NaH Promoted One-Pot Tandem Reactions of 3-(1-Alkynyl) Chromones to Form 2-Nitrogen-Substituted Xanthones

Wen-Di Duan, Yu-Fang Zhang, and Youhong Hu*

ABSTRACT: A silver-catalyzed dimerization of ethyl isocyanatoacetates could trigger the tandem reaction of 3-(1-alkynyl) chromones under the basic condition in a one-pot reaction to afford xanthone skeletons with 2-imidazolyl substitution in an efficient manner. With the control experiment in hand, a mechanism including dimerization of isocyanatoacetate/deprotonation/Michael addition/ring-opening/cyclization 1,2-elimination was deduced. Further investigation for the base was carried out, resulting in NaH as an optimal base to avoid the dimerization of 3-(1-alkynyl) chromones. The scope of this methodology was extended on the different substituents of 3-(1-alkynyl)-chromones and the potential of other N-heterocycle glycine ester anions to give the novel functional 2-nitrogen-derived xanthones.

INTRODUCTION

Tandem reaction is capable of constructing molecular complexity in an efficient manner using readily available intermediates.† Owing to multiple attributes in the reactivity of chromone moieties, our group has been applied 3-(1-alkynyl)chromones for the diversified synthesis of chromone-based scaffolds by the tandem reactions with different nucleophiles.‡ Since the α-hydrogen of isocyanatoacetate could be removed to afford an anion as a nucleophile and the terminal carbon of isocyan group could be nucleophilic as well on another aspect, isocyanatoacetate employed an excellent component in tandem reactions.§ Based on the information mentioned above, a cascade process was proposed. The consequent anion acquired by the deprotonation of isocyanatoacetate as a nucleophile could initiate the Michael addition to 3-(1-alkynyl)-chromone under basic conditions, resulting in the formation of the intermediate A. A could further undergo a transition-metal-assisted ring-closure reaction to generate B. The insertion of a transition metal was then followed by the elimination to form C. An aromatization reaction of C occurred to form a fused heterocycle compound D (Scheme 1a).

RESULT AND DISCUSSION

The investigation of the tandem reaction of 3-(1-alkynyl) chromones with ethyl isocyanatoacetates commenced by utilizing the reported condition with base and transition-metal salt as catalyst.¶ Most of the conditions resulted in messy reaction systems or recovered starting materials (Table S1). While AgOAc/K2CO3 system was employed in NMP under MW irradiation, a major product 2a was afforded, and the X-ray crystallography data of the chloro-analogue 2i was obtained to confirm the structure§ (Figure 1), which is a xanthone skeleton with a 2-imidazolyl substitution. Besides, the reaction system was meticulously analyzed and a byproduct 3a was identified in moderate amount (ca. 20% yield). Our group previously described the formation of product 3a for a tandem dimerization–salicylic acid–extrusion process.¶ It was noted that the structure of 2a with an imidazolyl group was formed, illustrating that the dimerization of isocyanatoacetates might be involved in the reaction. After reviewed Grigg’s work, ethyl isocyanatoacetate could be dimerized in competed AgOAc catalyzed reaction via a formal [3 + 2] dipolar addition (Scheme 2).§ The intermediate I was subsequently dero proto nated under basic conditions and then underwent the Michael addition to generate II; II went a ring-opening of pyrone moiety to form III. Afterward, alkyne–allene tautomerism was incorporated to produce IV; intramolecular nucleophilic addition transferred the negative charge from the phenol anion to form a carbanion V, which consecutively underwent 1,2-addition on the ethyl ester. Meanwhile, the ethoxy group was eliminated to deliver VI. An aromatization of VI gave 2a, ending the whole cascade with the construction of xanthone skeleton (Scheme 2, path A). Notably, the base could be critical for the formation of the byproduct 3a (Scheme 2, path B).

To confirm the mechanism of the tandem process, we conducted controlled experiments. Without AgOAc, the formation of 3a was predominant (Scheme 3a, 55% yield).
Treating ethyl isocyanate with AgOAc in dimethylformamide (DMF) formed ethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4-carboxylate I expeditiously in excellent yield (95%). Under MW irradiation, I could be deprotonated by NaH, and the tandem process was promoted to give the desired product 2a (67% yield) smoothly.

Owing the dimerization of ethyl isocyanoacetate involved in the reaction, 2 equiv of isocyanoacetate should be adopted in the tandem process. The removal of NMP is arduous due to its high boiling point. Thus, the solvent was replaced with DMF, and further investigations on bases were carefully performed. Deprotonated intermediate I is a relatively weak nucleophile; therefore, the base might significantly influence the reaction pathway. Among the various bases screened, Et3N showed less activity to this reaction and gave traces of 2a (Table 1, entry 3), whereas DBU gave a decreased yield of 2a (Table 1, entry 4). The reaction also provided a lower yield of 2a when the base was changed to tBuOK (Table 1, entry 5). When the base was replaced with MeONa, the yield of 2a was increased obviously (Table 1, entry 6). The screening of base ended with

Figure 1. ORTEP diagram of compound 2i with an ellipsoid contour probability of 50%.
NaH, which was found to be the best and gave a satisfying yield of 2a (Table 1, entry 7) without 3a. When the equivalents of NaH were increased from 1.0 to 1.5 in the reaction (Table 1, entry 8), a higher amount of byproduct 3a (∼30% yield) was observed compared with that in the initial stage. The screening of the solvents was carried out posteriorly, revealing that DMF is appropriate for the tandem reaction (Table 1, entries 9−12). Finally, the tandem process proceeded aptly with NaH as the base and DMF as the solvent in the one-pot reaction.

Recognizing the mechanism of the reaction, we explored the scope of 3-(1-alkynyl) chromones 1 under optimized conditions. Overall, substrates with the R1 substitution of benzene as well as heterocycle, or R2 substitution on chromone moiety yielded 2-imidazolylxanthone 2 in merit (38−85% yield). Electron-withdrawing groups (EWGs) on the terminal aromatic ring were unfavorable for this tandem process (Schemes 4 and 2b−d,i). It indicates that EWGs could stabilize carbanion V, decreasing its nucleophilicity in the ring-closing process. There was no apparent steric effect in the tandem reaction (Schemes 4 and 2d,g). For those substrates with substitution on chromone moiety, the reaction progressed smoothly to yield similar products (Schemes 4 and 2l,m). Additionally, alkyl-substituted alkyn could also achieve a reasonable yield (Schemes 4 and 2n).

Additionally, the scope of various heterocyclic N-substituted ethyl acetates (4a−d) was investigated (Scheme 5). Due to the lability of ethyl 2-(1H-pyrrol-1-yl)acetate (4a) under the basic condition at high temperature, the tandem process gave a low yield of the corresponding pyrroylxanthone 5a. Ethyl 2-(1H-imidazol-1-yl)acetate (4b) and ethyl 2-(1H-pyrazol-1-yl)-acetate (4c) gave the corresponding product 5b and 5c in moderate yield. Ethyl N,N-dimethylglycinate (4d) failed to bring in the N,N-dimethylxanthone scaffold.

In summary, a strategy has been developed for the synthesis of N-heterocycle functionalized xanthones from 3-(1-alkynyl)-

**Scheme 2. Plausible Mechanism**

**Scheme 3. Control Experiments**

| entry | base | solvent | yield (2a) (%) |
|-------|------|---------|---------------|
| 1^b   | K2CO3| NMP     | 23            |
| 2     | K2CO3| DMF     | 41            |
| 3     | Et3N | DMF     | trace         |
| 4     | DBU  | DMF     | 34            |
| 5     | BuOK | DMF     | 25            |
| 6     | MeONa| DMF     | 52            |
| 7     | NaH  | DMF     | 71            |
| 8^d   | NaH  | DMSO    | 30            |
| 9     | NaH  | 1,4-dioxane | 23          |
| 10    | NaH  | DMSO    | 19            |
| 11    | NaH  | toluene | trace         |
| 12^e  | NaH  | MeCN    | 23            |

Table 1. Optimization for the Reaction Conditions^d

^dUnless otherwise noted, the reactions were carried out with 0.5 mmol of 1a and 2 equiv of ethyl isocyanoacetate; 0.2 equiv of AgOAc was first mixed for 10 min, followed by 1 equiv of base in 1.5 mL of solvents under MW irradiation at 130 °C for 10 min. 1^1 equiv of ethyl isocyanoacetate and 1.5 equiv K2CO3 were added together into solvents; 3a was observed in 20% yield. No significant amount of 3a was found. 4^1.5 equiv of NaH was used, and 3a was observed in 30% yield. The reaction was run at 100 °C.
chromones and ethyl isocyanoacetate as substrates. Ethyl isocyanoacetate was dimerized to form imidazole intermediate I, which was subsequently deprotonated and then a tandem Michael addition/ring-opening/cyclization/1,2-addition took place to afford 3-hydroxy-2-(1H-imidazol-1-yl)-xanthone skeleton. Other anions of N,N-disubstituted glycinates were

Scheme 4. Scope of Various 3-(1-Alkynyl)Chromones

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\begin{align*}
\text{Scheme 5. Substrate Scope of Various N-Heterocycle-Substituted Ethyl Acetates}
\end{align*}
\]
acetylene (0.5 mmol) were charged into the vial. 1H NMR (400 MHz, CDCl3) δ 8.31 (dd, J = 7.9 Hz, 1H), 8.24 (s, 1H), 7.89 (s, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.75–7.64 (m, 4H), 7.40 (dd, J = 7.6, 7.6 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H); 13C{1H} NMR (125 MHz, CDCl3) δ 175.7, 161.3, 156.0, 155.0, 154.4, 138.7, 134.9, 134.4, 133.4, 131.8, 130.9 (q, JCF = 32.8 Hz), 129.0, 128.0 (q, JCF = 3.6 Hz), 126.5, 125.8, 125.1, 125.0, 124.0 (q, JCF = 273.4 Hz), 123.9, 122.6, 121.1, 118.7, 118.0, 115.2, 60.8, 14.1; HRMS (ESI): m/z [M + H]+ calcd. for C26H18F3N2O5: 495.1144; found: 495.1144.

**Ethyl 1-(3-Hydroxy-9-oxo-4-(4-fluoromethyl)phenyl)-9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2c).** Light yellow solid, 126 mg, 51% yield, eluent ratio (dichloromethane/methanol = 10:1); 1H NMR (600 MHz, CDCl3) δ 8.31 (d, J = 8.4 Hz, 1H), 8.24 (s, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 7.9 Hz, 2H), 7.71–7.63 (m, 3H), 7.40 (dd, J = 7.5, 7.5 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 175.8, 161.5, 156.1, 155.1, 154.4, 138.8, 135.0, 134.96, 133.5, 131.5, 130.5 (q, JCF = 33.2 Hz), 126.6, 125.9, 125.5 (q, JCF = 3.8 Hz), 124.6, 124.5, 124.10 (q, JCF = 270.6 Hz), 122.6, 121.2, 119.1, 118.1, 115.4, 60.9, 14.2; HRMS (ESI): m/z [M + H]+ calcd. for C24H16F4N3O3: 495.1168; found: 495.1164.

**Ethyl 1-(3-Hydroxy-9-oxo-4-(2-(fluorome-thyl)9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2d).** Light yellow solid, 109 mg, 44% yield, eluent ratio (dichloromethane/methanol = 10:1); 1H NMR (400 MHz, CDCl3) δ 8.16 (d, J = 6.0 Hz, 2H), 7.78 (d, J = 7.9 Hz, 1H), 7.58 (m, 3H), 7.45 (d, J = 7.6 Hz, 1H), 7.31 (dd, J = 7.5, 7.5 Hz, 1H), 7.05 (d, J = 8.4 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H);
\[ \text{ACS Omega} \quad \text{http://pubs.acs.org/journal/acsodf} \]

**Ethyl 1-(3-Hydroxy-4-oxo-4-(pyridin-4-yl)-9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2j).** Light yellow solid, 88 mg, 41% yield, eluent ratio (dichloromethane/methanol = 1:1), mp (°C): 268.1; \[^1\text{H}\text{NMR} (400 MHz, DMSO-\text{d}_6) \delta 8.38 (s, 1H), 8.28 (s, 1H), 8.17 (s, 1H), 8.08 (d, J = 7.8, 1H), 7.91 (s, 1H), 7.64 (dd, J = 7.5, 7.5 Hz, 1H), 7.34 (dd, J = 7.5, 7.5 Hz, 1H), 7.26 (d, J = 8.3 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); \[^{13}\text{C}\text{NMR} (150 MHz, DMSO-\text{d}_6)](\delta 173.9, 162.3, 155.2, 154.3, 139.0, 134.6, 132.3, 127.2, 125.6, 125.4, 124.3, 122.5, 121.0, 117.9, 59.6, 14.4; HRMS (ESI): \text{m/z} [\text{M} + \text{H}]^{+} \text{calcd. for C}_{25}\text{H}_{19}\text{N}_2\text{O}_5: 427.1246; \text{found: 428.1199.} \]

**Ethyl 1-(3-Hydroxy-4-oxo-4-(pyrimidine-5-yl)-9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2k).** Light yellow solid, 109 mg, 51% yield, eluent ratio (dichloromethane/methanol = 10:1), mp (°C): >300; \[^1\text{H}\text{NMR} (600 MHz, DMSO-\text{d}_6) \delta 9.03 (s, 1H), 8.98 (s, 2H), 8.25 (s, 1H), 8.17 (s, 1H), 8.08 (d, J = 7.8, 1H), 7.91 (s, 1H), 6.74 (dd, J = 7.5, 7.5 Hz, 1H), 7.34 (dd, J = 7.5, 7.5 Hz, 1H), 7.26 (d, J = 8.3 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); \[^{13}\text{C}\text{NMR} (150 MHz, DMSO-\text{d}_6)](\delta 173.3, 169.0, 163.0, 158.7, 155.6, 155.5, 138.8, 133.7, 131.7, 130.3, 127.4, 127.0, 125.8, 123.8, 121.9, 121.0, 117.7, 108.7, 104.5, 59.9, 14.8; HRMS (ESI): \text{m/z} [\text{M} + \text{H}]^{+} \text{calcd. for C}_{23}\text{H}_{17}\text{N}_2\text{O}_5: 429.1199; \text{found: 429.1193.} \]

**Ethyl 1-(3-Hydroxy-7-methoxy-9-oxo-4-phenyl-9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2l).** Light yellow amorphous solid, 146 mg, 64% yield, eluent ratio (dichloromethane/methanol = 10:1); \[^1\text{H}\text{NMR} (400 MHz, DMSO-\text{d}_6) \delta 8.25 (s, 1H), 7.88 (s, 1H), 7.74 (s, 1H), 7.66 (s, 1H), 7.59–7.48 (m, 5H), 7.26–7.18 (m, 2H), 4.29 (q, J = 7.2 Hz, 2H), 3.90 (3H), 3.00 (t, J = 7.1 Hz, 3H); \[^{13}\text{C}\text{NMR} (150 MHz, DMSO-\text{d}_6)](\delta 175.8, 162.2, 156.3, 154.0, 153.4, 131.0, 133.5, 130.9, 130.3, 129.2, 129.0, 126.1, 124.7, 127.2, 122.6, 121.5, 119.5, 119.2, 115.0, 105.8, 60.7, 56.0, 14.3; HRMS (ESI): \text{m/z} [\text{M} + \text{H}]^{+} \text{calcd. for C}_{25}\text{H}_{19}\text{N}_2\text{O}_5: 457.1400; \text{found: 457.1396.} \]

**Ethyl 1-(3-Hydroxy-7-fluoro-9-oxo-4-phenyl-9H-xanthen-2-yl)-1H-imidazole-4-carboxylate (2m).** Yellow amorphous solid, 111 mg, 50% yield, eluent ratio (dichloromethane/methanol = 10:1); \[^1\text{H}\text{NMR} (400 MHz, DMSO-\text{d}_6) \delta 8.24 (s, 1H), 8.15 (s, 1H), 7.85 (s, 1H), 7.71 (dd, J = 8.6, 3.2 Hz, 1H), 7.50–7.43 (m, 3H), 7.40–7.36 (m, 2H), 7.28–7.20 (m, 2H), 4.24 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H); \[^{13}\text{C}\text{NMR} (150 MHz, DMSO-\text{d}_6)](\delta 172.0, 162.5, 157.8 (d, J_{CF} = 238.9), 154.6, 151.5, 138.4, 135.5, 134.1, 131.7, 127.1, 126.6, 125.6, 122.4 (d, J_{CD} = 6.5 Hz), 120.6, 120.5, 119.5 (d, J_{CF} = 9.0 Hz), 116.3, 115.6, 110.0, 109.9, 59.4, 14.4; HRMS (ESI): \text{m/z} [\text{M} + \text{H}]^{+} \text{calcd. for C}_{25}\text{H}_{19}\text{N}_2\text{O}_5: 445.1200; \text{found: 445.1201.} \]
3-Hydroxy-2-(1H-pyrrol-1-yl)-4-(p-tolyl)-9H-xanthen-9-one (4a). White amorphous solid, 51 mg, 28% yield, eluent ratio (petroleum ether/ethyl acetate = 5:1); 1H NMR (500 MHz, CDCl3) δ 8.35 (d, J = 8.0 Hz, 1H), 8.32 (s, 1H), 7.67 (dd, J = 8.7, 7.1 Hz, 1H), 7.45 (d, J = 1.6 Hz, 4H), 7.40 (dd, J = 8.0, 7.1, 1H), 7.32 (d, J = 8.5 Hz, 1H), 7.08 (t, J = 2.1 Hz, 2H), 6.43 (t, J = 2.2 Hz, 2H), 6.00 (s, 1H), 2.52 (s, 3H); 13C{1H} NMR (125 MHz, CDCl3) δ 175.8, 155.7, 152.5, 152.1, 138.6, 134.0, 130.1, 129.6, 126.5, 126.1, 125.9, 123.7, 122.2, 121.6, 120.9, 117.6, 117.2, 115.4, 109.8, 13.7; HRMS (ESI): m/z [M + H]+ calcd. for C23H17N2O3: 369.1234; found: 369.1232.

3-Hydroxy-2-(1H-imidazol-1-yl)-4-(p-tolyl)-9H-xanthen-9-one (4b). White amorphous solid, 90 mg, 49% yield, eluent ratio (petroleum ether/ethyl acetate = 5:1); 1H NMR (600 MHz, CDCl3) δ 8.21 (d, J = 7.9 Hz, 1H), 8.24 (s, 1H), 8.00 (s, 1H), 7.64 (dd, J = 8.7, 7.1 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 7.41–7.35 (m, 3H), 7.29 (d, J = 8.4 Hz, 1H), 6.83 (s, 1H), 2.48 (s, 3H); 13C{1H} NMR (150 MHz, CDCl3) δ 175.6, 155.7, 154.9, 153.5, 138.3, 130.3, 129.5, 127.4, 126.5, 126.0, 123.7, 123.0, 121.5, 120.8, 119.6, 118.3, 117.3, 114.0, 21.0; HRMS (ESI): m/z [M + H]+ calcd. for C24H18NO3: 368.1289; found: 368.1292.

3-Hydroxy-2-(1H-pyrazol-1-yl)-4-(p-tolyl)-9H-xanthen-9-one (4c). White amorphous solid, 106 mg, 58% yield, eluent ratio (petroleum ether/ethyl acetate = 5:1); 1H NMR (400 MHz, CDCl3) δ 8.41 (s, 1H), 8.33 (d, J = 7.9 Hz, 1H), 8.29 (d, J = 2.6 Hz, 1H), 7.76 (d, J = 2.0 Hz, 1H), 7.65 (dd, J = 8.6, 7.1, 1H), 7.49–7.43 (m, 2H), 7.38–7.30 (m, 4H), 6.64–6.56 (m, 1H), 2.48 (s, 3H); 13C{1H} NMR (125 MHz, CDCl3) δ 176.5, 156.3, 153.5, 152.9, 139.0, 137.7, 134.4, 130.7, 129.0, 128.5, 127.7, 126.5, 124.0, 123.2, 121.2, 119.6, 118.2, 114.4, 113.8, 107.5, 21.4; HRMS (ESI): m/z [M + H]+ calcd. for C24H20N2O3: 369.1234; found: 369.1229.

ACKNOWLEDGMENTS
This study was financially supported by the State Key Laboratory of Drug Research (SIMM1803ZZ-01) and the Science and Technology Commission of Shanghai Municipality (18431907100).

REFERENCES
(1) For reviews of tandem reactions, see: (a) Christoffers, J.; Korjipelly, G.; Rosiak, A.; Rossle, M. Recent advances in metal-catalyzed asymmetric conjugate additions. Synthesis 2007, 2007, 1279–1300. (b) Vlaar, T.; Ruijter, E.; Orru, R. V. A. Recent Advances in Palladium-Catalyzed Cascade Cyclizations. Adv. Synth. Catal. 2011, 353, 809–841. (c) Amara, Z.; Caron, J.; Joseph, D. Recent contributions from the asymmetric aza-Michael reaction to alkaloids total synthesis. Nat. Prod. Rep. 2013, 30, 1211–1225. (d) Liu, S. Y.; Zhao, T.; Qu, J. P.; Wang, B. M. Expedit Synthetic of 1,4-Benzodiazepines via a Tandem Condensation/1,5-Hydride Transfer/Cyclization Process. Adv. Synth. Catal. 2018, 360, 4094–4098. For recent examples on tandem reactions see: (e) Li, Y.; Yu, J.; Bi, Y. C.; Yan, G. B.; Huang, D. Tandem Reactions of Ynones: via Conjugate Addition of Nitrogen-, Carbon-, Oxygen-, Boron-, Silicon-, Phosphorus-, and Sulfur-Containing Nucleophiles. Adv. Synth. Catal. 2019, 361, 4839–4881. (f) Lv, N. N.; Chen, Z. K.; Liu, Z. X.; Zhang, Y. H. Redox-Neutral Rhodium(III)-Catalyzed Annulation of Arylhydrazines with Sulfoxonium Ylides To Synthesize 2-Arylindoles. J. Org. Chem. 2019, 84, 13013–13021.
(2) (a) Hu, F.; Chen, T. J.; Yan, J. W.; Cheng, M.; Huang, L. P.; Hu, Y. H. Au-catalyzed cascade addition/cyclization/H-transfer reactions of 3-(1-alkynyl)chromones to construct 4H-Furo[3,2-c]-pyrans scaffold. RSC Adv. 2012, 2, 11238–11241. (b) Zhao, L. Z.; Xie, F. C.; Cheng, G.; Hu, Y. H. A Base-Promoted Tandem Reaction of 3-(1-Alkynyl)chromones with 1,3-Dicarbonyl Compounds: An Efficient Approach to Functional Xanthones. Angew. Chem. Int. Ed. 2009, 48, 6520–6523. (c) Huang, L. P.; Hu, F.; Ma, Q. D.; Hu, Y. H. CuBr-catalyzed cascade reaction of 2-substituted-3-(1-alkynyl)chromones to synthesize functionalized 3-acylfurans. Tetrahedron Lett. 2013, 54, 3410–3414. (d) Liu, Y.; Jin, S. Y.; Huang, L. P.; Hu, Y. H. Phase Transfer Reagent Promoted Tandem Ring-Opening and Ring-Closing Reactions of Unique 3-(1-Alkynyl) Chromones. Org. Lett. 2015, 17, 2134–2137. (e) Zhang, Y. F.; Duan, W. D.; Chen, J. J.; Hu, Y. H. Base-Promoted Cascade Reactions of 3-(1-Alkynyl)chromones with Pyridinium Ylides to Chromeno 2,3-d-azepine Derivatives. J. Org. Chem. 2019, 84, 4467–4472. (e) Xie, F. C.; Pan, X.; Lin, S. J.; Hu, Y. H. A base-promoted desalicyloylation dimerization of 3-(1-alkynyl)-chromones: An unusual approach to 2-alkynyl xanthones. Org. Biomol. Chem. 2010, 8, 1378–1381.
(3) For reviews on isocyanocacetates, see (a) Giustiniano, M.; Basso, M.; Mercalli, V.; Massarotti, A.; Novellino, E.; Tron, G. C.; Zhu, J. P. To each his own: isonitriles for all flavors. Functionalized isocyanides as valuable tools in organic synthesis. Chem. Soc. Rev. 2017, 46, 1295–1357. (b) Gulevich, A. V.; Zhanko, A. G.; Orru, R. V. A.; Nenajdenko, V. G. Isocyanacetoacetate Derivatives: Synthesis, Reactivity, and Application. Chem. Rev. 2010, 110, 5235–5331. (c) Qu, G.; Ding, Q. P.; Wu, J. Recent advances in isocyanide insertion chemistry. Chem. Soc. Rev. 2013, 42, 5257–5269. For Reaction Examples, see (d) Chen, D. P.; Shan, Y. Y.; Li, J. M.; You, J. M.; Sun, X. J.; Qu, G. Y. S. External Reductant-Free Palladium-Catalyzed Reductive
Insertion of Isocyanide: Synthesis of Polysubstituted Pyroles and Its Applications as a Cysteine Probe. Org. Lett. 2019, 21, 4044−4048.

(e) Pogaku, N.; Krishna, P. R.; Prapurna, Y. L. An Efficient Direct Access to Carbamates from Alcohols and TosMIC Mediated by Iodine in DMSO. Synlett 2018, 29, 2039−2042. (f) Teng, F.; Hu, W. M.; Hu, H. A. Z.; Luo, S.; Zhu, Q. Selective C-H or N-H Imidoylative Annulation of 2-(2-Isocyanophenyl)-1H-indoles Leading to Diverse Indole-fused Scaffolds. Adv. Synth. Catal. 2019, 361, 1414−1418.

(4) (a) Qi, X. Y.; Xiang, H. Y.; Yang, C. H. Synthesis of Functionalized Chromeno 2,3-b pyrrol-4(1H)-ones by Silver-Catalyzed Cascade Reactions of Chromones/Thiochromones and isocyanoacetates. Org. Lett. 2015, 17, 5590−5593. (b) Zhang, L. J.; Xu, X. X.; Shao, Q. R.; Pan, L.; Liu, Q. Tandem Michael addition/isocyanide insertion into the C-C bond: a novel access to 2-acylpyrroles and medium-ring fused pyroles. Org. Biomol. Chem. 2013, 11, 7393−7399. (c) Li, Y. F.; Xu, X. X.; Xia, C. Y.; Zhang, L. J.; Pan, L.; Liu, Q. Double nucleophilic attack on isocyanide carbon: a synthetic strategy for 7-aza-tetrahydroindoles. Chem. Commun. 2012, 48, 12228−12230.

(5) CCDC numbers 1987456(2i) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(6) Grigg, R.; Lansdell, M. I.; Thornton-Pett, M. Silver acetate catalyzed cycloadditions of isocyanoacetates. Tetrahedron 1999, 55, 2025−2044.

(7) Due to low solubility of compound 2j, additional MeOD were used in 13C NMR data acquisition to confirm the signal-to-noise ratio.