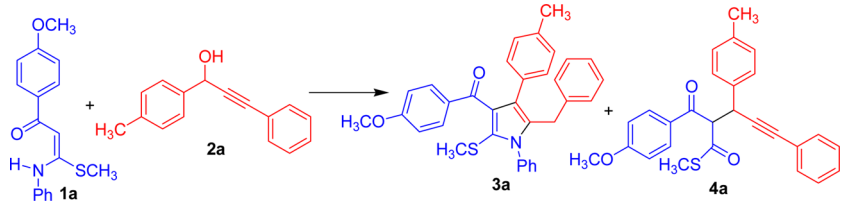


Table 1. Optimization Studies for the Synthesis of Substituted Pyrroles



entry	conditions	yield (%)[a] (3/4)
1	*p*-TSA·H_2O (50 mol%), acetonitrile, rt, 3 h	(-/77)
2	$InCl_3$ (20 mol%), acetonitrile, rt, 24 h	(43/-)
3	$InCl_3$ (20 mol%), acetonitrile, 82 °C, 3 h	(48/-)
4	$InCl_3$ (20 mol%), chlorobenzene, 100 °C, 3 h	(58/-)
5	$InCl_3$ (20 mol%), toluene, 100 °C, 3.5 h	(68/-)
6	$InCl_3$ (20 mol%), DCE, 84 °C, 3 h	(54/-)
7	$InCl_3$ (30 mol%), toluene, 100 °C, 3 h	(73/-)
8	$InCl_3$ (40 mol%), toluene, 100 °C, 3 h	(72/-)
9	$InBr_3$ (30 mol%), toluene, 100 °C, 3 h	(65/-)
10	$AgSbF_6$ (30 mol%), toluene 100 °C, 2.5 h	(61/-)
11	$Sc(OTf)_2$ (30 mol%), toluene 100 °C, 2.5 h	(35 /-)

[a]Isolated yield.

acetal **1a** and propargylic alcohol **2a** in the presence of monohydrated *p*-toluenesulfonic acid (*p*-TSA·H_2O) at room temperature (32 °C) in acetonitrile (Table 1, entry 1). But the reaction provided propargylated-1,3-dicarbonyl compounds **4a** in 77% yield, instead of desired pyrrole **3a**. The result could be explained by the release of H^+ ion from Bronsted acid *p*-TSA hydrolyzed the intermediate to furnish **4a** (see Scheme 2). The above outcome prompted us to replace the Bronsted acid *p*-TSA with Lewis acid. Consequently, we performed the reaction in the presence of $InCl_3$ (20 mol%) in acetonitrile at room temperature and got the expected pyrrole **3a** in moderate yield 43% (Table 1, entry 2). Heating the reaction at 82 °C with $InCl_3$ (20 mol%) afforded only 48% of product (Table 1, entry 3). To enhance the product formation, the reaction was screened with different solvents, such as chlorobenzene (100 °C), toluene (100 °C), and dichloroethane (84 °C) (Table 1, entries 4, 5, and 6) in the presence of $InCl_3$ (20 mol%). We found that toluene afforded the maximum yield of the desired pyrrole **3a** (68%). An effort to optimize the catalyst loading revealed that 30 mol% of $InCl_3$ provided the best result in toluene (100 °C), and the reaction completed within 3 h (Table 1, entry 7). Effectiveness of the other catalysts was also tested for this transformation. $InBr_3$ and $AgSbF_6$ provided the desired product **3a** in good yield, but $Sc(OTf)_2$ afforded only 35% of pyrrole **3a** (Table 1, entries 9−11). Hence, the best

Scheme 2. Mechanistic Routes to 3, 4, and 5

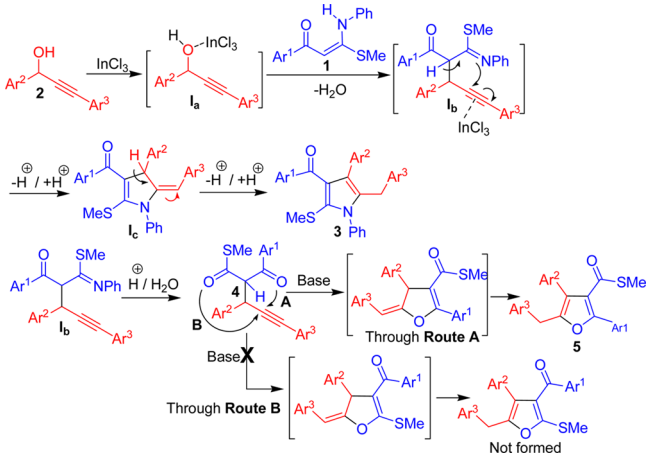


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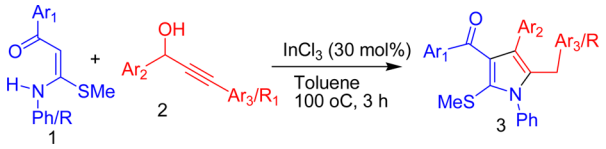
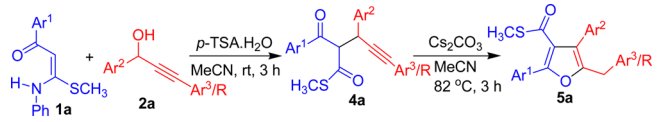
Table 2. Substrate Scope for the Synthesis of Pyrroles



entry	Ar^1	Ph/R	Ar^2	Ar^3/R^1	product **3** (Yield %)[a]
1	4-$OCH_3C_6H_4$	C_6H_5	4-$CH_3C_6H_4$	C_6H_5	**3a** (73)
2	4-$OCH_3C_6H_4$	C_6H_5	4-ClC_6H_4	4-$CH_3C_6H_4$	**3b** (76)
3	4-$OCH_3C_6H_4$	C_6H_5	4-ClC_6H_4	C_6H_5	**3c** (70)
4	3,4,5-$(OCH_3)_3C_6H_2$	C_6H_5	4-ClC_6H_4	4-$CH_3C_6H_4$	**3d** (75)
5	3,4,5-$(OCH_3)_3C_6H_2$	C_6H_5	4-$CH_3C_6H_4$	C_6H_5	**3e** (69)
6	3,4,5-$(OCH_3)_3C_6H_2$	C_6H_5	3-ClC_6H_4	4-$CH_3C_6H_4$	**3f** (74)
7	4-$CH_3C_6H_4$	C_6H_5	4-ClC_6H_4	*n*-C_5H_{11}	**3g** (67)
8	4-$CH_3C_6H_4$	C_6H_5	2-FC_6H_4	C_6H_5	**3h** (63)
9	4-$CH_3C_6H_4$	C_6H_5	3,4-$F_2C_6H_3$	4-$CH_3C_6H_4$	**3i** (71)
10	4-$CH_3C_6H_4$	C_6H_5	4-ClC_6H_4	C_6H_5	**3j** (70)
11	C_6H_5	C_6H_5	4-ClC_6H_4	C_6H_5	**3k** (72)
12	4-BrC_6H_4	C_6H_5	3,4-$F_2C_6H_3$	4-$CH_3C_6H_4$	**3l** (74)
13	4-$OCH_3C_6H_4$	*n*-C_4H_9	4-ClC_6H_4	4-$CH_3C_6H_4$	**3m** (31)
14	2-thienyl	C_6H_5	3-ClC_6H_4	4-$CH_3C_6H_4$	**3n** (74)
15	2-thienyl	C_6H_5	2-FC_6H_4	C_6H_5	**3o** (66)

[a]Isolated yield.

Table 3. Synthesis of Propargylated-1,3-dicarbonyl 4 and Furan 5



entry	Ar^1	Ar^2	Ar^3	1,3-dicarbonyl compound **4** (yield %)[a]	furan **5** (yield %)[a]
1	4-$OCH_3C_6H_4$	4-$CH_3C_6H_4$	C_6H_5	**4a** (77)	**5a** (63)
2	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	C_6H_5	**4b** (68)	**5b** (58)
3	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**4c** (74)	**5c** (61)
4	3,4,5-$(OCH_3)_3C_6H_2$	4-ClC_6H_4	4-$CH_3C_6H_4$	**4d** (78)	**5d** (56)
5	3,4,5-$(OCH_3)_3C_6H_2$	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**4e** (76)	**5e** (54)

[a]Isolated yield.

reaction condition was obtained when equivalent amounts of reactants **1a** and **2a** were treated with $InCl_3$ (30 mol%) in toluene at 100 °C for 3 h (Table 1, entry 7).

With the optimized reaction conditions in hand, we next started exploration of the substrate scope for the synthesis of highly substituted pyrroles **3** from different α-oxoketene-N,S-acetals **1** and propargylic alcohols **2**. The unsubstituted/mono as well as bulky trisubstituted aryl groups in the aroyl part of α-oxoketene-N,S-acetals show equal activity toward the formation of pyrrole **3** and provided good yields (Table 2, **3a**−**m**). In addition, the electron-deficient heteroaryl thionyl group in the α-oxoketene-N,S-acetals also reacted smoothly with the propargylic alcohols to furnish the corresponding pyrroles in good yields (**3n**,**o**). However, the replacement of *N*-phenyl group in the N,S-acetal with the *N*-alkyl group afforded only 31% of pyrrole **3m**. Propargylic alcohols bearing electron- rich/electron-deficient aryl group attached with the carbinol carbon are equally reactive for this conversion and furnished good yield of pyrrole **3**. Mono/disubstituted aryl group as well as *ortho*-/*meta*-/*para*-substituted aryl groups attached with the carbinol carbon also worked well for this transformation. Interestingly, the presence of aliphatic group at the alkyl end of propargylic alcohol shows similar reactivity as its aryl counterpart (**3g**).

The successful synthesis of highly substituted pyrroles prompted us to consider the synthetic usefulness of propargylated-1,3-dicarbonyl compound **4a**, which was formed through the reaction of **1a** and **2a** in the presence of *p*-TSA·H_2O (Table 1, entry 1). The literature investigation at this stage revealed that the propargylated-1,3-dicarbonyl compounds could be very useful synthons for the construction of highly functionalized furan derivatives via intramolecular cyclization in the presence of base or acid.[7] Hence, we decided to synthesize some propargylated-1,3-dicarbonyl compounds catalyzed by *p*-TSA·H_2O and further cyclize them using base to prepare furan. Interestingly, it is a new method for the synthesis of furan with −COSR functionality directly from α-oxoketene-N,S-acetal via propargylation/hydrolyzation/cyclization technique. The viability of the formation of propargylated-1,3-dicarbonyl compounds **4** from various α-oxoketene-N,S-acetals (**1**) and propargylic alcohols (**2**) in the presence of *p*-TSA·H_2O has been described in Table 3. The reaction with mono and trisubstituted α-oxoketene-N,S-acetals proceeded smoothly, and provided the desired product **4** in good yield. The substituted propargyl alcohols were also found equally reactive toward the formation of product **4**. It should be mentioned that the propargylated-1,3-dicarbonyl compounds **4** were obtained

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as diastereomeric mixture. Further, to cyclize the propargylated-1,3-dicarbonyl compounds **4**, we treated it with the base Cs_2CO_3 (1.0 equiv) and heated in acetonitrile at 82 °C for 3 h. To our delight, we found only one regioisomer of furan **5** in all cases in good yield (Table 3), and could not trace the other isomer. The structure of regioisomeric furan has been confirmed by satisfactory spectral (^{1}H, ^{13}C, mass, and 2D NMR) studies.

Taking into account the entire outcome, together with the related report, a plausible mechanistic pathway for the synthesis of pyrroles **3** from the reaction of α-oxoketene-N,S-acetals and propargylic alcohols are depicted in Scheme 2. The process starts with the coordination of $InCl_3$ with OH group of propargylic alcohol **2** to form corresponding propargylic cation, which subsequently is trapped by the α-oxoketene-N,S-acetals **1** to form $\mathbf{I_b}$. The coordination between the $InCl_3$ and the triple bond of $\mathbf{I_b}$ triggered the intramolecular cyclization through nitrogen atom to form a five membered intermediate $\mathbf{I_c}$, which upon intramolecular isomerization furnished pyrroles **3**. The formation of propargylated-1,3-dicarbonyl compound **4** also have been explained by the hydrolysis of C═N bond in $\mathbf{I_b}$ to C═O in the presence of *p*-TSA·H_2O. The propargylated-1,3-dicarbonyl compound **4** further underwent intramolecular cyclization/aromatization to give **5**. Though there is a possibility of formation of two regioisomeric furan rings as shown in Scheme 2 (route A and B) but only one isomer was formed making the protocol highly regioselective.

CONCLUSION

In conclusion, a novel and efficient one-pot protocol for the synthesis of highly substituted pyrroles from α-oxoketene-N,S-acetals and propargyl alcohols catalyzed by $InCl_3$ is developed. The reaction also provides propargylated-1,3-diketones after hydrolysis in the presence of Bronsted acid *p*-TSA·H_2O. Furthermore, propargylated-1,3-diketones were treated with base Cs_2CO_3 for regioselective synthesis of furan derivatives. The advantages of this method are pot-economy, air-tolerant, moderate to good yields, and economic viability of the catalyst. In addition, two different kinds of important heterocycles can be obtained by tuning the catalyst. Further applications of α-oxoketene-N,S-acetals on the extensions of this protocol are underway in the laboratory.

EXPERIMENTAL SECTION

General. The starting material α-oxoketene-N,S-acetals and propargylic alcohols were synthesized in the laboratory following the reported methods. The catalysts and bases were purchased from various suppliers and used as received. ^{1}H and ^{13}C NMR spectra were recorded on NMR spectrophotometer operating at 500 and 126 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0). IR spectra were measured in NaCl, and wavelengths are reported in cm^{-1}. Mass spectra were recorded under ESI/HRMS at 60 000 resolutions using ion trap mass analyzer. Melting points were uncorrected.

General Procedure for the Reaction of α-Oxoketene-N,S-acetals 1 and Propargyl Alcohols 2 for the Synthesis of Highly Substituted Pyrroles 3. α-Oxoketene-N,S-acetal **1** (0.25 mmol) and propargyl alcohol **2** (1 equiv) were added to a Schlenk tube containing 1.5 mL of toluene. $InCl_3$ (30 mol%) was added to the reaction mixture and the whole reaction mixture was heated at 100 °C for 3 h. After completion of reaction (checked by TLC), water was added to it and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was finally washed with brine solution. Then the organic layer was dried (Na_2SO_4), evaporated, and purified by silica-gel column chromatography using 5−7% of ethyl acetate in hexane as eluent. All the compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

General Procedure for the Reaction of α-Oxoketene-N,S-acetals and Propargyl Alcohols for the Synthesis of Propargylated-1,3-diketones 4. α-Oxoketene-N,S-acetal **1** (0.25 mmol) and propargyl alcohol **2** (1 equiv) were added to a Schlenk tube containing 1.5 mL of acetonitrile. *p*-TSA·H_2O (50 mol%) was added to the reaction mixture and the whole reaction mixture was stirred at room temperature (30 °C) for 3 h. After completion of reaction (checked by TLC), water was added to the reaction mixture and extracted with ethyl acetate (2 × 10 mL). The organic layer was then washed with brine solution. Thereafter, the organic layer was dried (Na_2SO_4), evaporated, and purified by silica-gel column chromatography using 5−7% of ethyl acetate in hexane as eluent. All the compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

General Procedure for the Cs_2CO_3 Promoted Cycloisomerization of Propargylated-1,3-diketones 4 for the Synthesis of Highly Substituted Furans 5. Cs_2CO_3 (1.0 equiv) was added to a 0.5 mL acetonitrilic solution of propargylated-1,3-diketones **4** (0.1 mmol) in a Schlenk tube covered with $CaCl_2$ guard tube, and the whole reaction mixture was heated at 82 °C for 3 h. After completion of the reaction (checked by TLC), the solvent was evaporated and the compound **5** was purified by silica-gel column chromatography using 8−10% of ethyl acetate in hexane as eluent. All the compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

Characterization Data of Isolated Compounds. *N-Phenyl-5-benzyl-4-(4-methylphenyl)-3-(4-methoxybenzoyl)-2-thiomethylpyrrole (**3a**).* Yield: 92 mg, 73% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid, mp 81−83 °C. IR (NaCl, cm^{-1}): 3058, 3026, 1727, 1646, 1598. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 9.0 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.08−7.05 (m, 5H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 9.0 Hz, 2H), 6.70−6.60 (m, 2H), 3.89 (s, 2H), 3.81 (s, 3H), 2.23 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.9, 163.1, 139.5, 137.8, 135.8, 132.4, 132.2, 131.9, 131.8, 129.5, 129.3, 129.2, 129.1, 128.7, 128.5, 128.2, 128.2, 126.0, 125.4, 124.5, 113.3, 56.4, 31.4, 21.3, 21.2. HRMS (ESI) calcd. for $C_{33}H_{29}NO_2S$ $[M+H]^+$ 504.1992; found 504.2004.

*N-Phenyl-4-(4-chlorophenyl)-3-(4-methoxybenzoyl)-5-(4-methylbenzyl)-2-thiomethylpyrro-le (**3b**).* Yield: 102 mg, 76% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3048, 2922, 1718, 1646, 1598, 1494. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 9.0 Hz, 2H), 7.38−7.32 (m, 3H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 7.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.58 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 3.80 (s, 2H), 2.26 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 163.3, 137.6, 136.1, 135.6, 133.4, 132.6, 132.4, 132.4, 132.2, 131.8, 131.5, 130.8, 129.1, 129.1, 128.8, 128.5, 127.9, 126.2, 123.2, 113.4, 55.4, 30.9, 21.2, 21.1. HRMS (ESI) calcd. for $C_{33}H_{28}ClNO_2S$ $[M+H]^+$ 538.1602; found 538.1617.

*N-Phenyl-3-benzoyl-5-benzyl-4-(4-chlorophenyl)-2-thiomethylpyrrole (**3c**).* Yield: 92 mg, 70% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3061, 3028, 2922, 1718, 1646, 1598, 1494. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 9.0 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.16 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 7.09−7.05 (m, 5H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.69−6.67 (m, 2H), 3.85 (s, 2H), 3.82 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 163.3, 139.1, 137.6, 133.3, 132.5, 132.4, 132.4, 131.7, 130.9, 129.1, 129.1, 128.8, 128.7, 128.5, 128.3, 128.1, 126.2, 126.0, 123.4, 113.4, 55.4, 31.3, 21.2. HRMS (ESI) calcd. for $C_{32}H_{26}ClNO_2S$ $[M+H]^+$ 524.1446; found 524.1457.

*N-Phenyl-4-(4-chlorophenyl)-3-(3,4,5-trimethoxybenzoyl)-5-(4-methylbenzyl)-2-thiomethyl-pyrrole (**3d**).* Yield: 90 mg, 75% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow solid, mp 101−103 °C. IR (NaCl, cm^{-1}): 3048, 2923, 1717, 1646, 1583. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (t, *J* = 7.0 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.11−7.07 (m, 8H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 2H), 3.84−3.82 (m, 11H), 2.28 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (126

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MHz, $CDCl_3$): δ 192.5, 152.7, 142.4, 137.5, 136.2, 135.8, 133.6, 133.4, 132.5, 132.4, 130.6, 129.1, 129.0, 128.9, 128.9, 128.7, 128.6, 127.8, 127.0, 123.2, 107.9, 61.0, 56.2, 30.9, 21.4, 21.2. HRMS (ESI) calcd. for $C_{35}H_{32}ClNO_4S$ $[M+H]^+$ 598.1813; found 598.1802.

N-Phenyl-5-benzyl-4-(4-methylphenyl)-3-(3,4,5-trimethoxybenzoyl)-2-thiomethylpyrrole (**3e**). Yield: 72 mg, 69% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow solid, mp 132−133 °C. IR (NaCl, cm^{-1}): 3059, 3025, 2923, 1717, 1646, 1583, 1465. ^1H NMR (500 MHz, $CDCl_3$): δ 7.38−7.29 (m, 4H), 7.11−7.04 (m, 8H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.72−6.71 (m, 2H), 3.89 (s, 2H), 3.81 (s, 3H), 3.80 (s, 6H), 2.22 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 152.5, 142.1, 139.6, 137.7, 136.0, 133.7, 131.9, 131.8, 129.4, 129.1, 129.0, 128.8, 128.7, 128.7, 128.3, 128.1, 126.6, 126.1, 124.4, 107.9, 60.9, 56.2, 31.4, 21.5, 21.2. HRMS (ESI) calcd. for $C_{35}H_{33}NO_4S$ $[M+H]^+$ 564.2203; found 564.2218.

N-Phenyl-4-(3-chlorophenyl)-5-(4-methylbenzyl)-3-(3,4,5-trimethoxybenzoyl)-2-thiomethyl-pyrrole (**3f**). Yield: 89 mg, 74% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow solid, mp 152−154 °C. IR (NaCl, cm^{-1}): 3049, 3000, 2923, 1650, 1583, 1462. ^1H NMR (500 MHz, $CDCl_3$): δ 7.41 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.15−7.03 (m, 9H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.57 (d, *J* = 8.0 Hz, 2H), 3.84−3.82 (m, 11H), 2.26 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.4, 152.6, 142.1, 137.5, 136.7, 136.0, 135.7, 134.0, 133.9, 132.5, 129.7, 129.0, 128.9, 128.8, 127.8, 127.6, 126.6, 123.1, 107.7, 60.8, 56.2, 30.8, 21.4, 21.1. HRMS (ESI) calcd. for $C_{35}H_{32}ClNO_4S$ $[M+H]^+$ 598.1813; found 598.1818.

N-Phenyl-4-(4-chlorophenyl)-5-n-hexyl-3-(4-methylbenzoyl)-2-thiomethylpyrrole (**3g**). Yield: 84 mg, 67% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid, mp 74−75 °C IR (NaCl, cm^{-1}): 3043, 2925, 2856, 1647, 1604, 1494. ^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.54−7.50 (m, 3H), 7.37 (d, *J* = 6.5 Hz, 2H), 7.16−7.08 (m, 6H), 2.48−2.44 (m, 2H), 2.35 (s, 3H), 1.96 (s, 3H), 1.17−1.14 (m, 2H), 1.07−1.03 (m, 2H), 0.97- 0.95 (m, 3H), 0.88−0.85 (m, 1H), 0.74 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.6, 143.2, 138.0, 136.4, 135.0, 133.8, 132.2, 131.0, 130.3, 129.2, 129.1, 128.9, 128.8, 128.4, 125.3, 122.3, 122.3, 31.1, 29.6, 28.8, 25.2, 22.4, 21.8, 21.2, 14.1. HRMS (ESI) calcd. for $C_{31}H_{33}ClNOS$ $[M+Na]^+$ 502.1960; found 502.1982.

N-Phenyl-5-benzyl-4-(2-fluorophenyl)-3-(4-methylbenzoyl)-2-thiomethylpyrrole (**3h**). Yield: 77 mg, 63% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3060, 3028, 2921, 1726, 1646, 1604, 1494. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.32 (t, *J* = 6.5 Hz, 2H), 7.23 (td, *J* = 7.5, 1.5 Hz, 1H), 7.09−7.07 (m, 5H), 7.02−7.01 (m, 3H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 9.0 Hz, 1H), 6.60−6.59 (m, 2H), 3.82 (s, 2H), 2.33 (s, 3H), 1.97 (s, 3H). ^1H NMR (500 MHz, $CDCl_3$): δ 193.1, 160.1 (d, *J* = 267.0 Hz), 142.8, 138.8, 137.7, 137.0, 136.5, 133.7, 132.4 (d, *J* = 2.8 Hz), 130.1, 129.2, 128.8, 128.7, 128.7, 128.6, 128.2 (d, *J* = 6.8 Hz), 127.0, 126.0, 124.0 (d, *J* = 3.5 Hz), 122.8, 122.6, 118.1, 115.5 (d, *J* = 22.6 Hz), 31.8, 21.8, 21.0. HRMS (ESI) calcd. for $C_{32}H_{26}FNOS$ $[M+H]^+$ 492.1792; found 492.1794.

N-Phenyl-4-(3,4-difluorophenyl)-3-(4-methylbenzoyl)-5-(4-methylbenzyl)-2-thiomethylpyr-role (**3i**). Yield: 93 mg, 71% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid, mp 126−128 °C. IR (NaCl, cm^{-1}): 3048, 2922, 2861, 1647, 1603, 1514. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 7.5 Hz, 2H), 7.03−6.99 (m, 1H), 6.92−6.90 (m, 4H), 6.56 (d, *J* = 7.5 Hz, 2H), 3.80 (s, 2H), 2.36 (s, 3H), 2.26 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.4, 150.0 (dd, *J* = 246.7, 12.6 Hz), 149.2 (dd, *J* = 246.2, 12.5 Hz), 143.4, 137.4, 136.3, 135.8, 135.7, 132.8, 131.9 (m), 130.2, 129.1, 129.1, 128.9, 128.9, 128.8, 127.8, 126.5, 125.8 (m), 122.6, 122.6, 118.5 (d, *J* = 17.1 Hz), 117.0 (d, *J* = 17.1 Hz), 30.8, 21.8, 21.1. HRMS (ESI) calcd. for $C_{33}H_{28}F_2NOS$ $[M+H]^+$ 524.1854; found 524.1844.

N-Phenyl-5-benzyl-4-(4-chlorophenyl)-3-(4-methylbenzoyl)-2-thiomethylpyrrole (**3j**). Yield: 89 mg, 70% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid, mp 95−97 °C. IR (NaCl, cm^{-1}): 3060, 3029, 1711, 1646, 1603, 1494. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.16−7.05 (m, 11H), 6.68−6.66 (m, 2H), 3.85 (s, 2H), 2.35 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.5, 143.3, 139.1, 137.5, 136.3, 133.3, 132.4, 132.4, 130.9, 130.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 128.3, 128.0, 126.4, 126.2, 123.5, 31.3, 21.8, 21.1. HRMS (ESI) calcd. for $C_{32}H_{26}ClNOS$ $[M+H]^+$ 508.1496; found 508.1505.

N-Phenyl-3-benzoyl-5-benzyl-4-(4-chlorophenyl)-2-thiomethylpyrrole (**3k**). Yield: 89 mg, 72% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3061, 3029, 2921, 1648, 1581, 1493. ^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.0 Hz, 2H), 7.43−7.36 (m, 2H), 7.34−7.29 (m, 4H), 7.15−7.05 (m, 9H), 6.68−6.66 (m, 2H), 3.85 (s, 2H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.7, 139.0, 138.9, 137.5, 133.2, 132.6, 132.5, 132.5, 131.0, 130.0, 129.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.1, 128.0, 127.1, 126.2, 123.7, 31.0, 21.1. HRMS (ESI) calcd. for $C_{31}H_{24}ClNOS$ $[M+H]^+$ 494.1340; found: 494.1343.

N-Phenyl-3-(4-bromobenzoyl)-4-(3,4-difluorophenyl)-5-(4-methylbenzyl)-2-thiomethylpyrr-ole (**3l**). Yield: 87 mg, 74% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow solid, mp 119−120 °C. IR (NaCl, cm^{-1}): 3050, 2922, 1720, 1649, 1584, 1514. ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.40 (t, *J* = 6.7 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.08 (d, *J* = 7.1 Hz, 2H), 7.03−6.86 (m, 5H), 6.54 (d, *J* = 7.9 Hz, 2H), 3.79 (s, 2H), 2.26 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.4, 150.1 (dd, *J* = 247.2, 12.8 Hz), 149.3 (dd, *J* = 247.1, 12.6 Hz), 137.7, 137.3, 135.8, 135.7, 133.2, 131.7 (m), 131.5, 131.4, 129.1, 129.0, 129.0, 128.9, 128.2, 127.8, 127.3, 125.8 (m), 122.7, 122.6, 118.6 (d, *J* = 17.2 Hz), 117.2 (d, *J* = 17.0 Hz), 30.8, 21.1. HRMS (ESI) calcd. for $C_{32}H_{24}BrF_2NOS$ $[M+H]^+$ 588.0803; found 588.0812.

N-n-Butyl-4-(4-chlorophenyl)-3-(4-methoxybenzoyl)-5-(4-methylbenzyl)-2-thiomethylpyrr-ole (**3m**). Yield: 40 mg, 31% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 2958, 2925, 2869, 1709, 1642, 1598, 1464. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 9.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.74 (d, *J* = 9.0 Hz, 2H), 3.99 (s, 2H), 3.90−3.86 (m, 2H), 3.80 (s, 3H), 2.34 (s, 3H), 2.30 (s, 3H), 1.55−1.53 (m, 2H), 1.31−1.26 (m, 2H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.9, 163.2, 136.2, 136.1, 133.6, 132.4, 132.1, 131.8, 130.8, 130.2, 129.6, 128.7, 128.3, 127.7, 124.8, 123.6, 113.3, 55.4, 44.8, 33.8, 30.7, 22.2, 21.2, 20.3, 13.9. HRMS (ESI) calcd. for $C_{31}H_{32}ClNO_2S$ $[M+H]^+$ 518.1915; found 518.1923.

N-Phenyl-4-(3-chlorophenyl)-5-(4-methylbenzyl)-3-(2-thienoyl)-2-thiomethylpyrrole (**3n**). Yield: 76 mg, 74% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3048, 2921, 2855, 1703, 1630, 1596. ^1H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, *J* = 6.0 Hz, 1H), 7.41−7.34 (m, 4H), 7.25 (d, *J* = 3.0 Hz, 1H), 7.15−7.06 (m, 5H), 6.93−6.89 (m, 3H), 6.56 (d, *J* = 8.0 Hz, 2H), 3.83 (s, 2H), 2.26 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 185.6, 145.7, 137.5, 136.7, 135.9, 135.6, 134.5, 134.2, 133.8, 133.8, 132.9, 129.6, 129.6, 129.5, 129.1, 129.1, 128.8, 127.9, 127.9, 127.7, 126.7, 126.7, 122.7, 30.9, 21.5, 21.1. HRMS (ESI) calcd. for $C_{30}H_{24}ClNOS_2$ $[M+H]^+$ 514.1055; found 514.1068.

N-Phenyl-5-benzyl-4-(2-fluorophenyl)-3-(2-thienoyl)-2-thiomethylpyrrole (**3o**). Yield: 64 mg, 66% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow sticky liquid. IR (NaCl, cm^{-1}): 3062, 2922, 2852, 1723, 1630, 1495. ^1H NMR (500 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.47 (dd, *J* = 3.5, 1.0 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.31−7.28 (m, 1H), 7.16−7.12 (m, 1H), 7.10 (d, *J* = 7.5 Hz, 2H), 7.04- 6.96 (m, 5H), 6.92 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.61−6.59 (m, 2H), 3.85 (s, 2H), 2.08 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 185.1, 161.0 (*J* = 244 Hz), 145.7, 138.7, 137.6, 134.3, 133.7, 133.3, 132.4 (*J* = 3.37 Hz), 129.3, 129.1, 128.9, 128.8, 128.7, 128.2, 128.2, 127.4, 127.0, 126.1, 124.2 (*J* = 3.37 Hz), 122.7 (*J* = 15.3 Hz), 117.5, 115.77 (*J* = 25.3 Hz), 31.8, 21.3. HRMS (ESI) calcd. for $C_{29}H_{22}FNOS_2$ $[M+H]^+$ 484.1200; found 484.1199.

S-Methyl-5-p-tolyl-2-(4-methoxybenzoyl)-3-(4-methylphenyl)-pent-4-yne-1-thioate (**4a**). Mixture of diastereomers (3:2). Yield: 82

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mg, 77% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid, mp 102−103 °C.

The data for the major isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, *J* = 9.0 Hz, 2H), 7.38−7.35 (m, 2H), 7.26- 7.24 (m, 2H), 7.16−7.10 (m, 3H), 7.04 (d, *J* = 7.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 5.11 (d, *J* = 10.5 Hz, 1H), 4.88 (d, *J* = 10.5 Hz, 1H), 3.86 (s, 3H), 2.33 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.8, 190.2, 164.1, 137.2, 135.3, 131.7, 131.6, 129.4, 129.4, 128.5, 128.0, 128.0, 123.1, 114.1, 89.3, 84.3, 68.1, 55.5, 39.1, 21.3, 12.1.

The data for the minor isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 9.0 Hz, 2H), 7.38−7.35 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16−7.10 (m, 3H), 7.00 (d, *J* = 7.5 Hz, 2H), 6.82 (d, *J* = 9.0 Hz, 2H), 5.08 (d, *J* = 10.5 Hz, 1H), 4.95 (d, *J* = 10.5 Hz, 1H), 3.79 (s, 3H), 2.34 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 189.3, 164.1, 137.0, 135.6, 131.8, 131.3, 130.0, 129.5, 128.4, 128.2, 127.9, 123.5, 113.9, 89.0, 84.9, 68.6, 55.4, 38.8, 21.1, 12.3. HRMS (ESI) calcd. for $C_{27}H_{24}O_3S$ $[M+Na]^+$ 451.1338; found 451.1349.

S-Methyl-5-Phenyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-pent-4-yne-1-carbothioate (**4b**). Mixture of diastereomer (3:2). Yield: 70 mg, 68% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid; mp 103−105 °C.

The data of major isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.32−7.28 (m, 2H), 7.24−7.22 (m, 2H), 7.20−7.18 (m, 2H), 7.09−7.03 (m, 3H), 6.96−6.92 (m, 2H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.81 (d, *J* = 11.0 Hz, 1H), 2.36 (s, 3H), 2.27 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.8, 191.5, 144.7, 137.3, 135.3, 134.6, 131.6, 129.6, 129.4, 129.1, 128.6, 128.3, 128.1, 123.1, 89.2, 84.4, 68.3, 39.2, 21.9, 21.3, 12.2.

The data of minor isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.32−7.28 (m, 2H), 7.24−7.22 (m, 2H), 7.09−7.03 (m, 5H), 6.96−6.92 (m, 2H), 5.05 (d, *J* = 11.0 Hz, 1H), 4.88 (d, *J* = 10.5 Hz, 1H), 2.36 (s, 3H), 2.28 (br, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.7, 190.7, 137.1, 135.6, 134.1, 131.8, 129.5, 129.4, 129.2, 128.5, 128.1, 128.0, 125.6, 123.5, 89.0, 85.0, 68.8, 38.8, 21.8, 21.2, 12.4. HRMS (ESI) calcd. for $C_{27}H_{24}O_2S$ $[M+Na]^+$ 435.1389; found 435.1379.

S-Methyl-5-p-tolyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-pent-4-yne-1-carbothioate (**4c**). Mixture of diastereomer (2:1). Yield: 79 mg, 74% (from 0.25 mmol of corresponding N,S-acetal). Pale yellow solid; mp 106−107 °C.

The data for the major isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.31−7.26 (m, 4H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.91 (s, 4H), 5.13 (d, *J* = 9.5 Hz, 1H), 4.87 (d, *J* = 10.5 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H), 2.24 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 191.3, 144.4, 137.7, 137.0, 135.2, 134.5, 131.3, 129.4, 129.2, 129.2, 128.6, 128.4, 119.9, 88.2, 84.4, 68.2, 39.0, 21.7, 21.3, 21.2, 12.0.

The data for the minor isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 4H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 5.11 (d, *J* = 9.5 Hz, 1H), 4.94 (d, *J* = 10.5 Hz, 1H), 2.33 (s, 6H), 2.32 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 190.6, 144.5, 137.8, 136.8, 135.6, 134.0, 131.5, 129.3, 129.2, 128.9, 128.8, 128.3, 120.3, 88.0, 85.0, 68.7, 38.7, 21.6, 21.4, 21.0, 12.2. HRMS (ESI) calcd. for $C_{28}H_{26}O_2S$ $[M+Na]^+$ 449.1546; found 449.1564.

S-Methyl-5-p-tolyl-2-(3,4,5-trimethoxybenzoyl)-3-(4-chlorophenyl)-pent-4-yne-1-carbothio-ate (**4d**). Mixture of diastereomer (2:1). Yield: 82 mg, 78% (from 0.20 mmol of corresponding N,S-acetal). Off white solid; mp 115−117 °C.

The data for the major isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.36 (s, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.89 (d, *J* = 10.5 Hz, 1H), 3.91 (s, 6H), 3.87 (s, 3H), 2.27 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.83, 190.10, 153.2, 143.5, 138.3, 136.7, 133.6, 131.8, 131.5, 130.1, 128.9, 128.8 119.6, 106.8, 87.6, 85.0, 68.6, 60.9, 56.4, 38.9, 21.5, 12.2.

The data for the minor isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.23−7.19 (m, 2H), 7.13 (s, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.00 (d, *J* = 11.0 Hz, 1H), 4.96 (d, *J* = 11.0 Hz, 1H), 3.92 (s, 6H), 3.87 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 189.4, 153.1, 143.6, 138.3, 137.4, 133.5, 131.6, 131.1, 130.0, 129.0, 128.8, 119.9, 106.5, 87.2, 85.8, 68.9, 60.9, 56.3, 38.4, 21.6, 12.4. HRMS (ESI) calcd. for $C_{29}H_{27}ClO_5S$ $[M+Na]^+$ 545.1160; found 545.1159.

S-Methyl-5-p-tolyl-2-(3,4,5-trimethoxybenzoyl)-3-(4-methylphenyl)-pent-4-yne-1-carbothioate (**4e**). Mixture of diastereomer (2:1). Yield: 76 mg, 76% (from 0.20 mmol of corresponding N,S-acetal). Pale yellow solid, mp 118−120 °C.

The data for the major isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (s, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 5.02 (d, *J* = 10.5 Hz, 1H), 4.87 (d, *J* = 10.5 Hz, 1H), 3.91 (s, 6H), 3.86 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.1, 190.6, 153.2, 143.4, 138.0, 137.3, 135.1, 131.5, 131.5, 129.4, 128.9, 128.5, 120.0, 106.8, 88.4, 84.6, 68.8, 61.0, 56.4, 39.3, 21.5, 21.3, 12.2.

The data for the minor isomer are as follows: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.10 (s, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 5.02 (d, *J* = 10.5 Hz, 1H), 4.94 (d, *J* = 10.5 Hz, 1H), 3.92 (s, 6H), 3.91 (s, 3H), 2.37 (s, 3H), 2.33 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.9, 189.9, 153.1, 143.3, 138.1, 137.1, 135.8, 132.1, 131.7, 129.4, 129.0, 128.0, 120.3, 106.4, 88.0, 85.3, 69.1, 60.9, 56.3, 38.9, 21.6, 21.2, 12.4. HRMS (ESI) calcd. for $C_{30}H_{30}O_5S$ $[M+Na]^+$ 525.1706; found 525.1716.

5-Benzyl-2-(4-methoxylphenyl)-4-(4-methylphenyl)-3-carbothiomethoxyfuran (**5a**). Yield: 27 mg, 63% (from 0.10 mmol of corresponding 1,3-diketone). Pale yellow solid; mp 100−102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63−7.62 (d, *J* = 8.5 Hz, 2H), 7.29−7.26 (m, 2H), 7.21−7.19 (m, 7H), 6.89 (d, *J* = 9.0 Hz, 2H), 3.96 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 3H), 2.39 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.3, 160.3, 152.0, 149.4, 138.2, 137.3, 129.8, 129.2, 129.2, 129.1, 128.7, 128.6, 126.6, 123.0, 122.6, 121.5, 113.9, 55.3, 32.5, 21.5, 12.6. HRMS (ESI) calcd. for $C_{27}H_{24}O_3S$ $[M+Na]^+$ 451.1338; found 451.1342.

5-Benzyl-2,4-bis(4-methylphenyl)-3-carbothiomethoxyfuran (**5b**). Yield: 24 mg, 58% (from 0.10 mmol of corresponding 1,3-diketone). Off white solid; mp 105−106 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.5 Hz, 2H), 7.29−7.26 (m, 3H), 7.21−7.16 (m, 8H), 3.97 (s, 2H), 2.38 (s, 3H), 2.37 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.5, 151.8, 149.7, 138.9, 138.1, 137.3, 129.8, 129.3, 129.2, 129.1, 128.7, 128.6, 127.4, 127.2, 126.7, 123.1, 122.2, 32.5, 21.6, 21.5, 12.6. HRMS (ESI) calcd. for $C_{27}H_{24}O_2S$ $[M+Na]^+$ 435.1389; found 435.1390.

5-(4-MethylBenzyl)-2,4-bis(4-methylphenyl)-3-carbothiomethoxyfuran (**5c**). Yield: 26 mg, 61% (from 0.10 mmol of corresponding 1,3-diketone). Off white solid; mp 101−102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.23−7.16 (m, 6H), 7.08 (s, 4H), 3.92 (s, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.6, 151.8, 150.0, 138.8, 137.2, 136.0, 135.1, 129.8, 129.4, 129.2, 129.2, 129.1, 128.5, 127.4, 127.2, 122.8, 122.1, 32.1, 21.6, 21.5, 21.2, 12.6. HRMS (ESI) calcd. for $C_{28}H_{26}O_2S$ $[M+Na]^+$ 449.1546; found 449.1545.

5-(4-Methylbenzyl)-2-(3,4,5-trimethoxyphenyl)-4-(4-chlorophenyl)-3-carbothiomethoxy- furan (**5d**). Yield: 29 mg, 56% (from 0.10 mmol of corresponding 1,3-diketone). Off white solid; mp 105−107 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.95 (s, 2H), 3.93 (s, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 2.32 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.4, 153.2, 151.4, 150.2, 139.1, 136.3, 134.6, 133.9, 131.1, 130.5, 129.5, 128.8, 128.3, 124.9, 122.1, 122.0, 104.9, 61.0, 56.2, 32.1, 21.2, 12.6. HRMS (ESI) calcd. for $C_{29}H_{27}ClO_5S$ $[M+Na]^+$ 545.1160; found 545.1163.

5-(4-Methylbenzyl)-2-(3,4,5-trimethoxyphenyl)-4-(4-methylphenyl)-3-carbothiomethoxy- furan (**5e**). Yield: 27 mg, 54% (from 0.10 mmol of corresponding 1,3-diketone). Off white solid; mp 119−121 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20−7.17 (m, 4H), 7.08 (s, 4H), 6.95 (s, 2H), 3.94 (s, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.8,

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153.2, 151.0, 149.9, 139.0, 137.3, 136.1, 135.0, 129.6, 129.4, 129.3, 129.0, 128.4, 125.2, 123.0, 122.4, 104.8, 61.0, 56.2, 32.1, 21.5 21.2, 12.7. HRMS (ESI) calcd. for $C_{30}H_{30}O_5S$ $[M+Na]^+$ 525.1706; found 525.1727.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02367.

Copies of ^1H and ^{13}C NMR (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*Phone: +91(471)2515420; Fax: +91(471)2491712; E-mail: ganeshnandi@gmail.com.

Notes

The authors declare no competing financial interest.

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