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A Method for the Analysis of Free Carbenes Present after the NHC-Organocatalytic Transformation**

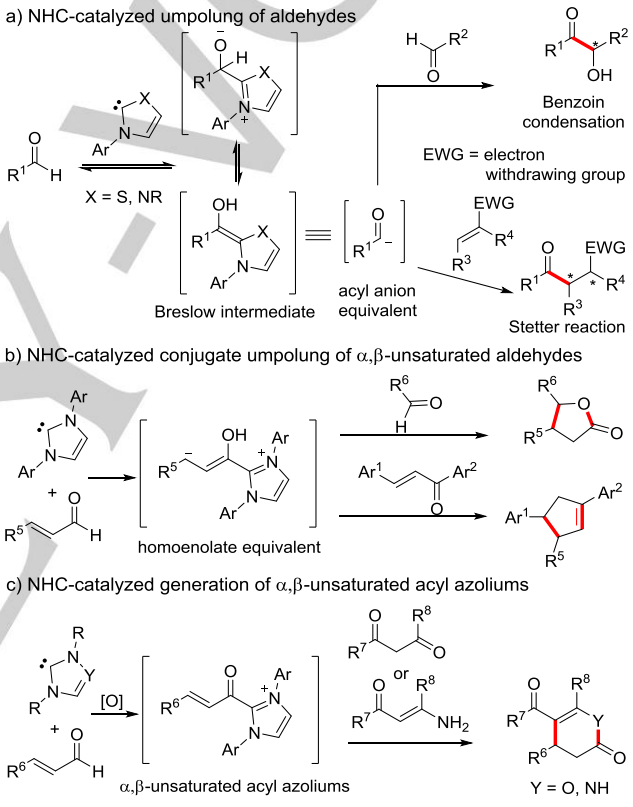
Tamal Kanti Das[a] and Akkattu T. Biju*[a,b]

Dedication ((optional))

Abstract: In N-heterocyclic carbene (NHC)-based organocatalysis, usually, the free carbene is generated in situ by treating the azolium salt with a base. Described herein is a method for the analysis of the NHC present in the reaction flask after the NHC-organocatalytic reaction. For this, the reaction mixture was treated with elemental sulfur after the reaction and isolated the formed thiourea/thione derivatives. The common NHC-catalyzed transformations such as benzoin reaction, Stetter reaction, homoenolate annulation reactions, and reaction proceeding via the α,β-unsaturated acyl azolium intermediate were studied. The results indicate that in most of the reactions tried, the carbenes are existing in free form after the reaction in 28-84%.

Introduction

N-Heterocyclic carbenes (NHCs)-based organocatalysis has emerged as one of the powerful synthetic strategy for the rapid construction of simple as well as complex molecules.[1] In most cases, NHCs are employed for the umpolung of aldehydes.[2] The resultant acyl anion equivalents (commonly known as "Breslow intermediates") can add to a wide variety of electrophiles such as aldehydes, ketones,[3] imines,[4] Michael acceptors,[5] and unactivated carbon-carbon multiple bonds.[6] The benzoin condensation[3] and the Stetter reaction[4] are the important transformations proceeding via the umpolung of aldehydes (Scheme 1a). Moreover, NHCs can also trigger the conjugate umpolung leading to the generation of homoenolate equivalent intermediates.[7] The homoenolates can be intercepted with aldehydes to form γ-butyrolactones,[8] and cyclopentenes are formed by the trapping of homoenolates with chalcones (Scheme 1b).[9] Recently, the umpolung concept using NHCs has been extended to Michael acceptors[10] and alkyl halides.[11,12] In addition to the NHC-catalyzed umpolung of electrophiles, NHCs are also used for catalyzing the normal mode of reactions (non-umpolung). One of the important intermediate in this category is the α,β-unsaturated acyl azolium intermediate, generated usually from enals under oxidative conditions[13,14] or reaction of NHCs with α,β-unsaturated acid fluorides.[15] This electrophilic intermediate can be trapped with various bifunctional nucleophiles to afford six-membered nitrogen and oxygen heterocycles (Scheme 1c).



Scheme 1. Important modes of NHCs in organocatalysis

In NHC-catalyzed transformations, in most cases, the free carbene is generated in situ from the imidazolium/thiazolium/ triazolium salt by treatment with a suitable base. Typically 1-20 mol % of the NHC precatalysts are used for the transformation. This amount of catalyst is assumed to be needed for the maximum conversion to the desired product. The analysis of the free NHC-catalyst present in the reaction vessel after the known catalytic transformations will give information on how much catalyst is used/decomposed in a given transformation, and thus give insight into the recovery of the precious catalyst after the reaction. To the best of our knowledge, such an analysis on free NHCs in organocatalytic reactions is unknown. Herein, we report a simple and efficient method for the analysis of the amount of NHCs left after the catalytic transformation. We have studied the common NHC-catalyzed transformations such as benzoin

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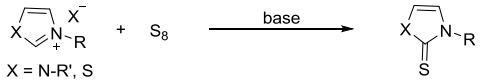
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

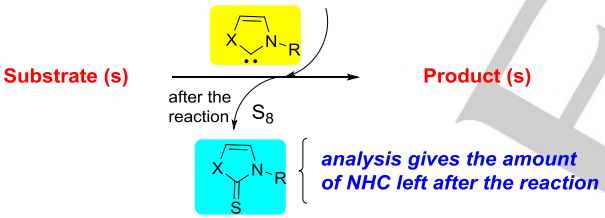
reaction, Stetter reaction, homoenolate annulation reactions, and reaction proceeding via the α,β-unsaturated acyl azolium intermediate (Scheme 1).

The underlying principle of the present analysis is the ability of NHCs to form thiourea/thione derivatives upon treatment with elemental sulfur (Scheme 2).[16] The thiourea/thione derivatives of NHCs are formed under mild reaction conditions, and are stable and isolable. In most of the cases, the conversion of NHCs to the corresponding thiourea/thione derivative by the reaction with sulfur is quantitative.



Scheme 2. Trapping of NHCs with elemental sulfur

We envisioned that the quantitative evaluation of the NHCs left behind after a given NHC-catalyzed reaction could be possible by the addition of elemental sulfur at the end of the transformation. The knowledge that sulfur is inert to most of the NHC-catalyzed reaction conditions gives the advantage of the present protocol. The sulfur addition enables the free NHCs present in the reaction mixture to form the corresponding thiourea/thione derivative. This thiourea/thione derivative is isolable by column chromatography or can be analyzed using ^{1}H NMR using an internal standard (Scheme 3). The amount of thiourea/thione formed likely corresponds to the free carbene present after the NHC-catalyzed transformation.

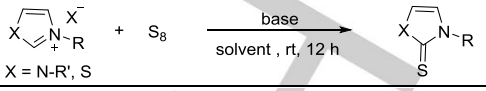


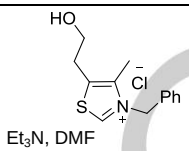
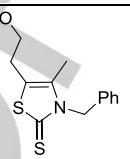
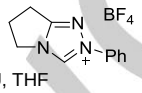
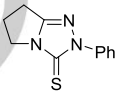
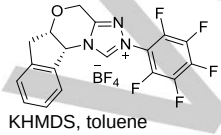
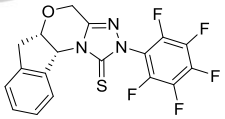
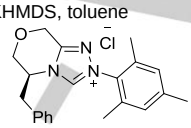
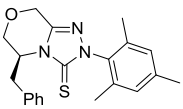
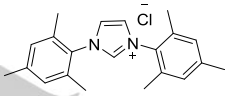
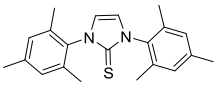
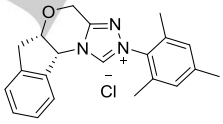
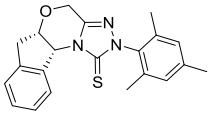
Scheme 3. The principle of the present work

Results and Discussion

The present study was initiated by the synthesis of various thiourea/thione derivatives from the corresponding azolium salts. The synthesis has been accomplished by treating the azolium salt with elemental sulfur in the presence of the base at rt (Table 1). For instance, the thione in entry 1 has been synthesized from the thiazolium salt by treatment with elemental sulfur in presence of Et_3N. It may be noted that except the thiourea derivative synthesized from IMes.HCl (entry 5), all the thione/thiourea synthesized in this study, to the best of our knowledge is unknown previously.[17]

Table 1. Synthesis of the thione/thiourea derivatives from azolium salts[a]

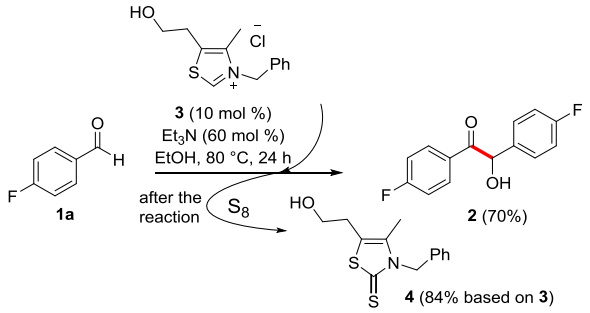


entry	azolium salt/base/solvent	thione/thiourea	yield(%)
1	 Et_3N, DMF		98
2	 DBU, THF		97
3	 KHMDS, toluene		89
4	 KO*t*-Bu, toluene		90
5	 DBU, DME		93
6	 DBU, CH_2Cl_2		89

[a]For the detailed procedure and for the characterization of thiourea/thione, see the Supporting Information

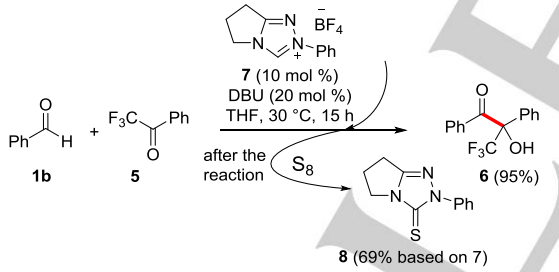
To examine the free carbenes present after the reaction, we first selected the benzoin condensation since it is the common reaction proceeding via the umpolung of aldehydes. Considering the fact that benzoin condensation is reversible in many cases,[18] we followed a very recent procedure by Lv, Zhang and co-workers.[19] In an initial experiment, the reaction of 4-fluorobenzaldehyde **1a** with carbene generated from the thiazolium salt **3** using Et_3N as the base was performed. The reaction afforded the benzoin product **2** in 74% yield. Moreover, we tested the conversion of thiazolium salt **3** to the thione derivative **4** under basic conditions and it was found to be quantitative at 30 °C. With these two background information, the formation of thione **4** under benzoin reaction condition was examined. Treatment of **1a** with 10 mol % **3** at 80 °C in EtOH followed by cooling the reaction mixture to 30 °C and subsequent addition of elemental sulfur to the reaction mixture furnished the benzoin **2** in 70% yield and the thione **4** was isolated in 84% yield based on the amount of **3** used (Scheme 4). The 84% formation of **4** after the benzoin reaction is an indication that ~84% of the carbene is still available after the benzoin reaction leading to 70% of the product **2**.[20] This also

indicates that the active NHC catalyst is not decomposing under the reaction conditions.



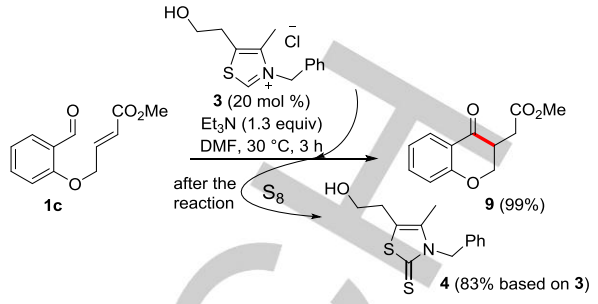
Scheme 4. Analysis of free NHCs in benzoin reaction

The high amount of free carbene present in the reaction flask after the homobenzoin reaction inspired us to investigate the amount of free NHCs in other transformations catalyzed by NHCs. We then focused our attention on intermolecular cross-benzoin reaction. The NHC-catalyzed cross-coupling of aromatic aldehydes with trifluoromethyl ketones to afford α-hydroxy α-trifluoromethyl ketones has been uncovered by Enders and Henseler.[21] Following this procedure, reaction of benzaldehyde **1b** with **5** in the presence of NHC generated from the triazolium salt **7** using DBU followed by the treatment of the reaction mixture with elemental sulfur resulted in the formation of **6** in 95% yield and the thiourea derivative **8** in 69% yield based on the amount of **7** used (Scheme 5). The formation of **8** in 69% yield indicates the availability of free carbene at the end of the cross-benzoin reaction.



Scheme 5. Free NHC-analysis in cross-benzoin reaction

With the information on free NHC remaining after the benzoin reaction, we then focused our attention on Stetter reaction. Following the procedure of Ciganek,[22] treatment of the aldehyde **1c** with the NHC generated from the thiazolium salt **3** using Et_3N as base followed by the addition of elemental sulfur after 3 h resulted in the formation of the chromanone **9** in 99% yield and the thione **4** in 83% yield (Scheme 6). The isolation of **4** in 83% yield sheds light on the presence of free carbene in the reaction medium after the intramolecular Stetter reaction.



Scheme 6. Free NHC analysis in intramolecular Stetter reaction

Having the data on existence of free NHC remaining after the intramolecular Stetter reaction, we considered the addition of substrate **1c** (1.0 equiv) to the reaction mixture after 3 h and stirred again for 3 h (without extra addition of **3** and Et_3N). Analysis of the reaction mixture revealed the formation of **9** in 95% yield with complete conversion of **1c** (cycle 2). Interestingly, addition of 1.0 equiv each of **1c** in three portions at an interval of 3 h to 20 mol% of **3** and Et_3N provided **9** in 88% yield (cycle 3). At this stage, 7% of **1c** was recovered. The formation of **9** in 88% yield even after third cycle indicates the amount of free carbene still available in the reaction mixture. Performing the addition of **1c** in four portions afforded **9** in 74% yield with observation of unreacted **1c** in 22% yield. The addition of 0.25 mmol each of **1c** in 5 portions afforded 64% of **9** and 28% of **1c** was recovered (cycle 5). Similarly, addition in 6 portions furnished **9** in 57% yield and **1c** was recovered in 33% yield (cycle 6). For the seventh cycle, **9** was still formed in 28% yield and **1c** was recovered in 61% yield. In all cases, the yield of **9** and the recovered amount of **1c** was determined by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard. These experiments clearly indicate that the free carbene is catalytically active in all these experiments. The details are presented in Figure 1.

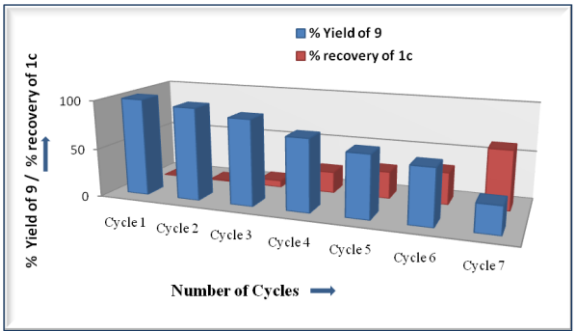
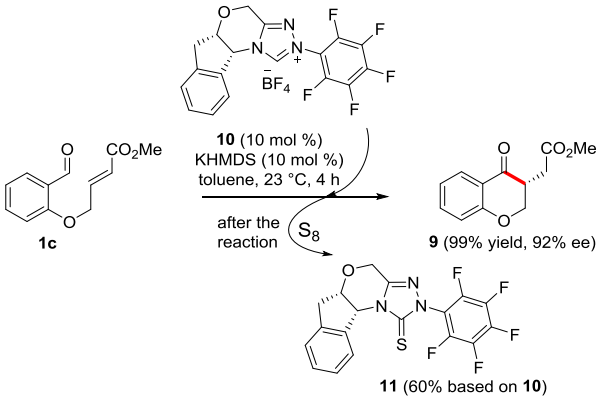


Figure 1. Details on intramolecular Stetter reaction with portion-wise addition of aldehyde

Next, the analysis of free NHCs in enantioselective intramolecular Stetter reaction was carried out. Following the procedure of Rovis and co-workers,[23] treatment of the aldehyde **1c** with NHC generated from the chiral triazolium salt **10** using

KHMDS as the base followed by the addition of elemental sulfur and subsequent stirring of the reaction mixture resulted in the isolation of the chiral chromanone **9** in 99% yield and 92% ee and the chiral thiourea was formed in 60% yield (Scheme 7). The isolation of 60% thiourea derivative **11** indicated the presence of catalytically active NHC after the enantioselective Stetter reaction.



Scheme 7. Free NHC analysis in enantioselective intramolecular Stetter reaction

We also tested the effect of portion-wise substrate addition with the same catalyst system on the enantioselectivity in the intramolecular Stetter reaction. In the first cycle, the intramolecular Stetter reaction furnished the chromanone **9** in 99% yield and 92% ee in 4 h following the Rovis protocol (cycle 1).[23] At this stage, another equivalent of the aldehyde **1c** was added to the reaction mixture and stirred for the indicated time. This reaction afforded **9** in 96% yield and 88% ee (cycle 2). Addition of **1c** in three portions (1.0 equiv each) after 4 h interval and processing the reaction mixture afforded **9** in 92% yield and 88% ee (cycle 3). The yield and ee of **9** obtained in cycles 1-3 are presented in Figure 2. This clearly indicates that the enantioselectivity of the product was not considerably changed upon portion-wise addition of the substrate and it also sheds light on the availability of free carbenes in the reaction system.

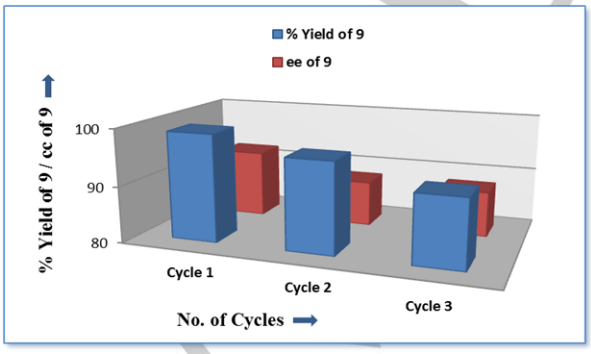
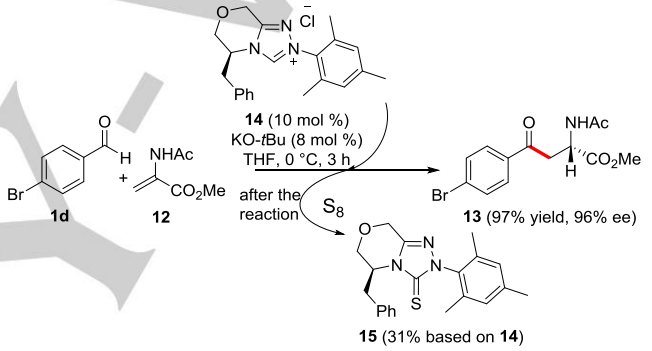


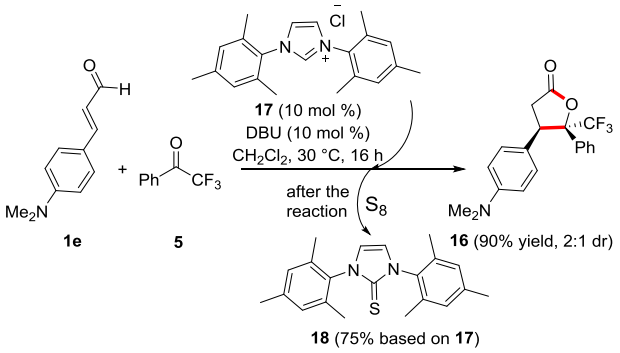
Figure 2. Effect of portion-wise addition of aldehyde in the enantioselectivity of the product in intramolecular Stetter reaction

The results of the enantioselective intramolecular Stetter reaction prompted us to investigate the free NHC present in the intermolecular version. For this, we attempted the Stetter reaction using dehydroamino ester as the Michael acceptor, which involves a stereoselective protonation. Following the procedure of Glorius and co-workers,[24] the treatment of aldehyde **1d** with *N*-acylamido acrylate **12** using NHC generated from the chiral triazolium salt **14** using KO-*t*Bu as base followed by stirring of the reaction mixture with elemental sulfur afforded the Stetter product **13** in 97% yield and 96% ee and the thiourea derivative **15** in 31% yield (Scheme 8). The low yield of **15** formed may indicate the rather less amount of free carbene present after the Stetter reaction. To confirm this, we tried the reaction of **14** with elemental sulfur using KO-*t*Bu under the present conditions. Notably, 40% of the thiourea was formed under the present conditions. This shows that the low yield of **15** formed in the present free NHC analysis may be due to the moderate conversion of **14** to **15** under the same conditions.



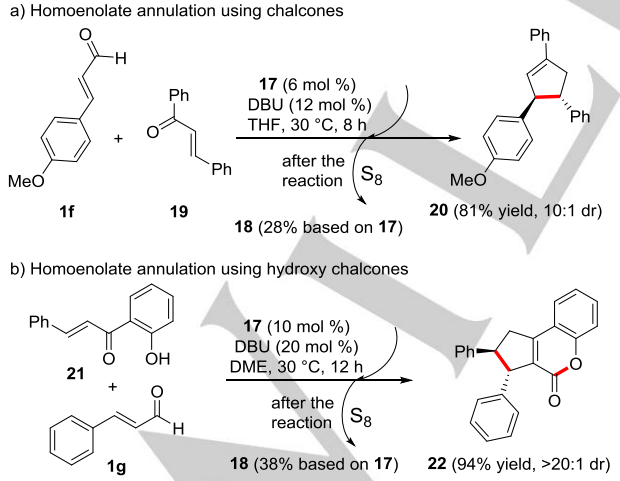
Scheme 8. Free NHC analysis in enantioselective intermolecular Stetter reaction

Having established a protocol for the analysis of free NHCs present in NHC-catalyzed reactions proceeding via the umpolung of aldehydes, we then focused our attention on the homoenolate annulation reactions. This is one of the important modes of NHC reactivity.[7,8] Following the procedure of Glorius and co-workers,[25] treatment of the aldehyde **1e** with **5** in the presence of NHC generated from IMes.HCl **17** using DBU as the base followed by the addition of elemental sulfur at the end of the reaction furnished the γ-butyrolactone **16** (90% yield and 2:1 dr) and the thiourea **18** in 75% yield (Scheme 9). The good amount formation of **18** shows the efficiency of the catalysis as well as the availability of free NHC at the end of the reaction.



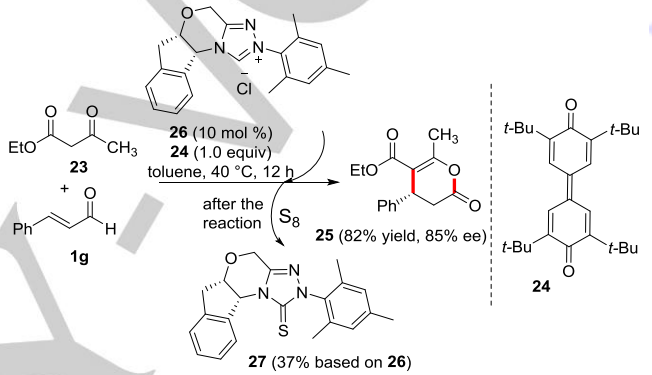
Scheme 9. Free NHC analysis in homoenolate annulation reaction

The cyclopentannulation reaction proceeding via the conjugate umpolung of enals has also been examined. Following the procedure of Nair and co-workers,[9] the mixing of aldehyde **1f** with chalcone **19** in the presence of carbene generated from **17** using DBU followed by the addition of elemental sulfur at the end of the reaction afforded the cyclopentene **20** (81% yield, 10:1 dr) and the thiourea derivative **18** in 28% yield (Scheme 10a). The low yield of thiourea formation indicates that the amount of catalytically active species present at the end of the reaction is less compared to all other previous reactions. In addition, we also studied the free NHC present after the related cyclopentane-fused coumarins synthesis from enals and hydroxy chalcones.[26] Treatment of **1g** with **21** in the presence of NHC generated from **17** followed by the addition of sulfur at the end of the reaction provided the cyclopentane-fused coumarin derivative **22** (94% yield, >20:1 dr) and the thiourea **18** was isolated in 38% yield (Scheme 10b). In this case also, the isolation of moderate amount of **18** indicates that the free NHC present in the reaction flask after the reaction is less.



Scheme 10. Free NHC analysis in cyclopentannulation reaction

Finally, we tested the free carbene present after the reaction proceeding via the α,β-unsaturated acyl azoliums. The NHC-catalyzed generation of α,β-unsaturated acyl azoliums under oxidative conditions followed by the interception with 1,3-dicarbonyls for the synthesis of dihydropyranones was developed by De Sarkar and Studer,[13] and the enantioselective version was subsequently demonstrated by Xiao and co-workers.[27] Following the procedure of Xiao and co-workers,[28] reaction of **1g** with ethyl acetoacetate **23** in the presence of NHC generated from the chiral triazolium salt **26** under oxidative conditions using **24** followed by the addition of elemental sulfur at the end of the reaction furnished the dihydropyranone **25** (82% yield, 85% ee) and the thiourea **27** was formed in 37% yield. The formation of low amount of thiourea shows that after the catalytic reaction, the amount of carbene available in the reaction flask is less.



Scheme 11. Free NHC analysis in NHC-catalyzed oxidative transformation

Conclusions

In conclusion, we have presented a method for the analysis of free carbenes present in the reaction flask after a given NHC-organocatalytic transformations. This was possible by the addition of elemental sulfur to the reaction mixture at the end of the organocatalytic reaction and isolating the formed thiourea/thione derivatives. This technique was used for the analysis of free NHCs present in benzoin reaction, Stetter reaction, homoenolate annulation reactions, and reaction proceeding via the α,β-unsaturated acyl azolium intermediates. In most of the NHC reactions studied, the results indicate that free carbenes are present at the end of the reaction. We believe that the present study with positive results on amount of NHCs remaining after the organocatalytic transformation will be helpful in this area of catalysis.[29]

Experimental Section

General Information: Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. Dry DME, CH_2Cl_2, EtOH were purchased from commercial sources and stored under argon over 4 Å molecular sieves. Dry toluene was purchased from commercial source and stored under argon over metallic sodium. Dry THF was prepared freshly by distilling over

sodium under argon before use. Et_3N was purchased from commercial source and stored under argon over potassium hydroxide. DBU was distilled and stored under argon. Elemental sulfur was crystallized from ethanol. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). HRMS measurements were carried out using ESI method and ion-trap mass analyzer.

General procedure for the synthesis of Thiones:[16a,b] An oven dried schlenk tube was equipped with a magnetic stir bar and the carbene precursor was added. The Schlenk tube was then evacuated and back filled with argon. The solvent and base was added into it and the resulting reaction mixture was kept stirring for 5 minutes at 30 °C. Then elemental sulfur was added and the reaction mixture was allowed to stir for another 12 h at 30 °C. After 12 h, the solvent was evaporated to obtain the crude reaction mixture which was purified by flash column chromatography on silica gel to afford the thione.

3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazole-2(3*H*)-thione (4) Following the general procedure, treatment of thiazolium salt **3** (135 mg, 0.5 mmol), Et_3N (106 mg, 146 µL, 1.0 mmol) with sulfur (32 mg, 1.0 mmol) in DMF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether/EtOAc = 60/40) of the crude reaction mixture afforded 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazole-2(3*H*)-thione 4 as a white solid (130 mg, 98% yield). R_f (Pet. Ether/EtOAc = 60/40): 0.17; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.25 (dt, *J* = 14.0, 6.9 Hz, 3H), 7.15 (d, *J* = 7.3 Hz, 2H), 5.46 (s, 2H), 3.68 (t, *J* = 6.1 Hz, 2H), 2.89 (s, 1H), 2.70 (t, *J* = 6.0 Hz, 2H), 2.03 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 187.0, 136.0, 134.9, 128.9, 127.8, 126.6, 120.1, 61.7, 50.7, 29.7, 13.3. **HRMS**: calculated [M+H]+ for $C_{13}H_{16}NOS_2$: 266.0668, found:266.0661. **FTIR (cm^{-1})**: 3385, 3019, 2970, 2360, 1609, 1496, 1430, 1375, 1318, 1215, 1109, 1045, 1011, 769, 701, 668, 503, 457, 434, 419.

2-Phenyl-2,5,6,7-tetrahydro-3*H*-pyrrolo[2,1-c][1,2,4]triazole-3-thione (8): Following the general procedure, treatment of triazolium salt **7**[30] (10 mg, 0.036 mmol) , DBU (17.0 mg, 17 µL, 0.108 mmol) with sulfur (3.2 mg, 0.1 mmol) in THF (1.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 70/30) of the crude reaction mixture using silica gel afforded 2-phenyl-2,5,6,7-tetrahydro-3*H*-pyrrolo[2,1-c][1,2,4]triazole-3-thione **8** as a white solid (7.7 mg, 97% yield). R_f (Pet. Ether/EtOAc = 60/40): 0.3; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.98 (d, *J* =7.8 Hz, 2H), 7.46 (t, *J* =7.5 Hz, 2H) , 7.34 (t, *J* =7.7 Hz, 1H), 4.00 (t, *J* =7.1 Hz, 2H), 3.02 (t, *J* = 8.0 Hz, 2H), 2.67 (q, *J* = 7.4 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.2, 156.6, 138.6, 128.8, 127.9, 123.7, 44.1, 26.0, 22.8. **HRMS**: calculated [M+H]+ for $C_{11}H_{12}N_3S$: 218.0746, found: 218.0744. **FTIR (cm^{-1})**: 3681, 3019, 2973, 2400, 2360, 1602, 1498, 1427, 1393, 1302, 1215, 1021, 928, 770, 701, 668, 507, 464, 452, 434, 420.

(5a*S*,10b*R*)-2-(Perfluorophenyl)-2,4,5a,10b-tetrahydro-1*H*,6*H*-indeno[2,1-b][1,2,4]triazolo[4,3-d][1,4]oxazine-1-thione (**11**) Following the general procedure, treatment of triazolium salt **10**[31] (23.0 mg, 0.05 mmol) , KHMDS (0.1 mL, 0.05 mmol) with sulfur (3.2 mg, 0.1 mmol) in toluene (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether/EtOAc = 20/80) of the crude reaction mixture using silica gel afforded 5a*S*,10b*R*)-2-(perfluorophenyl)-2,4,5a,10b-tetrahydro-1H,6H-indeno[2,1-b][1,2,4]triazolo[4,3-d][1,4]oxazine-1-thione **11** (18 mg, 89% yield). R_f (Pet. Ether/EtOAc = 90/10): 0.15; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 4.0 Hz, 2H), 7.28 – 7.20 (m, 1H), 5.71 (d, *J* = 3.3 Hz, 1H), 4.88 (d, *J* = 16.1 Hz, 1H), 4.67 (dd, *J* = 15.3, 10.1 Hz, 2H), 3.35 (dd, *J* = 16.7, 4.2 Hz, 1H), 3.21 (d, *J* = 16.7 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.4, 147.1, 139.9, 138.0, 129.3, 127.6, 127.0, 125.3, 78.4, 60.6, 60.6, 37.8, 29.9. **LCMS**: calculated [M]+ for $C_{18}H_{10}F_5N_3OS$: 411.3, found: 411.9. **FTIR (cm^{-1}):** 2923, 2852, 2360, 2339, 1589, 1517, 1486, 1433, 1373, 1347, 1106, 1078, 1038, 995, 909, 765, 502, 455, 431, 411.

(*S*)-5-Benzyl-2-mesityl-2,5,6,8-tetrahydro-3*H*-[1,2,4]triazolo[3,4-c][1,4]oxazine-3-thione (15): Following the general procedure, treatment of triazolium salt **14**[6c] (19.0 mg, 0.05 mmol), KO*t*-Bu (11.2 mg, 0.1 mmol) with sulfur (3.2 mg, 0.1 mmol) in toluene (1.0 mL) at rt for 12 h followed by flash column chromatography of the crude reaction mixture using silica gel afforded (*S*)-5-benzyl-2-mesityl-2,5,6,8-tetrahydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazine-3-thione **15** (17 mg, 90% yield). R_f (Pet. Ether/EtOAc = 90/10): 0.17; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 (d, *J* = 7.1 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 4.99 (d, *J* = 16.2 Hz, 1H), 4.68 (d, *J* = 15.5 Hz, 1H), 4.42 (d, *J* = 12.2 Hz, 1H), 4.15 (d, *J* = 12.2 Hz, 1H), 3.71 (t, *J* = 15.8 Hz, 2H), 2.94 (t, *J* = 12.5 Hz, 1H), 2.34 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 166.1, 145.4, 140.2, 136.8, 136.2, 132.9, 130.0, 129.4, 128.9, 127.2, 65.5, 62.4, 54.8, 35.5, 21.4, 18.0, 17.8; **HRMS**: calculated [M+H]+ for $C_{21}H_{24}N_3S$: 366.1635, found:366.1626. **FTIR (cm^{-1}):** 3019, 2976, 2927, 2400, 2360, 1574, 1439, 1390, 1350, 1215, 1115, 1056, 1033, 928, 770, 668, 502, 458, 434, 419.

1,3-Dimesityl-1,3-dihydro-2*H*-imidazole-2-thione (18): Following the general procedure, treatment of imidazolium salt **17** (85.0 mg, 0.25 mmol), DBU (76.0 mg, 75 µL, 0.5 mmol) with sulfur (16.0 mg, 0.5 mmol) in DME (1.0 mL) at rt for 12 h followed by flash column chromatography of the crude reaction mixture using silica gel 1,3-dimesityl-1,3-dihydro-2*H*-imidazole-2-thione **18** afforded (78.0 mg, 93% yield). Spectroscopic data were identical with the literature.[16]

(5a*S*,10b*R*)-2-Mesityl-2,4,5a,10b-tetrahydro-1*H*,6*H*-indeno [2,1-b][1,2,4]triazolo[4,3-d][1,4]oxazine-1-thione (**27**): Following the general procedure, treatment of triazolium salt **26**[32] (10.0 mg, 0.027 mmol) , DBU (8.2 mg, 8.0 µl, 0.05 mmol) with sulfur (2.0 mg, 0.05 mmol) in DCM (1.0 mL) at rt for 12 h followed by flash column chromatography of the crude reaction mixture using silica gel afforded (5a*S*,10b*R*)-2-mesityl-2,4,5a,10b-tetrahydro-1*H*,6*H*-indeno[2,1b][1,2,4]triazolo[4,3-d][1,4]oxazine-1-thione **27** (8.4 mg, 89% yield). R_f (Pet. Ether/EtOAc = 60/40): 0.22; **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 8.11 (d, *J* = 7.5 Hz, 1H), 7.37- 7.35 (m, 2H), 7.32-7.29 (m, 1H), 7.05 (s, 2H), 5.83 (d, *J* = 3.4 Hz, 1H) , 4.94 (d, *J* = 15.8 Hz, 1H) , 4.76 (d, *J* = 15.5 Hz, 1H) , 4.74 (d, *J* = 4.2 Hz, 1H), 3.42 (dd, *J1*= 4.4 Hz, *J2* = 16.5 Hz, 1H), 3.27 (d, *J* = 16.8 Hz, 1H), 2.39 (s, 3H), 2.19 (s, 3H), 2.15 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.6, 145.4, 140.2, 139.9, 138.8, 136.3, 136.1, 133.1, 129.4, 129.4, 129.0, 127.6, 126.9, 125.2, 78.5, 60.8, 60.1, 37.8, 21.4, 18.1, 17.8. **HRMS:** calculated [M+H]+ for $C_{21}H_{22}N_3OS$: 364.1478, found: 364.1467. **FTIR (cm^{-1}):** 2921, 2852, 2361, 1724, 1579, 1439, 1388, 1347, 1331, 1216, 1103, 1081, 1059, 1024, 758, 504, 454, 440, 422, 411.

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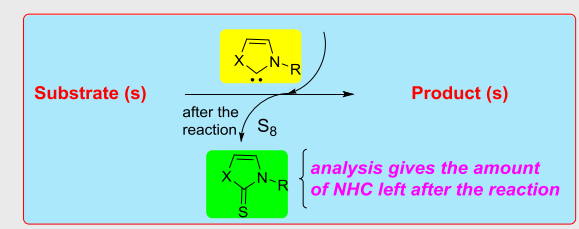

A systematic analysis of the NHC present in the reaction flask after the organocatalytic reaction has been demonstrated by treating the reaction with elemental sulfur after the reaction and isolated/analyzed the formed thiourea/thione derivatives.

*Tamal Kanti Das, Akkattu T. Biju**

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A Method for the Analysis of Free Carbenes Present after the NHC-Organocatalytic Transformation