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## Graphical Abstract

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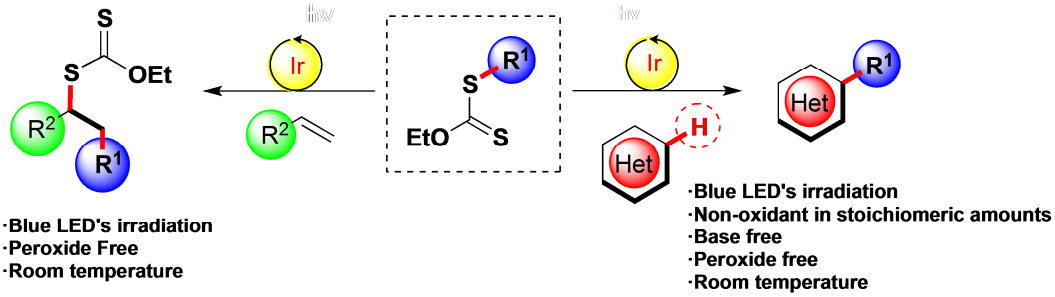

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# Visible light/Ir(III) photocatalytic initiation of xanthate-based radical-chain reactions: xanthate group transfer and oxidative addition to aromatic systems

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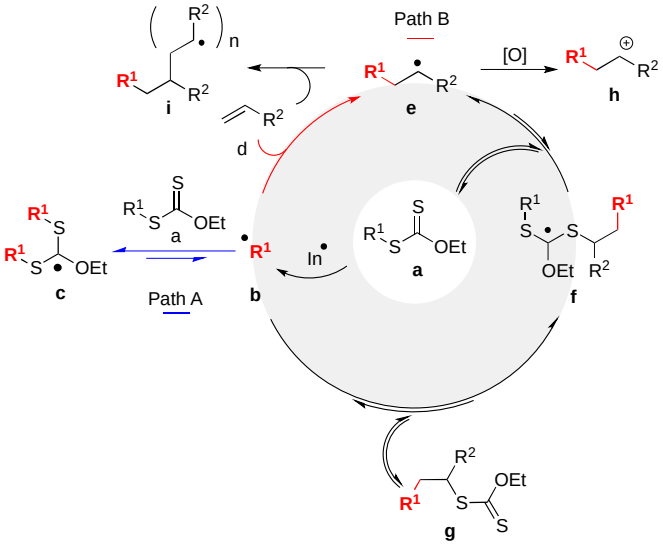
ABSTRACT

A photocatalyzed redox generation of radicals from *O*-ethyl xanthates to generate electrophilic radicals under photoredox catalysis, using $Ir(ppy)_3$ and blue LEDs irradiation is described. The protocol can be used in classical xanthate-based inter- and intra-molecular group transfer reactions and oxidative radical addition to several heteroaromatic systems. The process does not require high temperature and reactions are cleaner compared with the traditional peroxide initiation. In the oxidative addition to aromatic systems, the oxidation process is part of the catalytic cycle and does not require a stoichiometric oxidant such as DLP which is particularly difficult to separate from the product.



## 1. Introduction

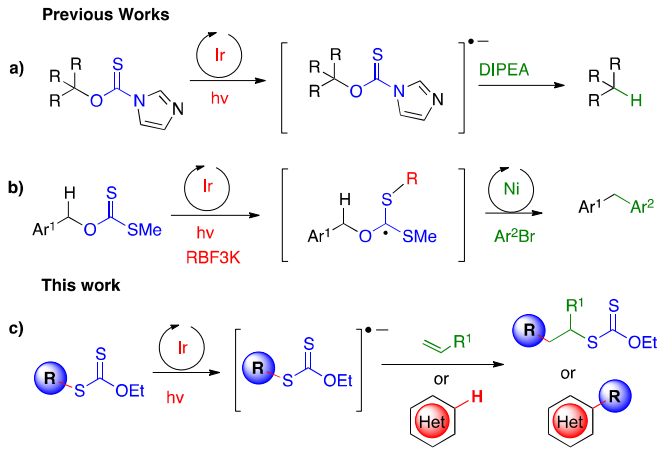
Since its inception by *Sir* Derek Barton[1] and further extended by Zard,[2] xanthate-based radical chemistry has become an important tool in organic synthesis. Because of the ease by which new carbon-carbon bonds are generated *via* radical addition to both activated and simple alkenes[3] as well as by oxidative addition to aromatic systems,[3] these protocols have been applied elegantly in the total synthesis of natural products[4] and in the development of new synthetic methodologies for the construction of molecules with a vast range of complexity.[4] Over the last three decades, Zard and co-workers have provided many different functionalized xanthates which, in turn, have generated free radicals, useful for various synthetic purposes. The main features of the reaction mechanism in the xanthate transfer process are: 1) once the radical **b** is generated from xanthate **a**, (by the action of an initiator In$^{\bullet}$, Scheme 1), the fast and degenerate reversible addition/fragmentation process between the radical **b** and its xanthate precursor (path A), extends the lifetime of radical **b**, allowing it to be captured even by unactivated alkenes and homo and heteroaromatic systems (**d**) in an inter- and intra-molecular processes, giving a new radical **e** (path B). 2) The equilibrium between the reactive radical species and the xanthates (**a** and **g**) maintains a low concentration of the reactive species (**b** and **e**), allowing the reactions to progress in a quite concentrated medium (even under solvent-free conditions). Interestingly, depending on the conditions and combination of xanthate and alkene, a polymerization process may (RAFT/MADIX polymerization process) or may not occur.




**Scheme 1.** Mechanism for xanthate radical process.

Under standard conditions however, the radical **e** is trapped by the xanthate **a** to finally afford the expected transfer-xanthate **g**.

3) Product **g** is itself a new xanthate, which may function as a substrate in other radical or ionic processes. Thus, several complex transformations can occur that take advantage of the rich sulfur-based chemistry. In some specific cases (*e. g.*, in the addition to an aromatic system), the presence of an oxidant (*e. g.*, peroxide itself) in the reaction media might induce the conversion of the radical **e** into the corresponding cation **h**, which might undergo a proton elimination to regenerate the olefinic system.




**Scheme 2.** Photoredox catalysis generation of radicals from thiocarbamates

The xanthate-based radical chain process is commonly initiated using organic peroxides such as dilauroyl peroxide (DLP) and dicumyl peroxide (DCP). However, these peroxides require high temperatures to be fragmented and byproducts can be difficult to eliminate from the product, especially when DLP is used. As an alternative, triethylborane can initiate the radical chain process at room temperature. Unfortunately, several equivalents of this reagent are usually required, with poor reproducibility of results. Photoredox catalysis has re-emerged as a powerful strategy to construct C-C and/or C-X bonds under mild conditions by the activation of simple substrates. Several novel methodologies and applications in total synthesis have been reported in the last decade, showing the versatility of this chemistry[5].

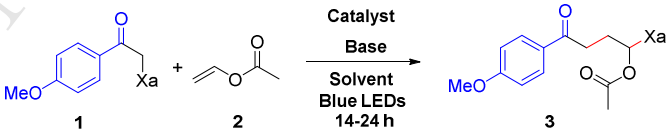
Recently, several research groups have developed photoredox catalytic systems to generate radical species from dithiocarbonates (xanthates) and thiocarbamates. Ollivier and co-workers reported a photocatalytic Barton–McCombie deoxygenation process of secondary and tertiary alcohols using $Ir(ppy)_3$, in the presence of DIPEA as the sacrificial electron donor, under blue LED irradiation (Scheme 2, a).[6a] Molander and co-workers developed a reductive cross-coupling reaction using Ni/Ir-based photoredox dual catalysis. In this case, the radical species were generated from the corresponding *O*-benzyl xanthates, also under blue LEDs irradiation (Scheme 2, b).[6b]

Based on these reports, we wondered if the radical initiation process *via* reduction of *O*-ethyl xanthates under photoredox catalysis would be useful for intra- and intermolecular radical additions to alkenes and oxidative addition to heteroaromatic systems.

## 2. Results and discussion

We first investigated the xanthate group transfer reaction between xanthate **1** and vinyl acetate **2** (Table 1). The reaction was performed using $Ir(ppy)_3$ (1 mol%) and 2,6-lutidine as a sacrificial electron donor in acetonitrile, under blue LED light (entry 1). Gratifyingly, under these conditions, the xanthate transfer product was obtained in 25 % yield. An increase in the catalyst loading to 2 mol% resulted in a slightly higher yield; however, the use of 5 mol% did not improve the yield (entry 3). Thus, 2 mol% was selected as the optimum. When the less reducing $Ru(bpy)_3$ was tested as a photocatalyst, the reaction did not proceed (entry 4). Substituting DMF for acetonitrile resulted in an improved yield (entry 5) and this solvent was selected for subsequent reactions. Under the same conditions, the use of $[Ir(dtbbpy)(ppy)]PF_6$ gave a slightly lower yield (entry 6). The use of triethylamine resulted only in decomposition of the starting material (entry 7). Surprisingly, when the reaction was performed without lutidine, **3** was isolated in higher yield (entry 8). This result suggested that the base does not play a determinant role in the xanthate group transfer process. Apparently, the efficient radical chain process, once initiated, persists long enough to afford an improved product yield without the need to regenerate the organometallic initiator by the action of the base. Another possible explanation for this observation is that the electron rich radical species **c** and **f** (Scheme 1) reduce Ir(IV) via a SET process to regenerate the initiator[7] consuming a portion of the substrate. Increasing the stoichiometric ratio between xanthate **1** and vinyl acetate **2** resulted in a better yield (entry 9). Using vinyl acetate as a solvent favored polymerization of the alkene. Interestingly, when the reaction was carried out without $Ir(ppy)_3$, product **3** was obtained in 25% yield (entry 10). This result clearly indicates that the reaction starts only with the blue LEDs irradiation, presumably *via* homolytic C–S scission.[8] Nevertheless, under these conditions the chain reaction is only moderately efficient and therefore catalyst assistance is required. Finally, the reaction did not proceed in the absence of irradiation (entry 11).

**Table 1.** Optimization of the xanthate transfer reaction conditions under photoredox catalysis.

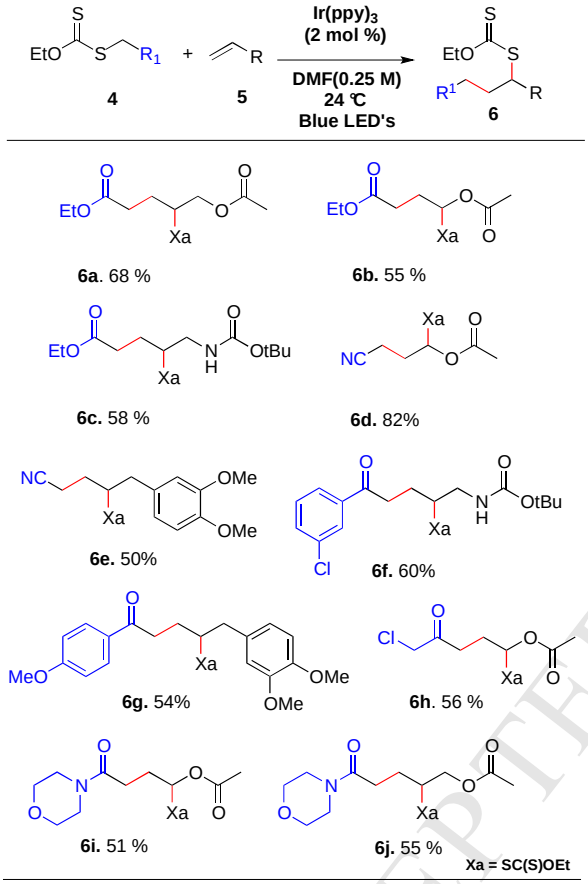



| entry | catalyst | base | solvent | yield[b] (%) |
|---|---|---|---|---|
| 1 | $Ir(ppy)_3$ (1 %) | Lutidine | MeCN | 25 |
| 2 | $Ir(ppy)_3$ (2 %) | Lutidine | MeCN | 29 |
| 3 | $Ir(ppy)_3$ (5 %) | Lutidine | MeCN | 30 |
| 4 | $Ru(bpy)_3$ (2 %) | Lutidine | MeCN | n.r. |
| 5 | $Ir(ppy)_3$ (2 %) | Lutidine | DMF | 55 |
| 6 | $[Ir(dtbbpy)(ppy)_2]PF_6$ (2 %) | Lutidine | DMF | 51 |
| 7 | $Ir(ppy)_3$ (2 %) | $NEt_3$ | DMF | 0 |
| 8 | $Ir(ppy)_3$ (2 %) | - | DMF | 57 |
| 9[c] | $Ir(ppy)_3$ (2 %) | - | DMF | 70 |
| 10[c] | - | - | DMF | 25 |
| 11[c,d] | $Ir(ppy)_3$ (2 %) | - | DMF | n.r. |

**base** (0.11 mmol, 1.1 equiv.) **solvent** (0.4 mL, 0.25 M).[b] Isolated yield. [c] These reactions were performed using **1** (0.2 mmol, 2.0 equiv) and **2** (0.1 mmol, 1.0 equiv.). [d] Reaction performed without blue LEDs irradiation.

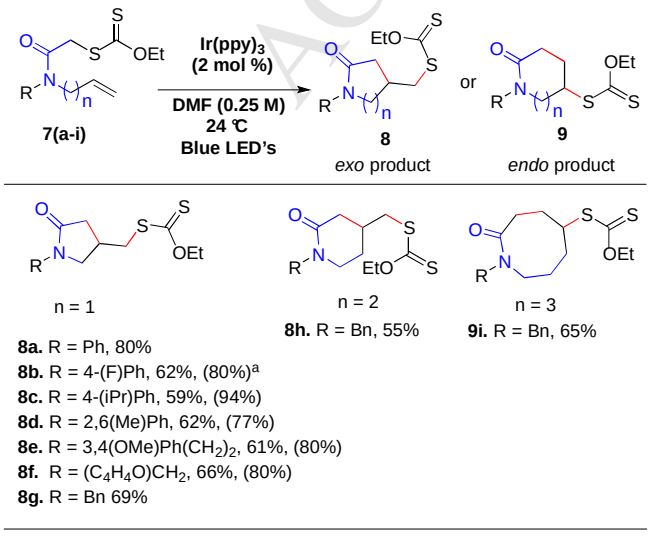
With the optimal conditions in hand, we proceeded to explore the scope of the radical initiation protocol (Scheme 3). The addition of the xanthate derived from ethyl acetate as compared to allyl acetate, vinyl acetate, or Boc-protected allyl amine was evaluated. Then, the corresponding xanthate transfer products **6a-c** were obtained in moderate yields. When we tested the xanthate derived from acetonitrile, the product **6d** was obtained in good yield with vinyl acetate as the radical acceptor and the product **6e**

was obtained in moderate yield when the simple alkene 4-allyl-1,2-dimethoxybenzene was utilized. Additionally, xanthates derived from ketones and amides were tested with various alkenes, giving rise the corresponding products **6f-j** in moderate yield. Importantly, the synthetized compounds may serve as substrates for several ionic and radical transformations. For example, xanthate **6h** is a synthetic equivalent of a 1,4-ketoaldehyde[9] useful for the synthesis of several heteroaromatic systems. On the other hand, substrate **6f** may be utilized for the synthesis of tetralones by ring-closure onto the aromatic ring[10] as well as for the synthesis of thiazolidine 2-ones.[11] Vinyl acetate derivatives have been used in the synthesis of α,β-unsaturated trifluoromethylketones.[12] It should be emphasized that some of the products were obtained in yields comparable to those



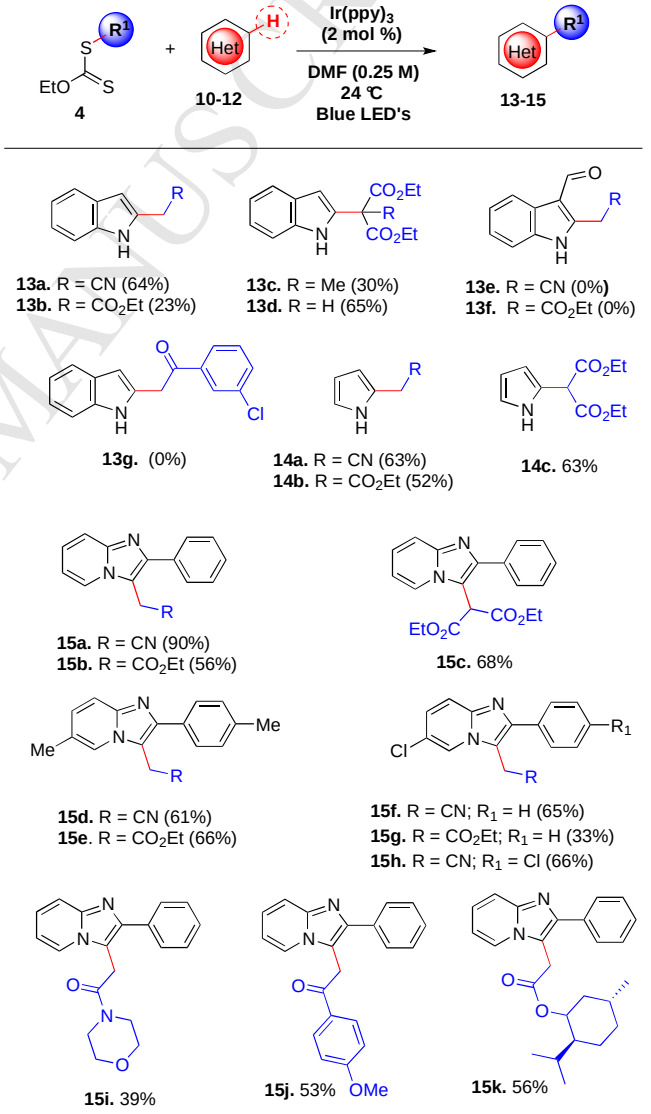

reported by Zard[13] (67% for compound **6d**) and Renaud[14] (74% for compound **6a**), using the classical peroxide initiation.

**Scheme 3.** Intermolecular additions of electrophilic radicals to alkenes.




**Scheme 4.** Xanthate group transfer in intramolecular reaction.

Then, we explored intramolecular reactions using substrates **7a-i** (Scheme 4). When n=1 (**7a-g**), the substrates underwent a 5-*exo* radical cyclization, giving rise to pyrrolidones **8a-g.** When n=2 (**7h**), a 6-*exo* radical cyclization was observed, affording piperidone **8h** (Scheme 4). In addition, when n=3 (**7i**), the reaction provided aza-octanone **9i,** *via* an 8-*endo* cyclization. The results obtained in this intramolecular radical addition are comparable to those reported for analogous substrates using the DLP initiation methodology.[15] It is important to point out that most of the reactions reach a stage in which the process stops, thus precluding full consumption of starting material. Thus, the calculated yields of heterocycles **8b-f** (up to 94%) are based on recovered starting material show the potential of this protocol.



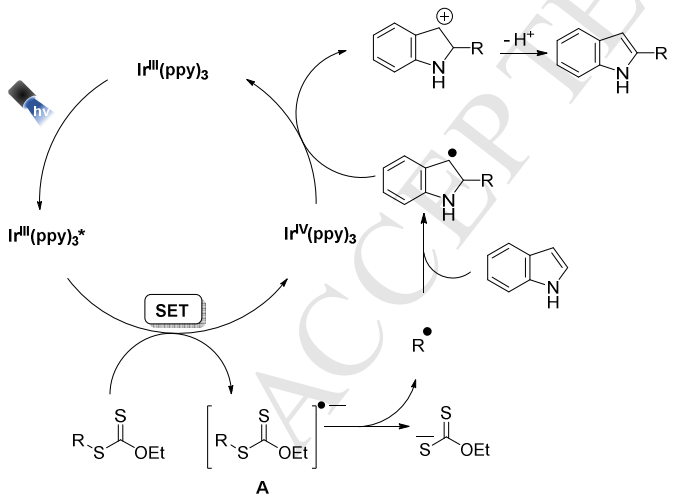

**Scheme 5.** Oxidative addition to heterocyclic systems.

To extend the scope of the photoredox initiation protocol, the more challenging direct intermolecular oxidative alkylation of heteroaromatic systems, was further explored (Scheme 5). It is worth mentioning that such a process permits the regioselective installation of an alkyl group onto heteroaromatic systems

through a direct C-H bond functionalization (Minisci type reaction).[16] Furthermore, the protocol might be utilized for construction of synthetically useful intermediates or for late stage functionalization of pharmaceutically important molecules.[17] Indeed, the use of photocatalytic conditions for the intermolecular alkylation of heteroaromatics has been recently described.[18] In those studies, only bromomalonates and bromoacetonitrile were employed for the radical addition onto selected heteroaromatic systems.[18]

Satisfactorily, when the radical addition of xanthates derived from acetonitrile, ethyl acetate and malonate were effected on indole and pyrrole, products **13a-d** and **14a-c** were obtained in moderate yields. However, when indole-3-carboxaldehyde was used as the radical acceptor, the expected products (**13e, f**) were not obtained under apparent inhibition of the process, and most of the starting materials were recovered. Similarly, the product **13g** was not observed when the *m*-chlorophenacyl xanthate precursor was employed. Recently, we and others reported the radical addition to imidazol[1,2-a]pyridine under DLP-initiation conditions.[19] Likewise, Sun and co-workers[18a] reported a cyanomethylation of this heterocyclic system using bromoacetonitrile under photoredox catalysis in the presence of $NaHCO_3$ as a base. Interestingly, when the radical addition to this aromatic system using xanthates derived from acetonitrile, ethyl acetate, malonate, even xanthates derived from ketones and amides was carried out, moderate product yields were obtained in the absence of a base (**15a-k**). Most of the experiments were conducted in 0.1 mmol scale. However, similar yields were observed when the experiment for the obtantion of the product **15a** was scaled up to 1 gram.

To gain insight into the reaction mechanism, the reduction potential of xanthate **1** was determined by cyclic voltammetry[20] (see supporting information). The value obtained for this xanthate was -1.60 V (SCE), which is in principle, suitable to be reduced to the radical anion **A** by the action of the $Ir(ppy)_3^*$ {$E_{1/2}$ $[Ir(ppy)_3]^+/Ir(ppy)_3^*$) = -1.73 V (SCE)}[5b].




**Scheme 6**. Proposal mechanism for the oxidative addition.

Thus, based on our experimental observations and previous reports,[6,18] we propose that the mechanism of the oxidative addition starts with a single electron transfer (SET) from the Ir(III) excited-state to the xanthate, giving rise to a radical-anion **A**, which undergoes a cleavage to generate a new radical and a xanthogenate anion (Scheme 6). The new carbon-centered radical adds to the aromatic ring, resulting in a new radical which is oxidized by Ir(IV) to regenerate the catalyst. Finally, proton abstraction regenerates the aromatic system to generate the final product.

## 3. Conclusions

In conclusion, we have developed a new radical initiation system from *O*-ethyl xanthates to generate electrophilic radicals under photoredox catalysis, using $Ir(ppy)_3$ and blue light. The protocol can be used in classical xanthate-based radical reactions such as xanthate group transfer and oxidative radical addition to aromatic rings. The process does not require high temperature and reactions are cleaner compared with the traditional peroxide initiation. In the oxidative addition to aromatic systems, the oxidation process is part of the catalytic cycle and does not require a stoichiometric oxidant such as DLP which is particularly difficult to separate from the product. Furthermore, the presence of a base is not necessary as in the photocatalytic processes previously reported.[18] We believe that this novel photocatalytic initiation process offers the opportunity to expand the applications of the xanthate-based radical chemistry, especially those cases when the nature of the initiator and the temperature might cause difficulties.

## 4. Experimental section

### *4.1. General*

Solvents (DMF and MeCN) were purchased from Sigma-Aldrich and were used without further purification. Triethylamine and 2,6-lutidine were purchased from Sigma-Aldrich and used without further purification. Catalysts ($Ir(ppy)_3$, $Ru(bpy)_3$ and $[Ir(dtbbpy)(ppy)_2]PF_6$) were purchased from Sigma-Aldrich and used without further purification. Melting points were determined on a Fisher apparatus and are not corrected. All reactions were performed under an argon atmosphere. Reaction progress was monitored by analytical thin layer chromatography using GF silicagel plates purchased from Merck. Visualization was achieved by short-wave UV light (254 nm) and/or staining with vanillin. 1H and 13C NMR spectra were recorded on a Jeol Eclipse-300 MHz, Bruker Avance III 400MHz and Bruker Fourier-300 MHz model spectrometers using $CDCl_3$ as solvent. Chemical shifts are reported as parts per million downfield from an internal tetramethylsilane standard (δ = 0.0 for 1H) or from solvent reference (CDCl3 δ =7.26 for 1H, δ =77.16 for 13C). NMR coupling constants are reported in hertz (Hz). Low- and high-resolution DART+ mass spectra were obtained on Jeol JMS-T100LC spectrometer. The reactions were carried out in a handmade reactor equipped with four 3 W LEDs and a fan.

### *4.2. General procedure for the xanthate transfer group reaction and oxidative addition to aromatic systems.*

In a 4.0 mL glass vial equipped with a stirring bar, were added the corresponding xanthate (0.2 mmol, 2.0 equiv.), the radical acceptor (0.1 mmol, 1.0 equiv.) (alkene 2 or 5; or heterocycle 10-12), $Ir(ppy)_3$ (0.002 mmol, 0.02 equiv.) and DMF (0.4 mL, [0.25 M]). Next, the resulting solution was degassed by three consecutive freeze−pump−thaw cycles and placed under argon atmosphere. Finally, the reaction mixture was stirred and irradiated in a Blue LEDs reactor (12 W) at 24 °C during 12-14 h. After that, the mixture was concentrated in *vacuo* and the product was purified by flash column chromatography on silica gel.

*4.2.1. 1-((ethoxycarbonothioyl)thio)-4-(4-methoxyphenyl)-4-oxobutyl acetate 3:*

Following the general procedure, **3** was obtained as a pale yellow oil (24.9 mg, 70 % yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.94 (m, 8.8 Hz, 2H), 6.94 (d, J = 8.8, 2H), 6.74 (t, J = 6.4 Hz, 1H), 4.55 – 4.74 (m, 2H), 3.88 (s, 3H), 3.09 (td, J = 7.1 Hz, 2.3 Hz, 2H), 2.43 (m, 2H), 2.34 – 2.43 (m, 2H), 2.07 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 210.0, 196.4, 169.4, 163.6, 130.3, 129.6, 113.8, 80.3, 70.3, 55.5, 33.8, 28.7, 20.9, 13.7. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{16}H_{21}O_5S_2$: 357.08304, found: 357.08364.

*4.2.2. ethyl 5-acetoxy-4-((ethoxycarbonothioyl)thio)pentanoate 6a:*

Following the general procedure, **6a** was obtained as a yellow pale oil (20.9 mg, 68% yield) after purification via flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.63 (q, J = 7.1 Hz, 2H), 4.26 (qd, J = 11.4, 5.5 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.07 – 3.92 (m, 1H), 2.04 – 2.23(m, 1H), 2.06 (s, 3H), 2.02 – 1.83 (m, 1H), 1.41 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 212.9, 172.7, 170.8, 70.4, 65.65, 60.73, 48.9, 31.6, 26.0, 20.9, 14.3, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{12}H_{21}O_5S_2$: 309.08304, found: 309.08326.

*4.2.3. Ethyl 4-acetoxy-4-((ethoxycarbonothioyl)thio)butanoate 6b:*

Following the general procedure, **6b** was obtained as a pale yellow oil (16.18 mg, 55% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 95:5).

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.67 (t, J = 6.4 Hz, 1H), 4.64 (dtt, J = 10.7, 7.0, 3.5 Hz, 2H), 4.15 (q, J =7.1 Hz, 2H), 2.45 (d, 2H), 2.35 – 2.19 (m, 2H), 2.08 (s, 3H), 1.42 (t, J = 6.0 Hz, 3H), 1.27 (t, J = 6.0 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 210.0, 172.1, 169.4, 80.0, 70.4, 60.9, 30.3, 29.5, 21.0, 14.3, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{11}H_{19}O_5S_2$: 295.06739, found: 295.06884.

*4.2.4. ethyl 4-((tert-butoxycarbonyl)amino)-4-((ethoxycarbonothioyl)thio)butanoate 6c:*

Following the general procedure, **6c** was obtained as a yellow pale oil (21.1 mg, 58% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.85 (br, 1H), 4.65 (q, J = 7.1 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.87 (dq, J = 9.1, 5.8 Hz, 1H), 3.58 – 3.28 (m, 2H), 2.63 – 2.34 (m, 2H), 2.23 – 1.80 (m, 2H), 1.51 - 1.37 (m, 12H), 1.25 (t, 7.2 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.4, 172.9, 156.0, 79.7, 70.4, 60.7, 51.4, 43.8, 31.7, 28.5, 26.7, 14.3, 13.9. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{15}H_{28}NO_5S_2$: 366.14089, found: 366.14042.

*4.2.5. 3-cyano-1-((ethoxycarbonothioyl)thio)propyl acetate 6d:*

Following the general procedure, **6d** was obtained as a yellow pale oil (19.95 mg, 82% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 95:5). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.67 (t, J = 6.2 Hz, 1H), 4.66 (q, J = 7.2 Hz, 2H), 2.62 – 2.47 (m, 1H), 2.45 – 2.26 (m, 1H), 2.13 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 208.9, 169.2, 118.2, 79.0, 70.6, 30.4, 20.8, 13.9, 13.7. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_9H_{14}NO_3S_2$: 248.04151, found: 248.04165.

*4.2.6. S-(4-cyano-1-(3,4-dimethoxyphenyl)butan-2-yl) O-ethyl carbonodithioate 6e:*

Following the general procedure, **6e** was obtained as a brown oil (16.9 mg, 50% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.87 – 6.70 (m, 3H), 4.65 (q, J = 7.1 Hz, 2H), 4.03 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.12 (dd, J = 14.1, 6.2 Hz, 1H), 2.82 (dd, J = 14.1, 8.5 Hz, 1H), 2.62 – 2.30 (m, 2H), 2.25 – 2.02 (m, 1H), 1.88 (m, 1H), 1.43 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 212.9, 149.0, 148.1, 130.0, 121.3, 119.0, 112.2, 111.2, 70.4, 55.9, 51.1, 40.6, 28.9, 15.2, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{16}H_{22}NO_3S_2$: 340.10411, found: 340.10400.

*4.2.7. tert-butyl (5-(3-chlorophenyl)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl)carbamate 6f:*

Following the general procedure, **6f** was obtained as a yellow pale oil (25.9 mg, 60% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.93 (t, J = 1.9 Hz, 1H). 7.84 (dt, J = 7.8, 1.1 Hz, 1H), 7.55 (ddd, J = 8.0, 2.2, 1.1 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 4.92 (s, 1H), 4.65 (q, J = 7.1 Hz, 2H), 3.88 – 4.02 (m, 1H), 3.55 (dt, J = 12.6, 6.0 Hz, 1H), 3.44 (dt, J = 13.7, 6.4 Hz, 1H), 3.23 – 3.11 (m, 2H), 2.26 (dq, J = 13.7, 7.0 Hz, 1H), 2.09 – 1.94 (m, 1H), 1.45 (s, 9H), 1.45 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 213.2, 197.7, 155.9, 138.2, 135.0, 133.1, 129.9, 128.1, 126.2, 79.6, 70.3, 51.3, 43.8, 35.8, 28.4, 25.5, 13.7. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{19}H_{27}ClNO_4S_2$: 432.10700 , found: 432.10631.

*4.2.8. S-(1-(3,4-dimethoxyphenyl)-5-(4-methoxyphenyl)-5-oxopentan-2-yl) O-ethyl carbonodithioate 6g:*

Following the general procedure, **6g** was obtained as a brown solid (24.19 mg, 54 % yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). m.p.40-42°C **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.89 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 6.84 (s, 1H), 6.80 – 6.79 (m, 2H), 4.59 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.19 – 2.97 (m, 4H), 2.86 (dd, J = 13.9, 8.3 Hz, 1H), 2.19 – 2.17 (m, 1H), 1.99 – 1.86 (m, 1H), 1.39 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 214.2, 197.7, 163.5, 148.8, 147.8, 131.0, 130.3, 129.8, 121.4, 113.7, 112.4, 111.1, 69.9, 55.9, 55.5, 52.3, 41.2, 35.7, 29.7, 27.4, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{23}H_{29}O_5S_2$: 449.14564, found: 449.14524.

*4.2.9. 5-chloro-1-((ethoxycarbonothioyl)thio)-4-oxopentyl acetate 6h:*

Following the general procedure, **6h** was obtained as a yellow pale oil (16.6 mg, 56% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.63 (t, J = 6.4 Hz, 1H), 4.74 – 4.48 (m, 2H), 4.10 (s, 2H), 2.89 – 2.66 (m, 2H), 2.45 – 2.17 (m, 2H), 2.08 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 209.8, 201.0, 169.6, 80.0, 70.5, 48.2, 35.4, 28.0, 21.0, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{10}H_{16}ClO_4S_2$: 299.01785, found: 299.01866.

*4.2.10. 1-((ethoxycarbonothioyl)thio)-4-morpholino-4-oxobutyl acetate 6i:*

Following the general procedure, **6i** was obtained as a yellow pale oil (17.0 mg, 51% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.67 (t, J = 6.4 Hz, 1H), 4.70 – 4.59 (m, 2H), 3.70 – 3.65 (m, 4H), 3.44 (t, J = 4.8 Hz, 2H), 2.50 – 2.40 (m, 2H), 2.36 – 2.26 (m, 2H), 2.08 (s, 3H), 1.42 (t, J = 7.1, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 210.2, 169.8, 169.5, 80.5, 70.5, 67.0, 66.7, 46.0, 42.2, 39.2, 28.9, 21.0, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{13}H_{22}N_{16}O_5S_2$: 336.09327 , found: 336.09394.

*4.2.11. 2-((ethoxycarbonothioyl)thio)-5-morpholino-5-oxopentyl acetate 6j:*

Following the general procedure, **6j** was obtained as a yellow pale oil (19.1 mg, 55% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.65 (q, J = 7.1 H, 2H), 4.37 – 4.23 (m, 2H), 4.07 – 3.97 (m, 1H), 3.69 – 3.64 (m, 4H), 3.64 – 3.59 (m, 1H), 3.45 (t, J = 4.9 Hz, 2H), 2.57 – 2.40 (m, 2H), 2.25 (dddd, J = 14.5, 9.0, 6.6, 4.5 Hz, 1H), 2.07 (s, 3H), 1.92 (dddd, J = 14.4, 10.0, 8.7, 5.8 Hz, 1H), 1.43 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 213.2, 170.8, 170.4, 70.5, 67.0, 66.7, 65.8, 49.4, 46.0, 42.2, 30.2, 26.2, 20.9, 13.9. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{14}H_{24}NO_5S_2$: 350.10959, found: 350.10949.

*4.2.12. O-ethyl S-((5-oxo-1-phenylpyrrolidin-3-yl)methyl) carbonodithioate 8a:*

Following the general procedure, **8a** was obtained as a pale yellow oil (23.6 mg, 80% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.58 (d, J = 7.4 Hz, 2H), 7.31 – 7.43 (m, 2H), 7.16 (t, J = 7.4 Hz, 1H), 4.66 (q, J = 7.1 Hz, 2H), 4.01 (dd, J = 9.8, 7.6 Hz, 1H), 3.65 (dd, J = 10.0, 5.6 Hz, 1H), 3.21 – 3.48 (m, 2H), 2.72 – 3.02 (m, 2H), 2.47 (dd, J = 16.3, 6.1- Hz, 1H), 1.43 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.7, 172.4, 139.0, 128.9, 124.7, 120.0, 70.5, 53.2, 39.5, 38.6, 30.8, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{14}H_{18}NO_2S_2$: 296.07790, found: 296.07803.

*4.2.13. O-ethyl S-((1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl)methyl) carbonodithioate 8b:*

Following the general procedure, **8b** was obtained as a pale yellow oil (19.4 mg, 62% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.45 – 7.69 (m, 2H), 6.97 – 7.16 (m, 2H), 4.66 (q, J = 7.1 Hz, 1H), 3.97 (dd, J = 9.9, 7.5 Hz, 1H), 3.62 (dd, J = 9.9, 5.7 Hz, 1H), 3.22 – 3.47 (m, 2H), 2.69 – 3.00 (m, 2H), 2.45 (dd, J = 16.5, 6.3 Hz, 1H), 1.43 (t, J = 7.1 Hz, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.7, 172.4, 159.6 (d, J = 324 Hz), 135.1, 121.8 (d, J = 8.1 Hz), 115.6 (d, J = 22.5) Hz, 70.5, 53.4, 50.9, 39.5, 38.3, 30.8, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{14}H_{17}FNO_2S_2$: 314.06847, found: 314.06874.

*4.2.14. O-ethyl S-((1-(4-isopropylphenyl)-5-oxopyrrolidin-3-yl)methyl) carbonodithioate 8c:*

Following the general procedure, **8c** was obtained as a pale yellow oil (19.9 mg, 59% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.22 (d, J = 8.6 Hz, 2H), 4.66 (q, J = 7.2 Hz, 2H), 3.99 (dd, J = 9.9, 7.3 Hz, 1H), 3.63 (dd, J = 9.9, 5.2 Hz, 1H), 3.25 – 3.41 (m, 2H), 2.74 – 2.93 (m, 3H), 2.45 (dd, J = 16.5, 6.3 Hz, 1H), 1.43 (t, J = 7.1 Hz, 3H), 1.24 (s, 3H), 1.22 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.8, 172.3, 145.5, 136.7, 126.8, 120.2, 70.5, 53.4, 39.6, 38.5, 33.6, 30.8, 24.0, 23.9, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{17}H_{24}NO_2S_2$: 338.12485, found: 338.12516.

*4.2.15. S-((1-(2,6-dimethylphenyl)-5-oxopyrrolidin-3-yl)methyl) O-ethyl carbonodithioate 8d:*

Following the general procedure, **8d** was obtained as a pale yellow oil (18.1 mg, 62% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.10 (m, 3H), 4.67 (q, J = 7.1 Hz, 2H), 3.73 (dd, J = 10.3, 7.7 Hz, 1H), 3.30 – 3.52 (m, 3H), 2.99 (hept, J = 7.2, 6.8 Hz, 1H), 2.80 (dd, J = 16.9, 8.7 Hz, 1H), 2.44 (dd, J = 16.9, 6.9 Hz, 1H), 2.22 (s, 3H), 2.20 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.8, 172.6, 135.9, 135.3, 128.7, 128.4, 70.5, 53.4, 39.9, 36.8, 32.0, 18.0, 17.8, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{16}H_{22}NO_2S_2$: 324.10920, found: 324.10869.

*4.2.16. S-((1-(3,4-dimethoxyphenethyl)-5-oxopyrrolidin-3-yl)methyl) O-ethyl carbonodithioate 8e:*

Following the general procedure, **8e** was obtained as a pale yellow oil (23.4 mg, 61% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.70 – 6.83 (m, 3H), 4.65 (q, J = 7.0 Hz, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 3.31 – 3.62 (m, 3H), 3.20 (dd, J = 13.7, 6.2 Hz, 1H), 2.95 – 3.12 (m, 2H), 2.80 (t, J = 7.3 Hz, 2H), 2.48 – 2.77 (m, 2H), 2.17 (dd, J = 16.3, 5.6 Hz, 1H), 1.42 (t, J = 7.1, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.9, 173.2, 149.0, 147.7, 130.9, 120.6, 111.8, 111.3, 70.4, 55.9, 52.2, 43.7, 39.8, 37.1, 33.2, 30.9, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{18}H_{26}NO_4S_2$: 384.13032, found: 384.12926.

*4.2.17. O-ethyl S-((1-(furan-2-ylmethyl)-5-oxopyrrolidin-3-yl)methyl) carbonodithioate 8f:*

Following the general procedure, **8f** was obtained as a pale yellow oil (19.8 mg, 66% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 1.9, 0.9 Hz, 1H), 6.32 (dd, J = 3.2, 1.9 Hz, 1H), 6.26 – 6.23 (m, 1H), 4.65 (q, J = 7.2, 2H), 4.45 (s, 2H), 3.51 (dd, J = 10.0, 7.7 Hz, 1H), 3.32 – 3.14 (m, 2H), 3.11 (dd, J = 10.0, 5.5 Hz, 1H), 2.75 – 2.70 (m, 1H), 2.63 (dd, J = 16.8, 8.7 Hz, 1H), 2.25 (dd, J = 16.8, 6.4 Hz, 1H), 1.42 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 213.9, 173.0, 149.8, 142.5, 110.4, 108.5, 70.4, 51.6, 39.8, 39.2, 36.9, 30.8, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{13}H_{18}NO_3S_2$: 300.07281, found: 300.07276.

*4.2.18. S-((1-benzyl-5-oxopyrrolidin-3-yl)methyl) O-ethyl carbonodithioate 8g:*

Following the general procedure, **8g** was obtained as a pale yellow oil (21.4 mg, 69% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.16 – 7.37 (m, 5H), 4.61 (q, J = 7.1 Hz, 2H), 4.30 – 4.52 (m, 2H), 3.39 (dd, J = 10.0, 7.8 Hz, 1H), 3.06 – 3.30 (m, 2H), 3.00 (dd, J = 10.0, 5.6 Hz, 1H), 2.54 – 2.82

(m, 2H), 2.26 (dd, J = 16.8, 6.4 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.9, 173.3, 136.3, 128.9, 128.3, 127.8, 70.5, 51.4, 46.7, 39.9, 37.1, 30.8, 13.9. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{15}H_{20}NO_2S_2$: 310.09355, found: 310.09332.

*4.2.19. S-((1-benzyl-2-oxopiperidin-4-yl)methyl) O-ethyl carbonodithioate 8h:*

Following the general procedure, **8h** was obtained as a pale yellow oil (17.8 mg, 55% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.23 – 7.35 (m, 5H), 4.55 – 4.76 (m, 3H), 4.49 (d, J = 14.7 Hz, 1H), 3.13 – 3.31 (m, 3H), 3.09 (dd, J = 13.8, 6.2 Hz, 1H), 2.67 – 2.81 (m, 1H), 2.07 – 2.32 (m, 2H), 1.97 – 2.06 (m, 1H), 1.47 – 1.65 (m, 1H), 1.44 (t, J = 7.0 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 214.3, 168.5, 137.0, 128.6, 128.1, 127.4, 70.3, 50.0, 46.0, 40.7, 38.0, 32.8, 28.3, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: $C_{16}H_{22}NO_2S_2$: 324.10919, found: 324.10955.

*4.2.20. S-(1-benzyl-2-oxoazocan-5-yl) O-ethyl carbonodithioate 9i:*

Following the general procedure, **9i** was obtained as a pale yellow oil (21.9 mg, 65% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.14 – 7.45 (m, 5H), 4.46 – 4.78 (m, 4H), 3.62 – 3.85 (m, 1H), 3.33 – 3.58 (m, 2H), 2.73 – 2.82 (m, 1H), 2.58 – 2.67 (m, 1H), 2.26 – 2.47 (m, 1H), 1.90 – 2.10 (m, 2H), 1.70 – 1.89 (m, 3H), 1.42 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 213.7, 173.7, 137.5, 128.6, 128.3, 127.5, 69.8, 48.4, 48.2, 46.3, 33.8, 32.4, 31.8, 28.0, 13.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{17}H_{24}NO_2S_2$: 338.12484, found: 338.12386.

*4.2.21. 2-(1H-indol-2-yl)acetonitrile 13a:*

Following the general procedure, **13a** was obtained as a brown solid (9.9 mg, 64% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). m.p. 96-98 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 7.9, 1.0, 1H), 8.17 (s, 1H), 7.35 (dd, J = 8.2, 1.0 Hz, 1H), 7.21 (ddd, J = 8.2, 7.1, 1.3 Hz, 1H), 7.13 (ddd, J = 8.0, 7.1, 1.1 Hz, 1H), 6.48 (dq, J = 2.1, 1.0 Hz, 1H), 3.92 (d, J = 1.0, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 136.7, 128.3, 125.9, 122.9, 120.7, 120.7, 116.4, 111.1, 103.0, 17.8. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for : $C_{10}H_9N_2$: 157.07657, found: 157.07688.

*4.2.22. ethyl 2-(1H-indol-2-yl)acetate 13b:*

Following the general procedure, **13b** was obtained as a brown solid (4.7 mg, 23% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). m.p 28-31 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.47 (dd, J = 7.9, 1.0 Hz, 1H), 7.08 (ddd, J = 8.2, 7.1, 1.3 Hz, 1H), 7.01 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 6.28 (dd, J = 2.0, 1.0 Hz, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.76 (d, J = 0.9 Hz, 2H), 1.23 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 170.8, 136.6, 130.7, 128.5, 121.9, 120.3, 120.0, 110.9, 102.0, 61.5, 34.1, 14.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for : $C_{12}H_{14}NO_2$: 204.10245, found: 204.10221.

*4.2.23. diethyl 2-(1H-indol-2-yl)-2-methylmalonate 13c:*

Following the general procedure, **13c** was obtained as a yellow pale solid (8.6 mg, 30% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.57 (dd, J = 7.8, 1.0, 1H), 7.37 (dd, J = 8.1, 1.0 Hz, 1H), 7.18 (ddd, J = 8.2, 7.0, 1.3 z, 1H), 7.08 (ddd, J = 8.0, 7.1, 1.1 Hz, 1H), 6.47 (dd, J = 2.0, 0.9 Hz, 1H), 4.25 (q, J = 7.1 Hz, 4H), 1.95 (s, 3H), 1.27 (t, J = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 170.5, 136.4, 134.9, 127.7, 122.4, 120.7, 119.9, 111.2, 101.5, 62.4, 54.5, 21.4, 14.1. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for : $C_{16}H_{20}NO_4$: 290.13923, found: 290.13982.

*4.2.24. diethyl 2-(1H-indol-2-yl)malonate 13d:*

Following the general procedure, **13d** was obtained as a brown oil (17.8 mg, 65% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 95:5). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.58 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.19 (t, J = 8.3 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.50 (s, 1H), 4.91 (s, 1H), 4.33 – 4.18 (m, 4H), 1.29 (t, J = 7.2 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 167.3, 136.7, 128.8, 127.8, 122.5, 120.7, 120.1, 111.3, 103.4, 62.5, 51.8, 14.1. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{15}H_{18}NO_4$ : 276.12358, found: 276.12307.

*4.2.25. 2-(1H-pyrrol-2-yl)acetonitrile 14a:*

Following the general procedure, **14a** was obtained as a yellow pale oil (6.3 mg, 63% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.26 (br, 1H), 6.78 (td, J = 2.7, 1.5 Hz, 1H), 6.19 – 6.16 (m, 1H), 6.14 (tdt, J = 2.6, 1.6, 0.8 Hz, 1H), 3.77 (d, J = 0.8 Hz, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 118.8, 118.6, 116.9, 109.3, 108.3, 16.9, **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_6H_7N_2$ : 107.06092 , found: 107.06091.

*4.2.26. ethyl 2-(1H-pyrrol-2-yl)acetate 14b:*

Following the general procedure, **14b** was obtained as a yellow pale oil (8.0 mg, 52% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 95:5). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 6.76 (td, J = 2.7, 1.5 Hz, 1H), 6.14 (q, J = 2.9 Hz, 1H), 6.02 (dddt, J = 3.3, 2.4, 1.6, 0.8 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.67 (d, J = 0.8, 2H), 1.28 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 171.4, 123.5, 117.8, 108.4, 107.4, 61.2, 33.4, 14.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_8H_{12}NO_2$: 154.08680, found: 154.08699.

*4.2.27. diethyl 2-(1H-pyrrol-2-yl)malonate 14c:*

Following the general procedure, **14c** was obtained as a yellow pale oil (14.1 mg, 63% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 95:5). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.05 (br, 1H), 6.92 – 6.71 (m, 1H), 6.25 – 5.99 (m, 2H), 4.75 (s, 1H), 4.22 (qd, J = 7.1, 2.1 Hz, 4H), 1.28 (t, J = 7.1 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 167.8, 121.7, 118.9, 108.7, 108.4, 62.2, 51.2, 14.1. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{11}H_{16}NO_4$: 226.10793, found: 226.10757.

*4.2.28. 2-(2-phenylimidazo[1,2-a]pyridin-3-yl)acetonitrile 15a:*

Following the general procedure, **15a** was obtained as a brown oil (20.9 mg, 90% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.07 (d, *J*=6.9, 1H), 7.74 – 7.66 (m, 3H), 7.57 – 7.48 (m, 2H), 7.48 – 7.40 (m, 1H), 7.34 (ddd, *J* = 9.1, 6.8, 1.2 Hz, 1H), 4.17 (s, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 145.5, 145.2, 133.2, 129.1, 128.7, 125.5, 123.0, 118.1, 115.1, 113.5, 107.9, 14.0. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{15}H_{12}N_3$: 234.10312, found: 234.10395.

*4.2.29. ethyl 2-(2-phenylimidazo[1,2-a]pyridin-3-yl)acetate 15b:*

Following the general procedure, **15b** was obtained as a yellow pale oil (15.6 mg, 56% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR:** (300 MHz, $CDCl_3$) δ 8.06 (d, J = 6.8 Hz, 1H), 7.77 (d, J = 7.7, 2H), 7.62 (d, J = 9.1 Hz, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.37 – 7.28 (m, 1H), 7.22 – 7.12 (m, 1H), 6.81 (t, J = 6.9 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.98 (s, 1H), 1.21 (t, J = 7.1Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 169.5. 145.1, 144.7, 134.1, 128.8, 128.1, 124.7, 123.9, 117.8, 113.1, 112.6, 61.8, 31.0, 14.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{17}H_{17}N_2O_2$: 281.12900, found: 281.12914.

*4.2.30. diethyl 2-(2-phenylimidazo[1,2-a]pyridin-3-yl)malonate 15c:*

Following the general procedure, **15c** was obtained as a brown solid (23.9 mg, 68 % yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 8:2). m.p. 165-168. °C. **$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.37 (d, J = 7.2 Hz, 1H), 7.78 (d, J = 6.8 Hz, 2H), 7.69 (d, J = 9.0 Hz, 1H), 7.52 (t, J = 7.2 Hz, 2H), 7.45 (d, J = 7.1 Hz, 1H), 7.31 – 7.23 (m, 1H), 6.85 (td, J = 6.9, 1.2 Hz, 1H), 5.42 (s, 1H), 4.26 (qd, J = 7.2, 1.7 Hz, 4H), 1.28 (td, J = 7.2, 1.2 Hz, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 166.8, 146.5, 145.9, 133.9, 129.2, 128.8, 128.4, 126.4, 125.3, 117.7, 112.1, 112.0, 62.6, 49.3, 14.1. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{20}H_{21}N_20_4$: 353.15013, found: 353.14971.

*4.2.31. 2-(6-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)acetonitrile 15d:*

Following the general procedure, **15d** was obtained as a brown solid (15.9 mg, 61% yield) after purification via flash column chromatography using silica gel (Hex:AcOEt; 7:3). m.p. 160-163 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.63 (d, J = 9.2, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.8, 2H), 7.17 (dd, J = 9.3, 1.6 Hz, 1H), 4.12 (s, 2H), 2.42 (s, 6H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 144.9, 144.5, 138.5, 130.3, 129.8, 128.7, 123.4, 120.7, 117.3, 117.3, 115.2, 107.3, 21.4, 18.6, 14.1. **HRMS** (DART+) (m/z) [M + H]+: calc. for $C_{17}H_{16}N_3$: 262.13442 , found: 262.13377.

*4.2.32. ethyl 2-(6-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)acetate 15e:*

Following the general procedure, **15e** was obtained as a brown solid (19.9 mg, 66 % yield) after purification via flash column chromatography using silica gel (Hex:AcOEt; 7:3). m.p. 95-100 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dt, J = 2.0, 1.1 Hz, 1H), 7.72 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 9.1 Hz, 1H), 7.28 (d, J = 7.8 Hz, 2H), 7.09 (dd, J = 9.2, 1.7 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 4.01 (s, 2H), 2.41 (s, 3H), 2.37 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 169.7, 144.4, 144.1, 137.8, 129.5, 128.6, 127.8, 126.1, 122.2, 121.5, 116.9, 112.6, 61.7, 31.0, 21.4, 18.6, 14.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{19}H_{21}N_2O_2$: 309.16030, found: 309.15950.

*4.2.33. 2-(6-chloro-2-phenylimidazo[1,2-a]pyridin-3-yl)acetonitrile 15f:*

Following the general procedure, **15f** was obtained as a brown solid (17.3 mg, 65% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). m.p. 140-144 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 2.0, 0.9 Hz, 1H), 7.71 – 7.65 (m, 3H), 7.55 – 7.49 (m, 2H), 7.47 – 7.43 (m, 1H), 7.30 (dd, J = 9.5, 1.9 Hz, 1H), 4.14 (s, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 146.3, 144.0, 132.8, 129.2, 129.0, 128.7, 127.0, 121.9, 121.0, 118.6, 114.7, 108.6, 14.1. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for: $C_{15}H_{11}ClN_3$ 268.06415, found: 268.06472.

*4.2.34. ethyl 2-(6-chloro-2-phenylimidazo[1,2-a]pyridin-3-yl)acetate 15g:*

Following the general procedure, **15g** was obtained as a brown solid (10.3 mg, 33% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 9:1). m.p. 105-108 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.20 (dd, J = 1.9, 0.9 Hz, 1H), 7.84 – 7.78 (m, 2H), 7.62 (dd, J = 9.5, 0.9 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 7.21 (dd, J = 9.5, 2.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.03 (s, 2H), 1.31 (t, J = 7.1 Hz, 3H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 169.2, 145.8, 143.6, 133.7, 128.9, 128.7, 128.4, 126.1, 121.9, 120.9, 118.1, 113.8, 62.0, 31.0, 14.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for: $C_{17}H_{16}ClN_3O_2$ 315.09003, found: 315.09028.

*4.2.35. 2-(6-chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)acetonitrile 15h:*

Following the general procedure, **15h** was obtained as a brown solid (19.9 mg, 66 % yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). m.p. 165-168. °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 1.9, 0.9 Hz, 1H), 7.66 (dd, J = 9.6, 0.9 Hz, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.6 Hz, 2H), 7.31 (dd, J = 9.6, 1.9 Hz, 1H), 4.12 (s, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 145.1, 144.0, 135.1, 131.2, 129.7, 129.3, 127.1, 122.1, 120.8, 118.5, 114.3, 108.5, 13.9. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{15}H_{10}Cl_2N_3$: 302.02518, found: 302.02525.

*4.2.36. 1-morpholino-2-(2-phenylimidazo[1,2-a]pyridin-3-yl)ethan-1-one 15i:*

Following the general procedure, **15i** was obtained as a brown oil (12.5 mg, 39% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 5:5). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.27 (dt, J = 6.9, 1.2 Hz, 1H), 7.56 – 7.62 (m, 3H), 7.39 – 7.44 (m, 2H), 7.31 – 7.36 (m, 1H), 7.14 – 7.18 (m, 1H), 6.80 (td, J = 6.8, 1.2 Hz, 1H), 4.08 (s, 2H), 3.49 (s, 4H), 3.21 – 3.27 (m, 2H), 3.15 (dd, J = 5.6, 3.7 Hz, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 166.73, 145.2, 143.3, 134.3, 128.8, 128.6, 128.1, 124.8, 117.4, 113.8, 112.5, 66.8, 66.4, 46.4, 42.4, 29.9. **HRMS** (ESI) (m/z) $[M + H]^+$: calc. for $C_{19}H_{20}N_3O_2$: 322.1555, found: 322.1553.

*4.2.37. 1-(4-methoxyphenyl)-2-(2-phenylimidazo[1,2-a]pyridin-3-yl)ethanone 15j:*

Following the general procedure, **15j** was obtained as brown oil (18.2 mg, 53% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 6:4). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.91 (m, 3H), 7.68 – 7.64 (m, 3H), 7.45 (t, J = 7.4 Hz, 2H), 7.42 – 7.33 (m, 1H), 7.19 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.89 (d, J = 8.9 Hz, 2H), 6.80 (td, J = 6.8, 1.0 Hz, 1H), 3.86 (s, 3H), 4.68 (s, 2H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 193.4**,** 164.2, 145.3, 144.8, 134.7, 131.0, 128.8, 128.8, 128.0, 124.5, 124.1, 117.7, 114.1, 112.4, 55.7, 34.6. **HRMS** (DART+) (m/z) $[M + H]^+$: calc. for $C_{22}H_{19}N_2O_2$: 343.14465, found: 343.14429.

*4.2.38. (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 2-(2-phenylimidazo[1,2-a]pyridin-3-yl)acetate 15k:*

Following the general procedure, **15k** was obtained as a yellow pale oil (21.8 mg, 56% yield) after purification *via* flash column chromatography using silica gel (Hex:AcOEt; 7:3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.12 (dt, J = 7.2, 1.2 Hz, 1H), 7.86 – 7.81 (m, 2H), 7.68 (dt, J = 9.0, 1.1 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.40 (d, J = 7.4 Hz, 1H), 7.25 – 7.21 (m, 1H), 6.87 (td, J = 6.8, 1.2 Hz, 1H), 4.74 (td, J = 10.9, 4.5 Hz, 1H), 4.11 – 3.98 (m, 2H), 2.00 (dtd, J = 12.0, 3.6, 1.8 Hz, 1H), 1.73 – 1.59 (m, 2H), 1.52 – 1.42 (m, 1H), 1.38 – 1.28 (m, 1H), 1.09 – 0.91 (m, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.87 – 0.81 (m, 1H), 0.79 (d, J = 7.0 Hz, 3H), 0.66 (d, J = 7.0 Hz, 3H).

**$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 169.3, 145.1, 144.7, 134.2, 128.8, 128.0, 126.3, 124.6, 123.8, 117.7, 113.4, 112.5, 76.0, 47.2, 40.9, 34.2, 31.5, 31.3, 26.4, 23.4, 22.1, 20.8, 16.3. **HRMS** ($DART^+$) (m/z) $[M + H]^+$: calc. for $C_{25}H_{31}N_2O_2$: 391.23855, found: 391.23825.

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20. The redox potentials were determined by cyclic voltammetry using a glassy-carbon electrode in a 10mM solution of [(n-Bu)4N]PF6, as supporting electrolyte, in degassed HPLC grade acetonitrile; using Fc+/Fc as internal standard under nitrogen atmosphere. Scan rate: 100 mVs-1, saturated calomel electrode used as reference electrode and platinum as counter electrode.

### Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.