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Mechanochemical Thiolation of α-Imino Ketones: A Catalyst-Free, One-Pot, Three-Component Reaction

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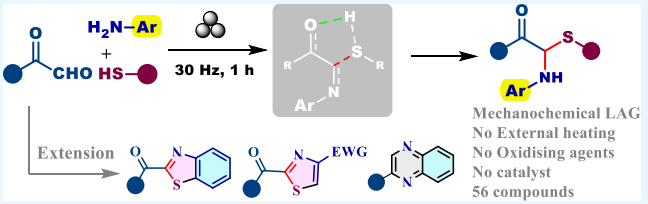
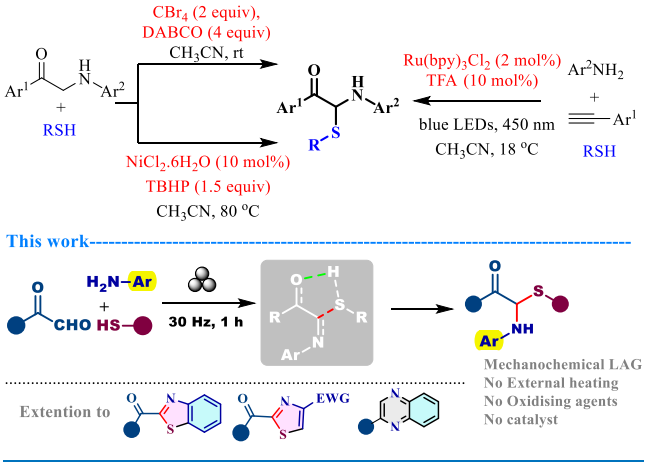
ABSTRACT: Herein, we report an efficient mechanochemical synthesis of α,α-amino thioketones involving a one-pot, three-component milling of 2-oxo aldehydes, amines, and thiols. Unlike previous methods, this protocol does not require any catalyst or oxidizing additive. The reaction proceeds through the thiolation of in situ formed α-imino ketones by liquid-assisted grinding. We have successfully extended this protocol to synthesizing benzothiazoles, thiazoles, and quinoxalines, demonstrating its efficiency and potential in the field. Importantly, we have shown the gram-scale synthesis, synthetic applications, and substrate scope of this protocol, instilling confidence in its practicality.



INTRODUCTION

Sulfur-containing compounds are of great interest due to their diverse roles in pharmaceutical chemistry,[1] organic chemistry,[2] material chemistry,[3] and living organisms.[4] In particular, α-amino ketones and α-amino esters are prevalent structures in many natural products, biologically active molecules, and pharmaceuticals.[5] Consequently, developing efficient methods for α-amino ketone derivatives has become a long-standing research area. These compounds are generally prepared by the C−H functionalization of α-amino ketones using various protocols.[6,7] However, the synthesis of α-amino ketones itself involves two steps: the use of electrophilic nitrogen like azodicarboxylate and organonitrogen compounds, followed by subsequent derivatization to obtain the required amine functionality.[8] Although the direct α-amination looks more straightforward, it suffers from the inherent nucleophilicity of both partners and the multistep synthesis of starting materials.[9] Therefore, in recent years, some catalytic methods using aziridine or an α-substituted intermediate to facilitate intermolecular umpolung reactions have been developed to install an α-amino substituent directly.[10] Although the direct C−H functionalization of α-amino ketones has been well studied, the incorporation of sulfur in α-amino ketones is limited to a few. In 2018, Huang and co-workers reported the thiolation of α-amino ketones by treating them with thiols in the presence of excessive reagents (2 equiv of CBr_4 and 4 equiv of DABCO).[11] Later, Shah's group reported a three-component synthesis under photoredox catalysis.[12] Recently, Xu and co-workers reported a nickel-catalyzed method, where 1.5 equiv of TBHP was required to reflux in acetonitrile to get the desired compounds (Scheme 1).[13] Despite some advantages, these methods suffer from using either excess reagents or stoichiometric additives, expensive catalysts, and presynthesized starting materials. Notably, all the reported methods involved forming α-imino ketone as the key intermediate, which underwent thiolation to furnish the desired α-amino α-thioketones under specific conditions. Recently, our group established a one-pot, multicomponent strategy for the Friedel−Crafts arylation of α-imino ketones and their cyclization reactions to access functionalized pyrroles and indoles.[14] Further, we disclosed the Povarov cyclization of

Scheme 1. Previous Works on the Synthesis of α,α-Amino Thioketones and Our Work



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these key building blocks to construct pyrroloquinolines in a diastereoselective manner.[15]

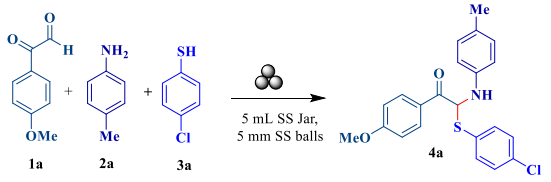
In recent years, organic synthesis under ball milling (mechanochemistry) is considered as a flagship approach in green chemistry and has become a valuable tool in synthetic organic chemistry.[16] Mechanochemistry allows environmentally friendly,[17] solvent-free synthesis of organic molecules, which provides access to a vast number of molecules that could not be achieved using conventional solution-based approaches.[18] Furthermore, in the year 2019, mechanochemistry was identified to meet the 12 principles of green chemistry, and it was selected as one of the ten world-changing innovations.[19] Despite many advantages of the mechanochemical organic synthesis, the preparation of organosulfur compounds using mechanochemistry is limited to a single report by Bolm's group, where a base-mediated synthesis of α-keto thioamide from acetophenone derivatives is developed under ball milling conditions.[20]

Inspired by the sustainable features attributed to mechanochemistry, we have initiated the mechanochemical organic synthesis in our laboratory and recently reported ring-opening cyclization of donor–acceptor cyclopropanes[21] and also the regioselective annulation of enaminones with propargyl alcohols.[22] In continuation, we report a metal-free thiolation of α-imino ketones through a one-pot, three-component approach under mechanochemical conditions.

RESULTS AND DISCUSSION

To investigate the mechanochemical reaction conditions, we chose readily available *p*-methoxyphenyl glyoxal (**1a**), *p*-toluidine (**2a**), and *p*-chlorothiophenol (**3a**) as the model substrates (Table 1). For the past few years, our group has successfully utilized alkaline earth catalysts as sustainable Lewis acid catalysts due to their high abundance on the earth's crust, biodegradability, nontoxicity, and moisture tolerance. Therefore, initially, we milled a mixture of **1a** (0.55 mmol), **2a** (0.55 mmol), **3a** (0.71 mmol) with 10 mol % $Ca(OTf)_2$ and silica (1 equiv) as grinding auxiliaries in a 5 mL SS jar with two SS balls (Ø 5 mm) at 25 Hz in a mixer mill. The milling resulted in 43% of the desired product **4a** in 1 h and 62% yield in 2 h (Table 1, entries 1,2). When we increased the milling frequency to 30 Hz, the reaction yield also increased (Table 1, entry 3). Milling with other grinding auxiliaries, such as talcum, alumina, and sodium chloride, does not yield better (Table 1, entries 4–6). Gratifyingly, when we switched to liquid-assisted grinding (LAG, acetonitrile, 25 μL), the reaction produced 82% **4a** (Table 1, entry 7). Interestingly, the same yield is reproduced without silica and the catalyst (Table 1, entries 8 and 9). Encouraged by the catalyst-free, three-component reaction, we milled them neat and found a lower yield of the product (entry 10). Increasing the quantity of acetonitrile (LAG) to 50 and 100 μL was not desirable as there was no further improvement (entries 11, 12). Milling for more or less time than 1 h is not beneficial (entries 13,14). Milling the reaction mixture with excess thiol did not show any notable increment in the yield of **4a** (Table 1, entry 15).

Table 1. Optimization of Reaction Conditions[a]



entry	reaction conditions	4a yield[b] (%)
1	10 mol % $Ca(OTf)_2$, silica, 25 Hz, 1 h	43
2	10 mol % $Ca(OTf)_2$, silica, 25 Hz, 2 h	62
3	10 mol % $Ca(OTf)_2$, silica, 30 Hz, 1 h	75
4	10 mol % $Ca(OTf)_2$, talcum, 30 Hz, 1 h	73
5	10 mol % $Ca(OTf)_2$, alumina, 30 Hz, 1 h	72
6	10 mol % $Ca(OTf)_2$, sodium chloride, 30 Hz, 1 h	70
7	10 mol % $Ca(OTf)_2$, silica, LAG, 30 Hz, 1 h	82
8	10 mol % $Ca(OTf)_2$, LAG, 30 Hz, 1 h	82
9[c]	LAG, 30 Hz, 1 h	83
10	30 Hz, 1 h	76
11	LAG (50 μL), 30 Hz, 1 h	83
12	LAG (100 μL), 30 Hz, 1 h	80
13	LAG, 30 Hz, 0.5 h	74
14	LAG, 30 Hz, 2 h	82
15[d]	LAG, 30 Hz, 1 h	84

[a]Reaction conditions: Unless mentioned, **1a** (100 mg, 0.55 mmol), **2a** (59 mg, 0.55 mmol), **3a** (103 mg, 0.71 mmol) were milled as per table, 25 μL of acetonitrile used as LAG, grinding auxiliary (1 eq, silica/alumina/talcum/NaCl). [b]Isolated yields. [c]Optimum conditions. [d]With 5 equiv of **3a**.

LAG is a phenomenon whereby the addition of small amounts of liquid can have a profound effect on the outcome of a milled reaction.[23] Therefore, we have also explored the nature of the liquid used for LAG of **1a**, **2a**, and **3a** with various other solvents, such as tetrahydrofuran (THF), toluene, 1,2-dichloroethane, *N*,*N*-dimethylformamide, dimethyl sulfoxide (DMSO), 1,1,1,3,3,3,-hexafluoroisopropanol, ethanol, water, 1,4-dioxane, and nitromethane, and observed that all of them vastly furnished the inferior results, as depicted in Figure 1. This study indicated that acetonitrile is the best for this catalyst-free, three-component, liquid-assisted grinding reaction. Based on these reaction screenings, we concluded that entry 9 was the best condition to obtain the desired compound.

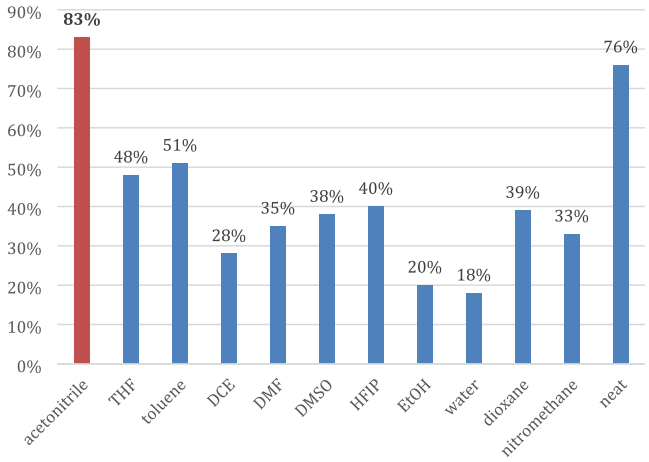


Figure 1. Study of LAG with various solvents (% of yields shown on the *Y* axis).

Having the optimized reaction conditions in hand (Table 1, entry 9), we focused on studying the generality of the reaction (Scheme 2). Initially, we studied the scope of various α-keto aldehydes (**1a**–**1e**) with *p*-toluidine **2a** and *p*-chlorothiophenol **3a** under the standard reaction conditions. As expected, the

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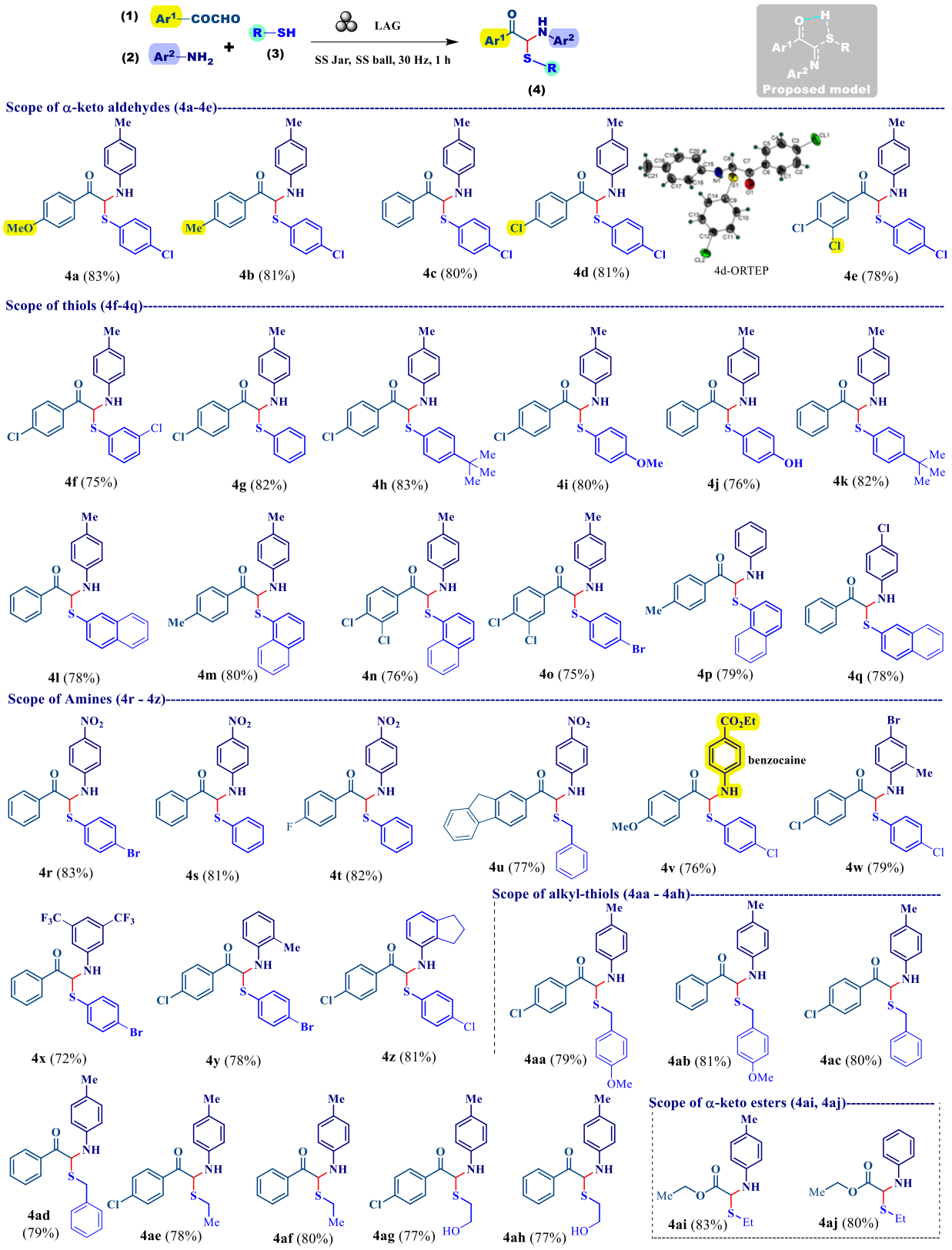
Scheme 2. Substrate Scope[a]



[a]Conditions: A mixture of 1 (100 mg, 0.55 mmol), 2 (0.55 mmol), 3 (0.71 mmol) and acetonitrile (25 μL, LAG) was milled in a 5 mL SS jar with 5 mm SS balls (two) at 30 Hz for 1 h in MM-400.

milling proceeded smoothly to furnish the desired α-amino and α-thio carbonyl compounds **4a**−**4e** in good yields. Furthermore, the structure of **4d** was unambiguously confirmed by obtaining the single-crystal X-ray data.[24] Next, a series of thiophenols were subjected to milling with α-keto aldehydes and amine **2a** to obtain the desired compounds **4f**−

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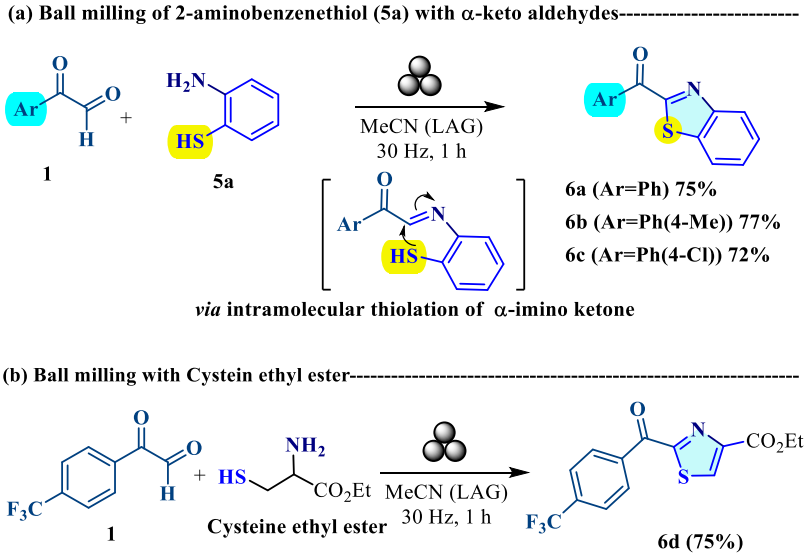
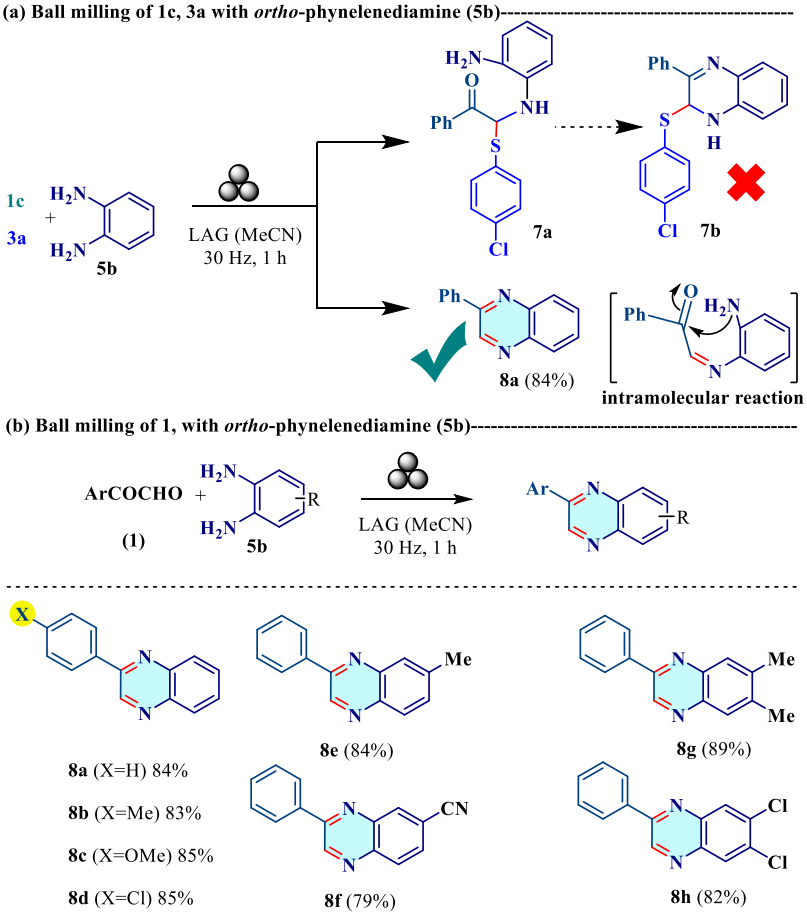
Scheme 3. Extension of the Protocol to the Synthesis of Benzothiazoles by Milling Aryl Glyoxal with 2-Amino Benzenethiol (a) and Cysteine Ethyl Ester (b)



Scheme 4. Ball Milling of Aryl Glyoxal with o-Phenylenediamine for the Synthesis of Quinoxalines



4q in good yields. Further, aryl amines bearing electron-donating groups, electron-withdrawing groups, and sterically hindered substitutions were milled with various keto aldehydes and thiols to furnish the desired compounds **4r**–**4z** without compromising the yields. Interestingly, our protocol is also compatible with various aliphatic thiols, such as *p*-methoxybenzylthiol (**3j**), benzylthiol (**3k**), ethanethiol (**3l**), and 2-mercaptoethan-1-ol (**3m**), to produce the corresponding *α*-amino and *α*-thio carbonyl compounds **4aa**–**4ah** in good yields. Besides, *α*-keto esters also reacted smoothly under the optimized ball milling conditions to furnish the *α*-amino and *α*-thio esters **4ai** and **4aj** in good yields (Scheme 2).

After successfully developing a catalyst-free, one-pot, three-component thiolation of *α*-amino ketone under solventless ball

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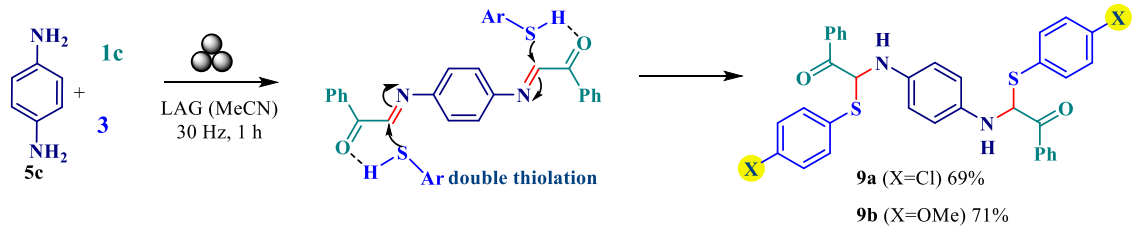
Scheme 5. Ball Milling of Aryl Glyoxal with *p*-Phenylenediamine



milling (Scheme 2), we extended the study to 2-amino thiophenol (**5a**), where the amine and SH group are within the same molecule. Under the standard milling conditions, various α-keto aldehydes were milled with **5a**, and the corresponding benzothiazoles **6a**−**6c** in good yields via the intramolecular thiolation of in situ formed α-imino ketones were obtained (Scheme 3). Next, we milled the cysteine ethyl ester (a nonessential amino acid derivative) with **1h** and obtained the corresponding thiazole derivative **6d** via the intramolecular thiolation of in situ formed α-imino ketones (Scheme 3).

Encouraged by this observation, we were curious to study o-phenylenediamine reactivity. As desired, **1c**, **3a**, and **5b** were subjected to LAG for 1 h, expecting the formation of **7b** via **7a** (Scheme 4). However, the reaction did not yield **7b** but furnished 2-phenyl quinoxaline **8a** in 84% yield. Realizing the fastness of a direct intramolecular reaction is due to the proximity effect (as indicated next to **8a**), we used excess (10 equiv) thiol **3a** and repeated the milling to overcome this issue. However, it still led to the formation of **8a**. Nevertheless, we generalized this catalyst-free mechanochemical synthesis of 2-aryl quinoxalines by milling α-keto aldehydes and *o*-phenylenediamine (Scheme 4) to prepare compounds **8a**−**8h** in good yields.

Next, we shifted our focus to utilize *p*-phenylenediamine (**5c**) in the reaction so that the α-imino ketones can be generated on both sides; hence, a bis-thiolation can be accomplished. Accordingly, we milled **5c** with 2 equiv of phenylglyoxal (**1c**) and 2 equiv of *p*-chlorophenyl thiol (**3a**) for one hour and obtained α-thiolated bis amino ketone **9a** in 69% yield. In a similar way, **9b** was prepared from **1c**, **5c**, and **3e** in 71% yield (Scheme 5).

Encouraged by the wide applicability of this protocol, we performed a gram-scale synthesis of **4d** (1.47 g) by milling **1d**, **2a**, and **3a** (Scheme 6). Subsequently, we have performed a series of postsynthetic modifications. Ketone **4d** was subjected to reduction with sodium borohydride in ethanol; surprisingly, we observed the substitution of the C−S bond with the hydride along with ketone reduction to furnish amino alcohol **10**. Next, ketone **4d** was subjected to Wittig olefination with the Horner−Wadsworth−Emmons reagent to obtain alkene **11a**. However, the isolated compound is characterized as 1,3-dihydro-2H-pyrrol-2-one **11b**. This was not surprising to us because, after the formation of desired alkene **11a**, the sec-amine underwent an intramolecular nucleophilic substitution at ester carbonyl, followed by double bond isomerization, which provided the dihydro-2H-pyrrol-2-one **11b** (see Scheme 6, eq-c, mechanism). A direct substitution of **4s** with indole was performed with TFA at room temperature[12] to obtain **12a**; however, the reaction furnished 2,2-di(1H-indol-3-yl)-1-phenylethan-1-one **12b**. Probably, after the formation of **12a**, *p*-nitroaniline also underwent substitution with indole (2-fold substitution). A method similar to that was used to prepare **12c**. Further, **12b** was treated with phenylacetylene and *n*-butyllithium to get propargyl alcohols **13** in 85% yield. Compound **13** is a key precursor for the carbazole construction (**14**).[25] Compound **4c** was also subjected to 2-fold substitution with *N*,*N*-dimethylaniline in the presence of 50 mol % TFA to get the desired compound **15** (Scheme 6).

To shed light on the reaction mechanism, we have isolated the intermediate **A1** (Scheme 7, eq-a), subjected it to the reaction conditions (stepwise), and obtained the corresponding product **4c**. Although we did not perform any study to indicate the role of hydrogen bonding in accelerating the reaction, we believe that it is essential in activating the electrophilicity of imino carbon through a five-membered transition state (as indicated), thus facilitating the addition of sulfur to get the final product **4**.[26] Based on these observations, we proposed a plausible reaction mechanism, as depicted in Scheme 7. Milling of α-ketoaldehyde (**1**) and primary amine (**2**) furnishes the α-imino ketone (**A**). Next, the thiolation of activated α-imino ketone through hydrogen bonding (see structure **B**) occurs to furnish the desired, α-amino, α-thio ketone **4**.

CONCLUSIONS

In conclusion, we have developed a green synthetic protocol for the thiolation of α-imino ketones under ball milling conditions from readily available starting materials. This one-pot, three-component reaction proceeds at room temperature without any catalyst, additive, or reflux in a solvent. Further, we have extended this strategy to constructing thiazoles, benzothiazoles, and quinoxalines. Besides, we demonstrated a gram-scale synthesis and postsynthetic modifications. The rationale for new observations during reduction, substitution, and Wittig olefination is discussed in detail. The generality of the reaction is well established by synthesizing 56 compounds. Considering its simplicity in terms of operation by ball milling, short reaction duration, cost-effectiveness and ready availability of starting materials, solventless and catalyst-free conditions, and adaptability to synthesize benzothiazoles and thiazoles, this protocol offers a convincing alternative to existing procedures for the synthesis of α,α-amino thioketones, and we expect this protocol to efficiently address the needs of the pharmaceutical industry within its domain.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents were used as received from commercial suppliers. Reactions were performed in oven-dried glassware with magnetic stirring. All reactions under the heating conditions were performed in an oil bath. Mechanochemical reactions were carried out in a RETSCH Mixer Mill MM-400. Milling vessels (5 mL volumetric capacity) and milling balls (5 mm diameter) were made of stainless steel. Reactions were monitored by thin-layer

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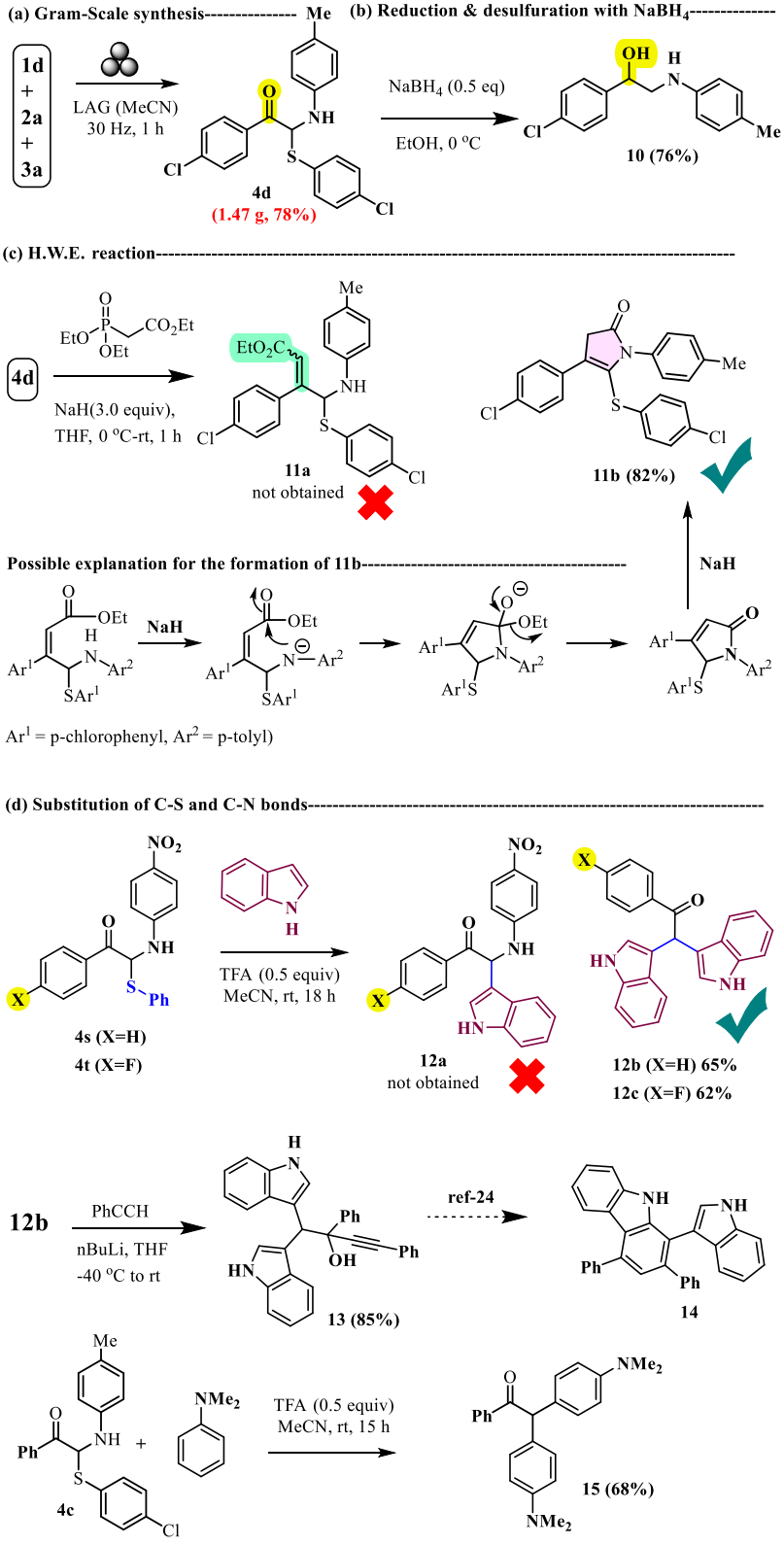
Scheme 6. Gram-Scale Synthesis and Postsynthetic Modifications



chromatography (TLC) with aluminum sheets, Merck silica gel 60 F254. TLC plates were visualized with UV light (254 nm), iodine treatment, or *p*-anisaldehyde stain. Column chromatography was carried out using silica gel 100−200 mesh as the stationary phase. NMR spectra were recorded at 500 MHz and (^{1}H) and at 125 and 100 MHz (^{13}C), respectively, on an Avance Bruker spectrometer. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (^{1}H: δ = 7.26 and ^{13}C: δ = 77.16 ppm) as an internal standard, and coupling constants (J) are given in Hz. HRMS spectra were recorded using ESI-TOF techniques. Melting points were measured with a LABINDIA MEPA melting apparatus. Single-crystal X-ray

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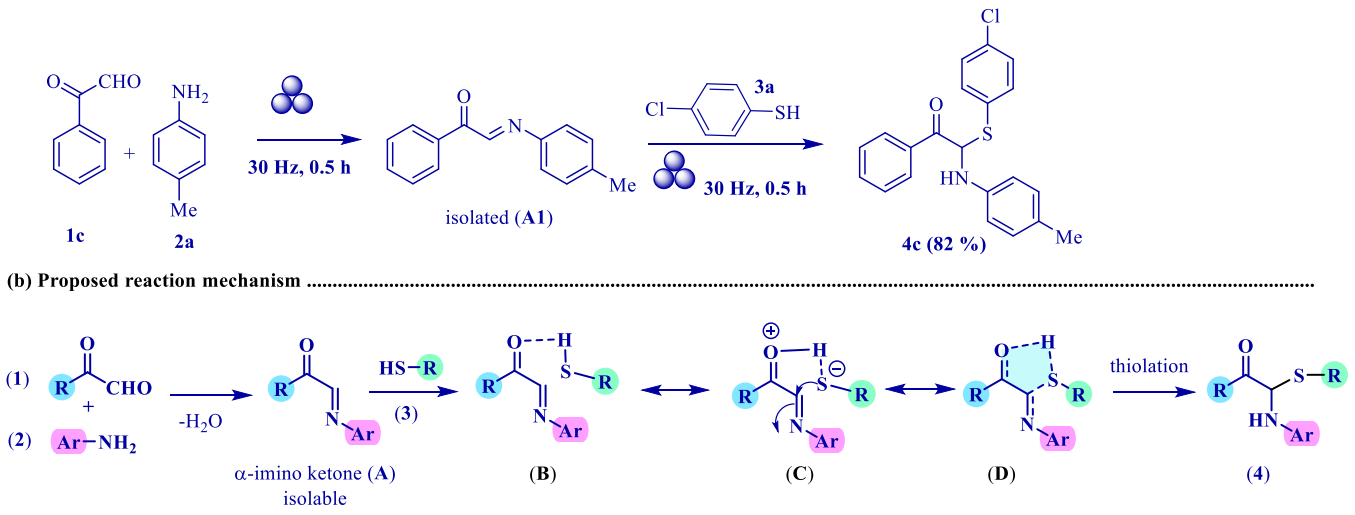
Scheme 7. Stepwise Reaction (a) and Possible Reaction Mechanism (b)



diffraction data were collected in Bruker D8-Quest diffractometers.

General Experimental Procedure for the Synthesis of Compound 4. A 5 mL SS milling jar equipped with two 5 mm SS balls was charged with glyoxal **1** (1 equiv), arylamine **2** (1 equiv), and thiol **3** (1.3 equiv) in MeCN (50 μL). After the jar was closed tightly, milling was carried out for 1 h at 30 Hz. After completion of the reaction (monitored by TLC), the crude residue was directly absorbed onto silica gel and purified by column chromatography (3% EtOAc in petroleum ether) to obtain the corresponding compound **4**.

Experimental Procedure for Gram-Scale Synthesis of Compound 4d. A 10 mL SS milling jar equipped with two 10 mm SS balls was charged with 4-chloro phenylglyoxal (869 mg, 4.672 mmol), *p*-toluidine (500 mg, 4.672 mmol), and thiol (874 mg, 6.074 mmol) in MeCN (100 μL). After closing the jar tightly, milling was carried out for 1 h at 30 Hz. After completion of the reaction (monitored by TLC), the crude residue was directly absorbed onto silica gel, and the product was purified by column chromatography (3% EtOAc in petroleum ether) to obtain the corresponding compound **4d**.

2-((4-Chlorophenyl)thio)-1-(4-methoxyphenyl)-2-(p-tolylamino)ethan-1-one (4a). Compound **4a** was obtained (using 5% EtOAc/petroleum ether) as a yellow solid (154 mg, 83%); mp: 103−104 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 6.24 (d, J = 9.5 Hz, 1H), 5.04 (d, J = 9.5 Hz, 1H), 3.90 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 187.2, 164.1, 140.4, 138.6, 135.9, 131.0, 130.0, 128.9, 128.6, 127.6, 126.8, 114.9, 114.1, 63.4, 55.6, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{22}H_{21}ClNO_2S]^+$: 398.0982; found: 398.0984. IR (film): ν_{max} 3382, 3016, 1668, 1328, 1228, 1086, 805, 548, cm^{-1}.

2-((4-Chlorophenyl)thio)-1-(p-tolyl)-2-(p-tolylamino)-ethan-1-one (4b). Compound **4b** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (144 mg, 81%); mp: 174−175 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.26 (d, J = 8.5 Hz, 1H), 5.02 (d, J = 9.0 Hz, 1H), 2.45 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 187.9, 144.8, 140.4, 138.6, 136.1, 131.7, 130.1, 129.7, 129.0, 128.8, 128.7, 127.4, 115.0, 63.5, 21.9, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{22}H_{21}ClNOS]^+$: 382.1032; found: 382.1037.

2-((4-Chlorophenyl)thio)-1-phenyl-2-(p-tolylamino)-ethan-1-one (4c). Compound **4c** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (138 mg, 80%); mp: 150−151 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, J = 7.5 Hz, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.0 Hz, 2H), 6.29 (d, J = 9.5 Hz, 1H), 5.01 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): 188.1, 140.3, 138.7, 136.1, 134.3, 133.7, 130.1, 129.1, 128.9, 128.8, 128.7, 127.3, 115.0, 63.7, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{19}ClNOS]^+$: 368.0876; found: 368.0878;

1-(4-Chlorophenyl)-2-((4-chlorophenyl)thio)-2-(p-tolylamino)ethan-1-one (4d). Compound **4d** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (152 mg, 81%); mp: 142−143 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 9.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.24 (d, J = 9.5 Hz, 1H), 4.98 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.8, 140.2, 140.1, 138.6, 136.2, 132.5, 130.1 (2), 129.3, 129.1, 128.9, 126.9, 115.0, 63.7, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{18}Cl_2NOS]^+$: 402.0486; found: 402.0487; IR (film): ν_{max} 3376, 3014, 1743, 1368, 1221, 1087, 804, 520, cm^{-1}.

2-((4-Chlorophenyl)thio)-1-(3,4-dichlorophenyl)-2-(p-tolylamino)ethan-1-one (4e). Compound **4e** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (159 mg, 78%); mp: 124−125 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (d, J = 2.5 Hz, 1H), 7.84 (dd, J = 2.0, 6.5 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.20 (s, 1H), 4.94 (bs, 1H), 2.32 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.3, 140.4, 138.4, 136.5, 134.5, 133.9, 131.1, 130.8, 130.2, 129.4, 129.3, 127.7, 127.6, 121.8, 115.3, 64.7, 20.6 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{17}Cl_3NOS]^+$: 436.0096; found: 436.0094.

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1-(4-Chlorophenyl)-2-((3-chlorophenyl)thio)-2-(p-tolylamino)ethan-1-one (4f). Compound **4f** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (141 mg, 75%); mp: 124−125 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 9.0 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.31 (dq, J = 5.0, 1.0 Hz, 1H), 7.17−7.13 (m, 3H), 6.98 (t, J = 2.0 Hz, 1H), 6.90 (dt, J = 5.0, 1.5 Hz, 1H), 6.80 (d, J = 8.5 Hz, 2H), 6.27 (d, J = 9.5 Hz, 1H), 5.04 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.9, 140.2, 139.9, 136.8, 135.3, 134.3, 132.6, 130.5, 130.1, 130.0, 129.8 (2), 129.3, 129.1, 115.1, 63.9, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{18}Cl_2NOS]^+$: 402.0486; found: 402.0487; IR (film): ν_{max} 3355, 3014, 1743, 1367, 1217, 1093, 777, 528 cm^{-1}.

1-(4-Chlorophenyl)-2-(phenylthio)-2-(p-tolylamino)-ethan-1-one (4g). Compound **4g** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (142 mg, 82%); mp: 82−83 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 9.0 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.35−7.32 (m, 1H), 7.25−7.21 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.02−7.00 (m, 2H), 6.81 (d, J = 8.5 Hz, 2H), 6.24 (d, J = 10.0 Hz, 1H), 4.98 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 187.1, 140.4, 140.0, 137.4, 132.9, 130.1, 129.7, 129.2, 128.9, 128.8, 128.6, 115.1, 63.7, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{19}ClNOS]^+$: 368.0876; found: 368.0874.

2-((4-(*tert*-Butyl)phenyl)thio)-1-(4-chlorophenyl)-2-(p-tolylamino)ethan-1-one (4h). Compound **4h** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (164 mg, 83%); mp: 148−149 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.0, Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 6.19 (d, J = 10.0 Hz, 1H), 4.97 (d, J = 10.0 Hz, 1H), 2.31 (s, 3H), 1.28 (s, 9H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 187.3, 152.9, 140.6, 139.8, 137.0, 133.0, 130.1, 130.0, 129.1, 128.6, 125.9, 125.1, 115.1, 63.7, 34.8, 31.3, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{25}H_{27}ClNOS]^+$: 424.1502; found: 424.1505. IR (film): ν_{max} 3350, 2958, 1739, 1297, 1229, 1094, 806, 553, cm^{-1}.

1-(4-Chlorophenyl)-2-((4-methoxyphenyl)thio)-2-(p-tolylamino)ethan-1-one (4i). Compound **4i** was obtained (using 5% EtOAc/petroleum ether) as a yellow solid (149 mg, 80%); mp: 110−111 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 6.17 (d, J = 10.0 Hz, 1H), 4.94 (d, J = 9.5 Hz, 1H), 3.77 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 187.1, 161.0, 140.5, 139.9, 138.9, 132.9, 130.1, 129.2, 128.6, 118.9, 115.1, 114.5, 63.6, 55.4, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{22}H_{21}ClNO_2S]^+$: 398.0982; found: 398.0984. IR (film): ν_{max} 3380, 3001, 1739, 1313, 1238, 1032, 806, 534, cm^{-1}.

2-((4-Hydroxyphenyl)thio)-1-phenyl-2-(p-tolylamino)ethan-1-one (4j). Compound **4j** was obtained (using 10% EtOAc/petroleum ether) as a pale yellow solid (125 mg, 76%); mp: 154−155 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, J = 7.0 Hz, 2H), 7.63 (t, J = 7.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.12 (d, J = 7.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 6.24 (d, J = 9.5 Hz, 1H), 5.40 (bs, 1H), 4.97 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 188.5, 157.3, 140.6, 139.3, 134.6, 133.6, 133.0, 130.1, 128.9, 128.7, 119.3, 116.1, 115.1, 63.5, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{21}H_{20}NO_2S]^+$: 350.1215; found: 350.1218; IR (film): ν_{max} 3389, 3013, 1740, 1367, 1215, 804, 527 cm^{-1}.

2-((4-(*tert*-Butyl)phenyl)thio)-1-phenyl-2-(p-tolylamino)ethan-1-one (4k). Compound **4k** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (150 mg, 82%); mp: 145−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, J = 8.5 Hz, 2H), 7.60 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.23−7.20 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.96−6.95 (m, 2H), 6.81 (d, J = 7.0 Hz, 2H), 6.25 (d, J = 9.5 Hz, 1H), 4.99 (d, J = 9.5 Hz, 1H), 2.31 (s, 3H), 1.28 (s, 9H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.4, 152.7, 140.7, 137.1, 134.7, 133.5, 130.0, 128.8, 128.7, 128.5, 125.9, 125.2, 115.1, 63.5, 34.8, 31.3, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{25}H_{28}NOS]^+$: 390.1892; found: 390.1891.

2-(Naphthalen-2-ylthio)-1-phenyl-2-(p-tolylamino)-ethan-1-one (4l). Compound **4l** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (140 mg, 78%); mp: 104−105 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 7.5 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.5 Hz, 1H), 7.65−7.62 (m, 2H), 7.54−7.44 (m, 5H), 7.16 (d, J = 8.5 Hz, 2H), 7.08 (dd, J = 1.5, 7.0 Hz, 1H), 6.84 (d, J = 8.5 Hz, 2H), 6.36 (d, J = 9.5 Hz, 1H), 5.04 (d, J = 10.0 Hz, 1H), 2.34 (s, 3H), ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.4, 140.6, 137.9, 134.7, 133.6, 133.5 (2), 130.1, 128.9, 128.8, 128.3, 128.0, 127.8, 127.1, 126.4, 126.2, 115.2, 63.8, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{25}H_{22}NOS]^+$: 384.1422; found: 384.1419.

2-(Naphthalen-1-ylthio)-1-(p-tolyl)-2-(p-tolylamino)-ethan-1-one (4m). Compound **4m** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (150 mg, 80%); mp: 148−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 8.0 Hz, 1H), 7.85−7.81 (m, 3H), 7.76 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.30−7.24 (m, 4H), 7.18−7.12 (m, 3H), 6.80 (d, J = 8.0 Hz, 2H), 6.40 (s, 1H), 4.99 (s, 1H), 2.45 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.5, 144.5, 141.1, 137.3, 136.6, 134.3, 132.4, 130.5, 130.1, 129.5, 129.1, 128.7, 128.3, 126.9, 126.4, 126.1, 125.3, 121.6, 115.1, 64.6, 21.8, 20.6 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{26}H_{24}NOS]^+$: 398.1579; found: 398.1582.

1-(3,4-Dichlorophenyl)-2-(naphthalen-1-ylthio)-2-(p-tolylamino)ethan-1-one (4n). Compound **4n** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (161 mg, 76%); mp: 142−143 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 2.0 Hz, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.72 (dd, J = 2.0, 6.5 Hz, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.43−7.39 (m, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.26−7.24 (m, 1H), 7.21−7.18 (m, 1H), 7.15 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 6.31 (s, 1H), 4.95 (s, 1H), 2.34 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.1, 140.3, 138.1, 137.3, 136.2, 134.2, 134.1, 133.5, 130.9, 130.8, 130.7, 130.2, 129.0, 128.4, 127.7, 126.6, 126.5, 126.3(2), 125.3, 115.0, 64.5, 20.7 ppm; HRMS (ESI-TOF) m/z: [M + H]$^+$ calculated for $[C_{25}H_{20}Cl_2NOS]^+$: 452.0643; found: 452.0637.

2-((4-Bromophenyl)thio)-1-(3,4-dichlorophenyl)-2-(p-tolylamino)ethan-1-one (4o). Compound **4o** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (168 mg, 75%); mp: 138−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.34 (d, J = 7.5 Hz, 2H), 7.12 (d, J = 7.5 Hz, 2H), 6.82 (d, J =

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7.5 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 6.19 (d, J = 8.5 Hz, 1H), 4.94 (d, J = 9.0 Hz, 1H), 2.31 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.6, 139.9, 138.8, 138.3, 133.9, 133.7, 132.2, 131.0, 130.6, 130.2, 129.2, 127.6, 127.4, 124.8, 115.1, 63.9, 20.7 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{21}H_{17}BrCl_2NOS]^+$: 479.9591; found: 479.9594.

2-(Naphthalen-1-ylthio)-2-(phenylamino)-1-(p-tolyl)-ethan-1-one (4p). Compound **4p** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (163 mg, 79%); mp: 152−153 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.40−7.37 (m, 1H), 7.34−7.25 (m, 6H), 7.17−7.14 (m, 1H), 6.91−6.88 (m, 3H), 6.41 (s, 1H), 5.09 (bs, 1H), 2.46 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.1, 144.7, 143.2, 137.5, 136.4, 134.1, 131.8, 130.6, 129.5(2), 129.0, 128.3, 126.9, 126.7, 126.4, 126.2, 125.3, 119.3, 114.9, 63.5, 21.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{25}H_{22}NOS]^+$: 384.1422; found: 384.1425.

2-(Naphthalen-2-ylthio)-1-phenyl-2-(p-tolylamino)-ethan-1-one (4q). Compound **4q** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (124 mg, 78%); mp: 137−138 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.63 (t, J = 6.5 Hz, 2H), 7.55−7.44 (m, 5H), 7.29 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 1H), 6.83 (d, J = 8.0 Hz, 2H), 6.27 (d, J = 9.0 Hz, 1H), 5.14 (d, J = 9.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.3, 141.6, 137.9, 134.2, 133.8, 133.5, 133.4, 133.3, 129.4, 128.9, 128.8, 128.4, 127.9, 127.8, 127.2, 126.5, 125.5, 124.1, 116.2, 62.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{24}H_{19}ClNOS]^+$: 404.0876; found: 404.0878. IR (film): ν_{max} 3329, 3043, 1740, 1305, 1227, 1092, 810, 578, cm^{-1}.

2-((4-Bromophenyl)thio)-2-((4-nitrophenyl)amino)-1-phenylethan-1-one (4r). Compound **4r** was obtained (using 5% EtOAc/petroleum ether) as a pale yellow solid (133 mg, 83%); mp: 171−172 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, J = 7.5 Hz, 2H), 8.04 (d, J = 8.0 Hz, 2H), 7.69 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.5 Hz, 2H), 7.37 (d, J = 7.0 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 7.0 Hz, 2H), 6.21 (d, J = 8.0 Hz, 1H), 5.79 (d, J = 8.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 188.3, 148.5, 140.1, 138.7, 134.4, 133.4, 132.3, 129.1, 128.9, 126.6, 126.2, 125.2, 113.9, 61.4, ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{20}H_{16}BrN_2O_3S]^+$: 443.0065; found; 443.0070; IR (film): ν_{max} 3368, 3013, 1734, 1368, 1216, 1100, 811, 539 cm^{-1}

2-((4-Nitrophenyl)amino)-1-phenyl-2-(phenylthio)-ethan-1-one (4s). Compound **4s** was obtained (using 5% EtOAc/petroleum ether) as a pale white solid (107 mg, 81%); mp: 179−180 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, J = 8.5 Hz, 2H), 8.05 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 7.0 Hz, 1H), 7.56 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.0 Hz, 1H), 7.23 (t, J = 8.0 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.22 (d, J = 8.0 Hz, 1H), 5.80 (d, J = 8.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.4, 148.7, 139.9, 137.3, 134.2, 133.6, 130.2, 129.1 (2), 128.9, 127.5, 126.3, 113.9, 61.3 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{20}H_{17}N_2O_3S]^+$: 365.0960; found; 365.0956; IR (film): ν_{max} 3370, 3014, 1739, 1593, 1367, 1316, 1224, 991, 748, 556 cm^{-1}.

1-(4-Fluorophenyl)-2-((4-nitrophenyl)amino)-2-(phenylthio)ethan-1-one (4t). Compound **4t** was obtained (using 5% EtOAc/petroleum ether) as a pale yellow solid (114 mg, 82%); mp: 185−186 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, J = 9.5 Hz, 2H), 8.11−8.08 (m, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.25−7.21 (m, 4H), 7.00 (d, J = 7.5 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 6.18 (d, J = 8.0 Hz, 1H), 5.78 (d, J = 8.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 187.1, 166.3(d, J_{C-F} = 256.2 Hz), 148.6, 139.9, 137.2, 131.7(d, J_{C-F} = 9.4 Hz), 130.3, 129.9, 129.2, 127.4, 126.3, 116.3(d, J_{C-F} = 21.8 Hz), 113.9, 61.3 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{20}H_{16}FN_2O_3S]^+$: 383. 0866; found; 383.0864; IR (film): ν_{max} 3369, 3012, 1732, 1368, 1221, 1105, 992, 837, 596 cm^{-1}.

2-(Benzylthio)-1-(9H-fluoren-2-yl)-2-((4-nitrophenyl)-amino)ethan-1-one (4u). Compound **4u** was obtained (using 10% EtOAc/petroleum ether) as a yellow solid (130 mg, 77%); mp: 155−156 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 7.5 Hz, 1H), 7.44−7.38 (m, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.18−7.15 (m, 3H), 7.10−7.08 (m, 2H), 6.69 (d, J = 9.0 Hz, 2H), 6.06 (d, J = 8.0 Hz, 1H), 5.32 (d, J = 8.0 Hz, 1H), 3.97 (s, 2H), 3.55 (dd, J = 7.5, 13.0 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.7, 147.5, 144.7, 143.6, 142.6, 140.4, 136.9, 132.2, 132.1, 129.1, 128.5(2), 128.1, 127.3, 127.1, 125.5, 125.4, 121.2, 120.0, 116.3, 111.0, 59.7, 37.1, 32.4 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{28}H_{23}N_2O_3S]^+$: 467.1429; found; 467.1426.

Ethyl 4-((1-((4-chlorophenyl)thio)-2-(4-methoxyphenyl)-2-oxoethyl)amino)benzoate (4v). Compound **4v** was obtained (using 15% EtOAc/petroleum ether) as a yellow semisolid (110 mg, 76%); NMR (500 MHz, $CDCl_3$): δ 8.02−8.00 (m, 4H), 7.17 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.20 (d, J = 8.5 Hz, 1H), 5.52 (d, J = 8.5 Hz, 1H), 4.36 (q, J = 7.0 Hz, 2H), 3.91 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 187.2, 166.8, 164.3, 146.8, 138.6, 136.4, 131.6, 131.2, 129.2, 126.7, 126.3, 121.1, 114.3, 114.0, 61.6, 60.6, 55.7, 14.6 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calculated for $[C_{24}H_{22}ClNO_4SNa]^+$: 478.0856; found; 478.0851; IR (film): ν_{max} 3458, 3010, 1732, 1598, 1367, 1223, 1093, 820, 768, 525 cm^{-1}.

2-((4-Bromo-2-methylphenyl)amino)-1-(4-chlorophenyl)-2-((4-chlorophenyl)thio)ethan-1-one (4w). Compound **4w** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (102 mg, 79%); mp: 123−124 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.35 (dd, J = 2.0, 8.5 Hz, 1H), 7.23−7.22 (m, 1H), 7.17 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 1H), 6.80 (d, J = 8.5 Hz, 2H), 6.15 (d, J = 5.5 Hz, 1H), 4.95 (d, J = 6.5 Hz, 1H), 1.99 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 187.5, 140.5, 139.9, 138.3, 136.6, 133.3, 132.8, 130.1, 129.9, 129.4, 129.2, 127.1, 125.8, 114.4, 111.6, 63.1, 16.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{21}H_{17}BrCl_2NOS]^+$: 479.9591; found; 479.9592.

2-((3,5-Bis(trifluoromethyl)phenyl)amino)-2-((4-bromophenyl)thio)-1-phenylethan-1-one (4x). Compound **4x** was obtained (using 5% EtOAc/petroleum ether) as a white solid (84 mg, 72%); mp: 174−175 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.5 Hz, 2H), 7.35 (d, J = 8.5 Hz, 3H), 7.25 (d, J = 2.0 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.21 (d, J = 8.5 Hz, 1H), 5.62 (d, J = 8.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 188.3, 144.1, 138.6, 134.4, 133.5, 132.8, (q, J_{C-F} = 33.0 Hz), 132.3, 129.2, 128.9, 126.9, 125.1, 124.7, 122.5, 114.3, 112.4, 62.0 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{22}H_{15}BrF_6NOS]^+$: 533.9962; found;

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533.9967. IR (film): ν_{max} 3355, 2968, 1739, 1385, 1269, 1002, 813, 527, cm^{-1}.

2-((4-Bromophenyl)thio)-1-(4-chlorophenyl)-2-(o-tolylamino)ethan-1-one (4y). Compound **4y** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (162 mg, 78%); mp: 143−144 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 1H), 7.12 (d, J = 7.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 6.84 (t, J = 7.5 Hz, 1H), 6.77 (d, J = 8.0 Hz, 2H), 6.28 (s, 1H), 4.99 (bs, 1H), 2.06 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 187.0, 140.4, 140.3, 138.8, 132.5, 132.1, 130.7, 130.1, 129.4, 127.5, 127.2, 124.7, 123.5, 119.3, 112.7, 62.9, 17.3 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{21}H_{18}BrClNOS]^+$: 445.9981; found; 445.9985.

1-(4-Chlorophenyl)-2-((4-chlorophenyl)thio)-2-((2,3-dihydro-1H-inden4yl)amino)ethan1-one (4z). Compound **4z** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (131 mg, 81%); mp: 125−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.25−7.16 (m, 3H), 6.89−6.82 (m, 4H), 6.30 (d, J = 9.6 Hz, 1H), 4.87 (d, J = 9.6 Hz, 1H), 2.96 (t, J = 7.2 Hz, 2H), 2.72−2.64 (m, 1H), 2.54−2.47 (m, 1H), 2.14−2.07 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 187.1, 145.6, 140.3, 138.7, 138.5, 136.3, 132.6, 130.1, 129.9, 129.3, 129.1, 127.7, 127.1, 115.9, 110.5, 63.1, 33.5, 29.5, 24.8 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{23}H_{20}Cl_2NOS]^+$: 428.0643; found; 428.0640; IR (film): ν_{max} 3377, 2948, 1739, 1369, 1217, 1086, 823, 535 cm^{-1}.

1-(4-Chlorophenyl)-2-((4-methoxybenzyl)thio)-2-(p-tolylamino)ethan-1-one (4aa). Compound **4aa** was obtained (using 5% EtOAc/petroleum ether) as a yellow solid (152 mg, 79%); mp: 118−119 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 6.69 (d, J = 8.5 Hz, 2H), 5.98 (d, J = 8.5 Hz, 1H), 5.11 (d, J = 8.5 Hz, 1H), 3.73 (s, 3H), 3.50 (d, J = 13.0 Hz, 1H), 3.43 (d, J = 12.5 Hz, 1H), 2.28 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.9, 158.7, 141.0, 140.1, 132.6, 130.3, 130.1, 129.9, 129.1, 128.7, 128.5, 114.8, 113.9, 60.4, 55.3, 31.5, 20.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{23}H_{23}ClNO_2S]^+$: 412.1138; found: 412.1140.

2-((4-Methoxybenzyl)thio)-1-phenyl-2-(p-tolylamino)ethan-1-one (4ab). Compound **4ab** was obtained (using 5% EtOAc/petroleum ether) as a white solid (143 mg, 81%); mp: 124−125 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 7.0 Hz, 2H), 7.57 (t, J = 6.5 Hz, 1H), 7.46 (t, J = 6.5 Hz, 2H), 7.05 (d, J = 7.0 Hz, 2H), 6.97 (d, J = 7.0 Hz, 2H), 6.74 (d, J = 6.5 Hz, 2H), 6.67 (d, J = 7.0 Hz, 2H), 6.04 (d, J = 7.0 Hz, 1H), 5.15 (d, J = 8.0 Hz, 1H), 3.71 (s, 3H), 3.50 (d, J = 12.5 Hz, 1H), 3.44 (d, J = 12.0 Hz, 1H), 2.27 (s, 3H) ppm; $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): 190.0, 158.7, 141.1, 134.3, 133.7, 130.3, 129.9, 128.8(2), 128.7, 128.4, 114.8, 113.9, 60.3, 55.3, 31.5, 20.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{23}H_{24}NO_2S]^+$: 378.1528; found: 378.1523; IR (film): ν_{max} 3017, 1739, 1367, 1224, 815, 519 cm^{-1}.

2-(Benzylthio)-1-(4-chlorophenyl)-2-(p-tolylamino)-ethan-1-one (4ac). Compound **4ac** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (143 mg, 80%); mp: 145−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.16−7.12 (m, 3H), 7.07−7.05 (m, 4H), 6.73 (d, J = 8.0 Hz, 2H), 5.99 (d, J = 4.0 Hz, 1H), 5.12 (s, 1H), 3.54 (d, J = 13.0 Hz, 1H), 3.47 (d, J = 12.5 Hz, 1H), 2.28 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 188.8, 140.9, 140.0, 136.8, 132.5, 130.1, 129.9, 129.1 (2), 128.5, 128.4, 127.1, 114.8, 60.4, 32.1, 20.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{22}H_{21}ClNOS]^+$: 382.1032; found: 382.1034; IR (film): ν_{max} 3458, 3017, 1733, 1368, 1221, 1088, 811, 527 cm^{-1}.

2-(Benzylthio)-1-phenyl-2-(p-tolylamino)ethan-1-one (4ad). Compound **4ad** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (128 mg, 79%); mp: 104−105 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.15−7.14 (m, 3H), 7.08−7.05 (m, 4H), 6.74 (d, J = 8.0 Hz, 2H), 6.06 (s, 1H), 5.15 (bs, 1H), 3.55 (d, J = 13.0 Hz, 1H), 3.49 (d, J = 12.5 Hz, 1H), 2.28 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.9, 141.0, 137.0, 134.3, 133.7, 129.9, 129.2, 128.8, 128.7, 128.4, 127.0, 114.8, 60.3, 32.1, 20.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{22}H_{22}NOS]^+$: 348.1422; found: 348.1426.

1-(4-Chlorophenyl)-2-(ethylthio)-2-(p-tolylamino)-ethan-1-one (4ae). Compound **4ae** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (177 mg, 78%); mp: 121−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 5.97 (d, J = 8.0 Hz, 1H), 5.17 (d, J = 7.5 Hz, 1H), 2.31−2.27 (m, 5H), 1.03 (t, J = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.6, 140.9, 140.0, 132.5, 130.1, 129.9, 129.1, 128.3, 114.6, 59.5, 21.1, 20.6, 14.0 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{17}H_{19}ClNOS]^+$: 320.0876; found: 320.0882; IR (film): ν_{max} 3369, 2966, 1739, 1517, 1368, 1225, 1090, 806, 532 cm^{-1}.

2-(Ethylthio)-1-phenyl-2-(p-tolylamino)ethan-1-one (4af). Compound **4af** was obtained (using 3% EtOAc/petroleum ether) as a yellow solid (107 mg, 80%); mp: 95−96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 7.5 Hz, 2H), 7.61−7.58 (m, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 8.0 Hz, 2H), 6.03 (d, J = 8.5 Hz, 1H), 5.19 (d, J = 8.0 Hz, 1H), 2.35−2.28 (m, 2H), 2.27 (s, 3H), 1.04 (t, J = 7.5 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.9, 141.2, 134.2, 133.6, 129.9, 128.8, 128.7, 128.2, 114.6, 59.5, 21.2, 20.6, 14.1 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{17}H_{20}NOS]^+$: 286.1266; found: 286.1262.

1-(4-Chlorophenyl)-2-((2-hydroxyethyl)thio)-2-(p-tolylamino)ethan-1-one (4ag). Compound **4ag** was obtained (using 5% EtOAc/petroleum ether) as a yellow solid (121 mg, 77%); mp: 90−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.0 Hz, 2H), 6.01 (d, J = 5.5 Hz, 1H), 5.22 (d, J = 4.0 Hz, 1H), 3.50 (s, 2H), 2.60−2.48 (m, 2H), 2.27 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.4, 141.0, 140.4, 132.7, 130.2, 130.1, 129.3, 129.1, 115.0, 61.6, 60.2, 31.1, 20.5 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{17}H_{19}ClNO_2S]^+$: 336.0825; found: 336.0826; IR (film): ν_{max} 3318, 3021, 1740, 1368, 1224, 998, 843, 533 cm^{-1}.

2-((2-Hydroxyethyl)thio)-1-phenyl-2-(p-tolylamino)-ethan-1-one (4ah). Compound **4ah** was obtained (using 5% EtOAc/petroleum ether) as a yellow solid (109 mg, 77%); mp: 98−99 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 7.5 Hz, 2H), 7.61 (t, J = 7.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 6.07 (d, J = 5.5 Hz, 1H), 5.25 (s, 1H), 3.51 (s, 2H), 2.63−2.51 (m, 2H), 2.27

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(s, 3H), ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 190.3, 140.8, 133.9 (2), 130.1, 128.9, 128.8, 114.7, 61.4, 59.5, 30.8, 20.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{17}H_{20}NO_2S]^+$: 302.1215; found: 302.1214.

Ethyl 2-(Ethylthio)-2-(p-tolylamino)acetate (4ai). Compound **4ai** was obtained (using 3% EtOAc/petroleum ether) as a yellow liquid (98 mg, 83%); ^1H NMR (500 MHz, $CDCl_3$): δ 7.03 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 8.0 Hz, 2H), 5.03 (d, J = 8.0 Hz, 1H), 4.61 (d, J = 7.0 Hz, 1H), 4.29 (q, J = 7.0 Hz, 2H), 2.63−2.52 (m, 2H), 2.25 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H), 1.20 (t, J = 7.5 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.9, 141.2, 129.7, 128.2, 114.4, 61.8, 58.5, 22.7, 20.4, 14.5, 14.1 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{13}H_{20}NO_2S]^+$: 254.1215; found: 254. 1213; IR (film): ν_{max} 3456, 3009, 1732, 1441, 1367, 1215, 1021, 805, 524 cm^{-1}.

Ethyl 2-(Ethylthio)-2-(phenylamino)acetate (4aj). Compound **4aj** was obtained (using 3% EtOAc/petroleum ether) as a yellow liquid (103 mg, 80%); ^1H NMR (500 MHz, $CDCl_3$): δ 7.24−7.20 (m, 2H), 6.80 (t, J = 7.5 Hz, 1H), 6.73 (d, J = 7.5 Hz, 2H), 5.04 (d, J = 8.5 Hz, 1H), 4.75 (d, J = 8.5 Hz, 1H), 4.29 (q, J = 7.0 Hz, 2H), 2.64−2.54 (m, 2H), 1.33 (t, J = 7.5 Hz, 3H), 1.20 (t, J = 7.5 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.1, 143.7, 129.4, 119.2, 114.4, 62.1, 58.2, 22.9, 14.6, 14.2 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{12}H_{18}NO_2S]^+$: 240.1058; found: 240.1060; IR (film): ν_{max} 3457, 3008, 1731, 1439, 1368, 1220, 1019, 899, 748, 525 cm^{-1}.

Benzo[d]thiazol-2-yl(phenyl)methanone (6a). Compound **6a** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (72 mg, 75%); mp: 76−77 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.0 Hz, 2H), 8.24 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 6.8 Hz, 1H), 7.58−7.54 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.5, 167.3, 154.0, 137.1, 135.1, 134.0, 131.4, 128.6, 127.7, 127.0, 125.9, 122.3 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_{10}NOS]^+$: 240.0483; found; 240.0484.

Benzo[d]thiazol-2-yl(p-tolyl)methanone (6b). Compound **6b** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (78 mg, 77%); mp: 97−98 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 8.5 Hz, 2H), 8.23 (d, J = 8.5 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.59−7.51 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.0, 167.6, 154.0, 145.1, 137.1, 132.5, 131.5, 129.4, 127.6, 126.9, 125.8, 122.3, 21.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{12}NOS]^+$: 254.0640; found; 254.0644; IR (film): ν_{max} 3457, 3020, 1741, 1368, 1217, 1115, 885, 574 cm^{-1}.

Benzo[d]thiazol-2-yl(4-chlorophenyl)methanone (6c). Compound **6c** was obtained (using 3% EtOAc/petroleum ether) as a pale yellow solid (79 mg, 72%); mp: 93−94 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.56 (d, J = 8.5 Hz, 2H), 8.24 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 7.0 Hz, 1H), 7.62−7.53 (m, 4H) ppm;$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 184.1, 167.2, 154.2, 140.9, 137.4, 133.8, 132.9, 129.0, 127.9, 127.2, 126.0, 122.3 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_9ClNOS]^+$: 274.0093; found; 274.0094; IR (film): ν_{max} 3457, 3013, 1742, 1368, 1215, 1114, 886, 531 cm^{-1}.

Ethyl 2-(4-(trifluoromethyl)benzoyl)thiazole-4-carboxylate (6d). Compound **6d** was obtained (using 10% EtOAc/petroleum ether) as a pale white solid (83 mg, 75%); mp: 82−83 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.67 (d, J = 8.0 Hz, 2H), 8.51 (s, 1H), 7.81 (d, J = 8.5 Hz, 2H), 4.47 (q, J = 7.5 Hz, 2H), 1.44 (t, J = 7.5 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 182.8, 167.3, 160.9, 149.2, 137.3, 135.4, 135.1, 133.7, 131.8, 125.7(q, J_{C-F} = 3.6 Hz), 62.0, 14.4 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_{11}F_3NO_3S]^+$: 330.0412; found; 330.0412.

2-Phenylquinoxaline (8a). Compound **8a** was obtained (using 10% EtOAc/petroleum ether) as a white solid (80 mg, 84%); mp: 75−76 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.33 (s, 1H), 8.21−8.12 (m, 4H), 7.81−7.75 (m, 2H), 7.59−7.53 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.9, 143.4, 142.4, 141.7, 136.8, 130.3, 130.2, 129.7, 129.6, 129.2, 127.6 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_{11}N_2]^+$: 207.0922; found; 207.0921. IR (film): ν_{max}3055, 1539, 1307, 1205, 1023, 796, 682, 549 cm^{-1}.

2-(p-Tolyl)quinoxaline (8b). Compound **8b** was obtained (using 10% EtOAc/petroleum ether) as a white solid (85 mg, 83%); mp: 93−94 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.31 (s, 1H), 8.15−8.09 (m, 4H), 7.78−7.71 (m, 2H), 7.37 (d, J = 7.5 Hz, 2H), 2.45 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.8, 143.3, 142.4, 141.5, 140.5, 134.0, 130.2, 129.9, 129.6, 129.3, 129.2, 127.5, 21.5 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{13}N_2]^+$: 221.1079; found; 221.1081. IR (film): ν_{max}3053, 1540, 1308, 1122, 1040, 826, 747, 551 cm^{-1}.

2-(4-Methoxyphenyl)quinoxaline (8c). Compound **8c** was obtained (using 10% EtOAc/petroleum ether) as a white solid (93 mg, 85%); mp: 100−101 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.29 (s, 1H), 8.18 (d, J = 8.5 Hz, 2H), 8.13−8.08 (m, 2H), 7.76 (t, J = 7.0 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.5 Hz, 2H), 3.90 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.5, 151.4, 143.1, 142.4, 141.3, 130.2, 129.4, 129.3, 129.1(2), 129.0, 114.6, 55.5 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{13}N_2O]^+$: 237.1028; found; 237.1029.

2-(4-Chlorophenyl)quinoxaline (8d). Compound **8d** was obtained (using 10% EtOAc/petroleum ether) as a brown solid (95 mg, 85%); mp: 137−138 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.16−8.11 (m, 4H), 7.81−7.74 (m, 2H), 7.54 (d, J = 8.5 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.7, 143.0, 142.3, 141.8, 136.7, 135.3, 130.6, 129.9, 129.7, 129.5, 129.3, 128.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_{10}ClN_2]^+$: 241.0533; found; 241.0536.

7-Methyl-2-phenylquinoxaline (8e). Compound **8e** was obtained (using 10% EtOAc/petroleum ether) as a white solid (76 mg, 84%); mp: 129−130 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.28 (s, 1H), 8.18 (d, J = 7.0 Hz, 2H), 8.05 (d, J = 8.5 Hz, 1H), 7.88 (s, 1H), 7.62 (d, J = 8.5 Hz, 1H), 7.56 (t, J = 7.0 Hz, 2H), 7.52 (d, J = 7.5 Hz, 1H), 2.61 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.1, 143.3, 141.7, 140.8, 140.2, 137.0, 132.7, 130.0, 129.2, 128.0, 127.6, 127.5, 21.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{13}N_2]^+$: 221.1079; found; 221.1082. IR (film): ν_{max}3052, 1739, 1538, 1367, 1206, 1024, 828, 763, 570 cm^{-1}.

3-Phenylquinoxaline-6-carbonitrile (8f). Compound **8f** was obtained (using 10% EtOAc/petroleum ether) as a white solid (69 mg, 79%); mp: 174−175 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.44 (s, 1H), 8.50 (s, 1H), 8.24 (d, J = 8.0 Hz, 3H), 7.94−7.92 (m, 1H), 7.62−7.58 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.1, 145.3, 143.9, 140.7, 135.8, 135.2, 131.4, 131.3, 131.2, 129.5, 126.9, 118.2, 112.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{10}N_3]^+$:

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232.0875; found; 232.0879. IR (film): ν_{max}3052, 2227, 1540, 1312, 1130, 1022, 840, 768, 517 cm^{-1}.

6,7-Dimethyl-2-phenylquinoxaline (8g). Compound **8g** was obtained (using 10% EtOAc/petroleum ether) as a white solid (77 mg, 89%); mp: 130−131 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.22 (s, 1H), 8.16 (d, J = 7.0 Hz, 2H), 7.90 (s, 1H), 7.85 (s, 1H), 7.55 (t, J = 7.0 Hz, 2H), 7.49 (t, J = 7.5 Hz, 1H), 2.51 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 151.0, 142.4, 141.3, 140.8, 140.6, 140.1, 137.2, 129.9, 129.1, 128.7, 128.2, 127.4, 20.4(2) ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{16}H_{15}N_2]^+$: 235.1235; found; 235.1238.

6,7-Dichloro-2-phenylquinoxaline (8h). Compound **8h** was obtained (using 10% EtOAc/petroleum ether) as a brown solid (63 mg, 82%); mp: 157−158 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.32 (s, 1H), 8.28−8.18 (m, 4H), 7.58 (d, J = 7.5 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 152.8, 144.4, 141.2, 140.4, 136.1, 135.1, 134.1, 130.9, 130.3, 129.9, 129.4, 127.7 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{14}H_9Cl_2N_2]^+$: 275.0143; found; 275.0146. IR (film): ν_{max}3045, 1589, 1442, 1101, 939, 871, 761, 539 cm^{-1}.

2,2′-(1,4-Phenylenebis(azanediyl))bis(2-((4-chlorophenyl)thio)-1-phenylethan-1-one) (9a). Compound **9a** was obtained (using 10% EtOAc/petroleum ether) as a yellow solid (202 mg, 69%); mp: 139−140 °C; ^1H NMR (500 MHz, $CDCl_3$): δ Hz, 4H), 7.21 (d, J = 8.0 Hz, 4H), 6.98 (d, J = 8.5 Hz, 4H), 6.91 (s, 4H), 6.32 (d, J = 9.5 Hz, 2H), 4.96 (d, J = 10.0 Hz, 2H), ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): 188.2, 138.6, 136.2, 135.9, 134.4, 133.8, 129.1, 129.0, 128.7, 127.5, 116.5, 64.4 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{34}H_{27}Cl_2N_2O_2S_2]^+$: 629.0891; found; 629.0895.

2,2′-(1,4-Phenylenebis(azanediyl))bis(2-((4-methoxyphenyl)thio)-1-phenylethan-1-one) (9b). Compound **9b** was obtained (using 10% EtOAc/petroleum ether) as a yellow solid (206 mg, 71%); mp: 131−132 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, J = 7.5 Hz, 4H), 7.63 (t, J = 7.5 Hz, 2H), 7.53 (t, J = 7.5 Hz, 4H), 6.98 (d, J = 9.0 Hz, 4H), 6.92 (s, 4H), 6.77 (d, J = 9.0 Hz, 4H), 6.26 (d, J = 9.5 Hz, 2H), 4.89 (d, J = 9.5 Hz, 2H), 3.79 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 188.3, 160.9, 139.0, 136.1, 134.7, 133.5, 128.9, 128.7, 119.4, 116.5, 114.4, 64.2, 55.4 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{36}H_{33}N_2O_4S_2]^+$: 621.1882; found; 621.1888.

1-(4-Chlorophenyl)-2-(p-tolylamino)ethan-1-ol (10). Compound **10** was obtained (using 10% EtOAc/petroleum ether) as a white solid (50 mg, 76%); mp: 99−100 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 4H), 7.01 (d, J = 8.0 Hz, 2H), 6.61 (d, J = 8.4 Hz, 2H), 4.90 (dd, J = 3.6, 4.8 Hz, 1H), 3.89 (bs, 1H), 3.38 (dd, J = 3.6, 9.6 Hz, 1H), 3.22 (dd, J = 4.8, 8.4 Hz, 1H), 2.54 (bs, 1H), 2.25 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.4, 140.6, 133.7, 129.9, 128.8, 127.8, 127.4, 113.9, 71.8, 52.4, 20.5 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{15}H_{17}ClNO]^+$: 262.0999; found; 262.0998. IR (film): ν_{max} 3319, 3172, 2915, 1739, 1218, 1073, 814, 570 cm^{-1}.

4-(4-Chlorophenyl)-5-((4-chlorophenyl)thio)-1-(p-tolyl)-1,3-dihydro-2H-pyrrol-2-one (11b). Compound **11b** was obtained (using 20% EtOAc/petroleum ether) as a pale yellow solid (87 mg, 82%); mp: 202−203 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, J = 9.0 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H), 7.21−7.17 (m, 4H), 4.80 (s, 2H), 2.33 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.0, 151.9, 136.7, 136.4, 134.4, 133.1, 131.9, 130.8, 130.2, 129.8, 129.3(2), 129.2, 126.9, 118.9, 53.3, 20.9 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{23}H_{18}Cl_2NOS]^+$: 426.0486; found; 426.0485. IR (film): ν_{max} 3008, 1739, 1681, 1375, 1206, 1090, 807, 541 cm^{-1}.

2,2-Di(1H-indol-3-yl)-1-phenylethan-1-one (12b). Compound **12b** was obtained (using 25% EtOAc/petroleum ether) as a brown solid (63 mg, 65%); mp: 222−223 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 7.0 Hz, 2H), 8.02 (bs, 2H), 7.55 (d, J = 8.0 Hz, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 8.0 Hz, 2H), 7.07 (t, J = 7.5 Hz, 2H), 6.92 (d, J = 2.5 Hz, 2H), 6.50 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 198.5, 136.8, 136.5, 132.6, 128.5, 128.4, 126.4, 124.2, 121.5, 119.0, 118.6, 113.4, 111.4, 42.1 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{24}H_{19}N_2O]^+$: 351.1497; found; 351.1497. IR (film): ν_{max} 3374, 3023, 1738, 1342, 1218, 1000, 742, 579 cm^{-1}.

1-(4-Fluorophenyl)-2,2-di(1H-indol-3-yl)ethan-1-one (12c). Compound **12c** was obtained (using 25% EtOAc/petroleum ether) as a brown solid (60 mg, 62%); mp: 204−205 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.12−8.10 (m, 2H), 8.02 (bs, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 7.5 Hz, 2H), 7.09−7.03 (m, 4H), 6.89 (s, 2H) 6.43 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.0, 165.7(d, J_{C-F} = 253.2 Hz), 136.6, 133.4, 131.6(d, J_{C-F} = 9.0 Hz), 126.7, 124.0, 122.4, 119.9, 119.0, 115.8 (d, J_{C-F} = 21.7 Hz), 114.3, 111.5, 42.3 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calculated for $[C_{24}H_{17}FN_2NaO]^+$: 391.1223; found; 391.1220.

1,1-Di-(1H-indol-3-yl)-2,4-diphenylbut-3-yn-2-ol (13).[4] The reaction of phenylacetylene (14.5 mg, 0.568 mmol), n-BuLi (3 mL of a 1.6 M solution in hexane, 0.568 mmol), THF (10 mL), and 2,2-di(1H-indol-3-yl)-1-phenylethanone (50 mg, 0.142 mmol) following the general procedure **13** yielded the pure product as a brown solid (55 mg, 85% yield, mp = 178−180 °C); ^1H NMR (400 MHz, DMSO-d_6): δ 10.76−10.64 (m, 2H), 7.63 (d, J = 7.6 Hz, 2H), 7.52−7.43 (m, 3H), 7.37 (d, J = 2.4 Hz, 1H), 7.34−7.29 (m, 3H), 7.25−7.18 (m, 4H), 7.15 (t, J = 7.5 Hz, 2H), 7.07 (t, J = 7.3 Hz, 1H), 6.97−6.88 (m, 2H), 6.82−6.77 (m, 2H), 6.15 (s, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.3, 145.8, 135.3, 135.2, 131.1, 128.5, 128.3, 128.1, 127.9, 127.1, 126.6, 126.3, 124.3, 124.1, 122.7, 120.2, 119.0, 118.9, 117.9, 117.8, 115.4, 115.0, 110.9, 110.8, 94.7, 85.0, 75.6, 46.2 ppm; HRMS(ESI-TOF) m/z: $[M + H]^+$: calculated for $[C_{32}H_{24}N_2O]^+$: 452.1883; found: 452.1884.

1-(1H-Indol-3-yl)-2,4-diphenyl-9H-carbazole (14).[5] Isolated as a brown viscous compound; yield: 67% (35 mg); ^1H NMR (500 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.13 (s, 1H), 7.77 (d, J = 7.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.0 Hz, 2H), 7.50−7.46 (m, 3H), 7.32−7.27 (m, 6H), 7.17−7.12 (m, 4H), 7.00−6.97 (m, 1H), 6.88 (d, J = 2.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 142.2, 141.2, 140.2, 140.0, 139.3, 136.5, 136.2, 130.0, 129.4, 128.5, 127.7, 127.6, 127.1, 126.3, 125.6, 124.8, 123.8, 123.2, 122.5, 120.4, 120.2, 119.6, 119.1, 114.9, 112.2, 111.6, 110.6 ppm; HRMS (ESI-TOF): m/z calculated for $C_{32}H_{23}N_2$ $[M + H]^+$ 435.1861, found 435.1867

2,2-Bis(4-(dimethylamino)phenyl)-1-phenylethan-1-one (15). Compound **15** was obtained (using 25% EtOAc/petroleum ether) as a pale white solid (67 mg, 68%); mp: 161−162 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, J = 7.0 Hz, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 8.0 Hz, 2H), 7.12

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(d, J = 8.5 Hz, 4H), 6.67 (d, J = 9.0 Hz, 4H), 5.84 (s, 1H), 2.90 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.5, 149.9, 138.9, 138.2, 132.5, 129.9, 129.0, 128.6, 128.3, 113.2, 58.1, 40.7 ppm; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $[C_{24}H_{27}N_2O]^+$: 359.2123; found; 359.2121. IR (film): ν_{max} 3457, 3020, 1741, 1368, 1217, 1115, 885, 574 cm^{-1}.

1-(4-Chlorophenyl)-2-(p-tolylimino)ethan-1-one (A1). To a solution of phenyl glyoxal (250 mg, 1.64 mmol) in acetonitrile was added toluidine (175.9 mg, 1.64 mmol) in a ball mill under standard conditions. After completion of the reaction, keto imine was purified by a filter column to obtain A1 as a brownish red colored viscous compound. ^1H NMR (500 MHz, $CDCl_3$): δ 7.87(s, 1H), 7.85−7.83 (m,2H), 7.53−7.50(m, 3H), 7.44(t, J = 7.5 Hz, 2H), 7.14(d, J = 8 Hz, 2H), 2.32(s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ 165.8, 135.5, 135.2, 134.3, 131.8, 129.7, 128.8, 127.1, 120.5, 21.0; HRMS (ESI-TOF): m/z $[M + H]^+$ calculated for $C_{15}H_{13}ClNOH$: 224.1075; found: 224.1072.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c09218.

Experimental procedures, characterization data, NMR spectra, and details of single-crystal data of compounds **4d** (PDF)

Calculation of statistics and refinement (TXT)

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Notes

The authors declare no competing financial interest.

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