A Practical Route to 2,3-Di-/1,2,3-Trisubstituted Indolizines from α-EWG Ketene *S*,*S*-Acetals and Their Application in Bis(1-indolizinyl)methane Synthesis

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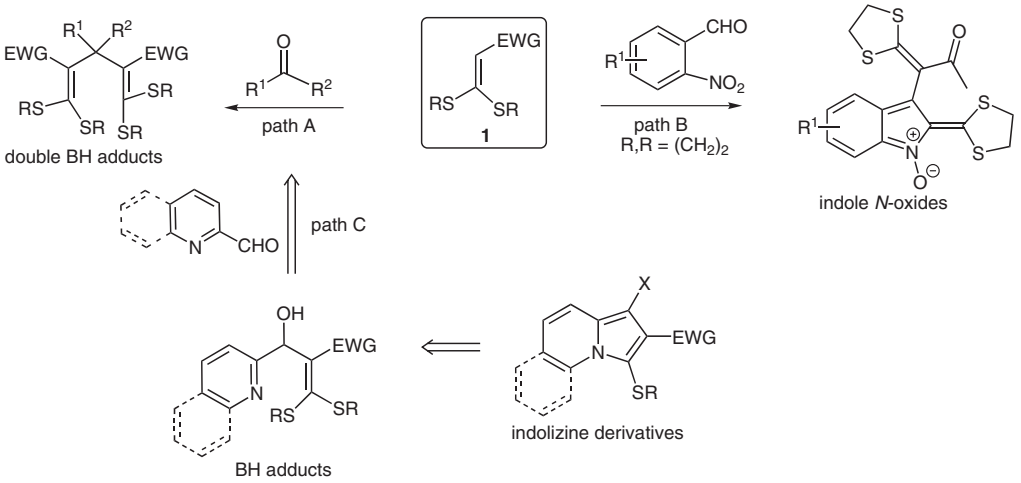
Abstract: An easy synthesis of 2,3-di-/1,2,3-trisubstituted indolizines has been developed via a formal [3+2] annulation of α-EWG ketene *S*,*S*-acetals with 2-pyridine-/2-quinolinecarbaldehyde. The disubstituted products are formed via an intramolecular aza-Michael addition and subsequent elimination of acetic acid, followed by desulfenylation assisted by acetic acid, whereas the trisubstituted products are obtained via a similar conjugate addition followed by elimination of alkanethiol. This strategy has been applied to the synthesis of bis(1-indolizinyl)methanes by the condensation of a 2,3-disubstituted indolizine with aldehydes/ketones in the presence of a catalytic amount of $BF_3{\cdot}OEt_2$.

Key words: indolizines, α-EWG ketene *S*,*S*-acetals, bis(1-indolizinyl)methanes, annulation, condensation

Indolizines are important heterocycles broadly found in naturally occurring and biological molecules[1,2] and used in the area of therapy[3] and dyestuffs.[1,4] Recently, much attention has been focused on the synthesis of the indolizine structural motif.[5] In general, the synthetic approaches to indolizine derivatives have mainly employed the Scholtz or Tschitschibabin reaction,[6] 1,3-dipolar cycloadditions,[7] and 1,5-dipolar cyclizations.[8] In addition to these procedures, a variety of other methods, including cyclization of the silicon-capped (*Z*)-2-pyridinevinylacetylenes with basic alcohol solutions,[9] reactions of propargylamines or amides with heteroaryl bromides by a catalyzed tandem coupling and cycloisomerization reaction,[10] or Pt(II)-catalyzed cycloisomerization of pyridinepropargylic alcohols and derivatives[11] can also be used. Recently, a new access to 2-substituted or 2,3-disubstituted indolizines starting from the Baylis–Hillman (BH) adducts based on 2-pyridinecarbaldehyde and activated alkenes having no or one β-substituent has been reported.[12] In this regard, although many approaches have been described,[1,5–12] the development of new synthetic methods, especially for the production of polysubstituted indolizines, from readily available starting materials with high selectivity and conversion under mild conditions is highly desired.

α-EWG ketene *S*,*S*-acetals (EWG = electron-withdrawing group) and related compounds are versatile synthons[13] and have found wide application in the synthesis of various carbo-[14] and heterocyclic compounds.[15] In our research on the synthetic applications of α-EWG ketene *S*,*S*-acetals,[16] we recently showed that their α-carbon atom possess a high nucleophility[17–19]and could add to aldehydes or ketones in the presence of Lewis acid via Baylis–Hillman-type reaction[20] to afford the double BH adducts (Scheme 1, Path A).[18] In the case of the reaction with *o*-nitrobenzaldehydes, substituted indole *N*-oxides were formed by the $TiCl_4$-mediated BH reaction and subse-



Scheme 1

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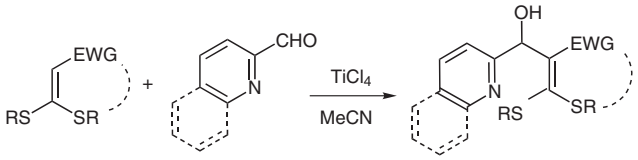
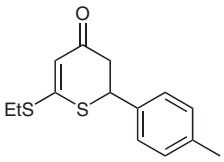
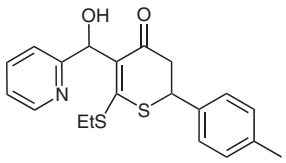
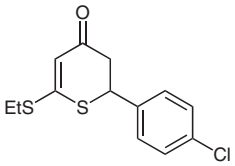
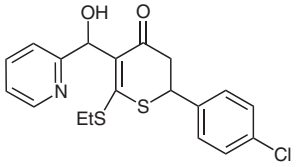
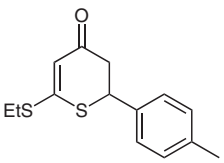
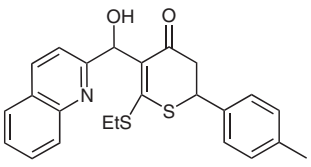
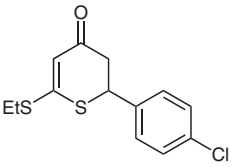
quent cyclization reaction (Scheme 1, Path B).[19] Combining with our previous studies,[16b,e–g,i,k,17–19] in the present work, 2-pyridinecarbaldehyde and 2-quinolinecarbaldehyde were chosen as probes to react with α-EWG ketene *S*,*S*-acetals **1** with the consideration that a formal [3+2] annulation between them would be realizable for the construction of substituted indolizines (Scheme 1, Path C).[12,21] As expected, BH adducts were obtained, catalyzed by $TiCl_4$, in high yields in acetonitrile. Then, the annulation of these new BH adducts was examined in the presence of acetic anhydride, which afforded 2,3-disubstituted and 1,2,3-trisubstituted indolizines in good yields. It is noteworthy that the efficiency of this methodology was demonstrated by the straightforward synthesis of bis(1-indolizinyl)methanes via the condensation of 2,3-disubstituted indolizines with various aldehydes or ketones in the presence of catalytic amount of $BF_3{\cdot}OEt_2$. Here, we wish to present these experimental results and the possible mechanism of the annulation of BH adducts to indolizine derivatives.

The reaction between 3,3-bis(ethylthio)acrylonitrile (**1a**) and 2-pyridinecarbaldehyde (**2A**) was first carried out using $TiCl_4$ as a catalyst in different solvents. The best results were obtained when **1a** was treated with **2A** in

Table 1 BH Reactions between α-EWG Ketene *S*,*S*-Acetals **1** and 2-Pyridine-/2-Quinolinecarbaldehyde **2**



1 **2** **3**

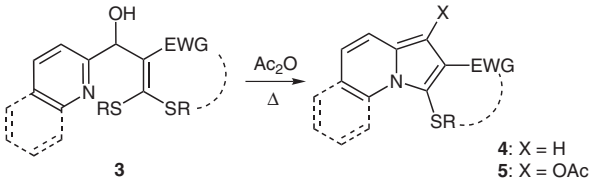
Entry[a]	Substrate **1**	R	EWG	Aldehyde **2**	Product **3**	Time (h)	Yield[b] (%)
1	**1a**	Et	CN	**2A**	**3Aa**	2	85
2	**1b**	*n*-Bu	CN	**2A**	**3Ab**	4	83
3	**1c**	Bz	CN	**2A**	**3Ac**	5	78
4	**1d**	Et	MeCO	**2A**	–[c]	5	–
5	**1e**			**2A**	**3Ae** 	6	73
6	**1f**			**2A**	**3Af** 	7	55
7	**1a**	Et	CN	**2B**	**3Ba**	4	79
8	**1b**	*n*-Bu	CN	**2B**	**3Bb**	5	67
9	**1c**	Bz	CN	**2B**	**3Bc**	7	69
10	**1e**			**2B**	**3Be** 	10	66
11	**1f**			**2B**	–[c]	10	–

[a] **1**:**2**:$TiCl_4$ = 1:1:1.1, r.t.
[b] Isolated yields after silica column chromatography.
[c] Unidentified mixture.

acetonitrile in the presence of $TiCl_4$ for two hours at room temperature, thus providing the desired 3,3-bis(ethylthio)-2-[hydroxyl(pyridin-2-yl)methyl]acrylonitrile (**3Aa**) in 85% yield (Table 1, entry 1). Under identical conditions, α-EWG ketene *S*,*S*-acetals **1b–d** were selected to react with **2A**. It is clear from Table 1 that the reactions of **1b** and **1c** proceeded smoothly to afford the corresponding adducts **3Ab** and **3Ac** (entries 2 and 3), while **1d** gave an unidentified mixture (entry 4). The cyclic α-EWG ketene *S*,*S*-acetals **1e** and **1f**, which could be readily prepared according to our previous report,[16g] were also tested as nucleophiles to react with **2A**. To our delight, the desired BH adducts **3Ae** and **3Af** were obtained in good yields (entries 5 and 6). Similarly, BH adducts **3Ba–Bc** and **3Be** were successfully synthesized in 66–79% yields from the reaction of **1a–c** and **1e** with 2-quinolinecarbaldehyde (**2B**) (entries 7–10), respectively. In the case of the reaction of **1f** and **2B**, a complex mixture was obtained (entry 11).

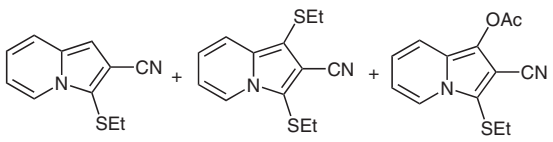
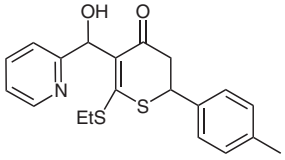
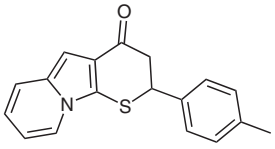
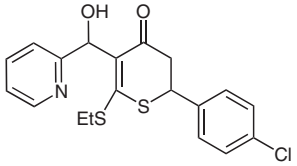
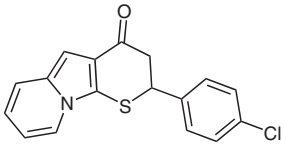
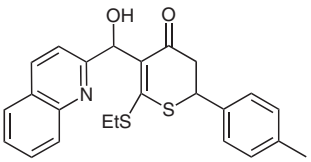
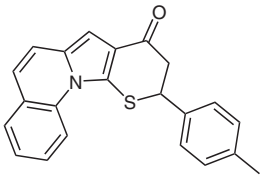
Then, the annulation of adducts **3** were tested. Kaye and co-workers reported that the annulation of acetylated BH adducts derived from activated alkenes having no β-sub-

Table 2 Annulations of BH Adducts **3**



3

4: X = H
5: X = OAc

Entry	Substrate **3**	R	EWG	Product **4** or **5**	X	Time (h)	Yield [a] (%)
1[b]	**3Aa**	Et	CN	 **4Aa** **4Aa'** **5Aa**	H (**4Aa**) SEt (**4Aa′**) OAc (**5Aa**)	6	31 47 5
2[c]	**3Aa**	Et	CN	**4Aa**	H	6	88
3[d]	**3Ab**	*n*-Bu	CN	**4Ab**	H	6	77
4[c]	**3Ac**	Bz	CN	**4Ac**	H	7	79
5[c]	**3Ae** 			**4Ae** 	H	5	66
6[c]	**3Af** 			**4Af** 	H	5	55
7[d]	**3Ba**	Et	CN	**5Ba**	OAc	7	87
8[d]	**3Bb**	*n*-Bu	CN	**5Bb**	OAc	7	79
9[d]	**3Bc**	Bz	CN	**5Bc**	OAc	9	83
10[d]	**3Be** 			**4Be** 	H	5	82

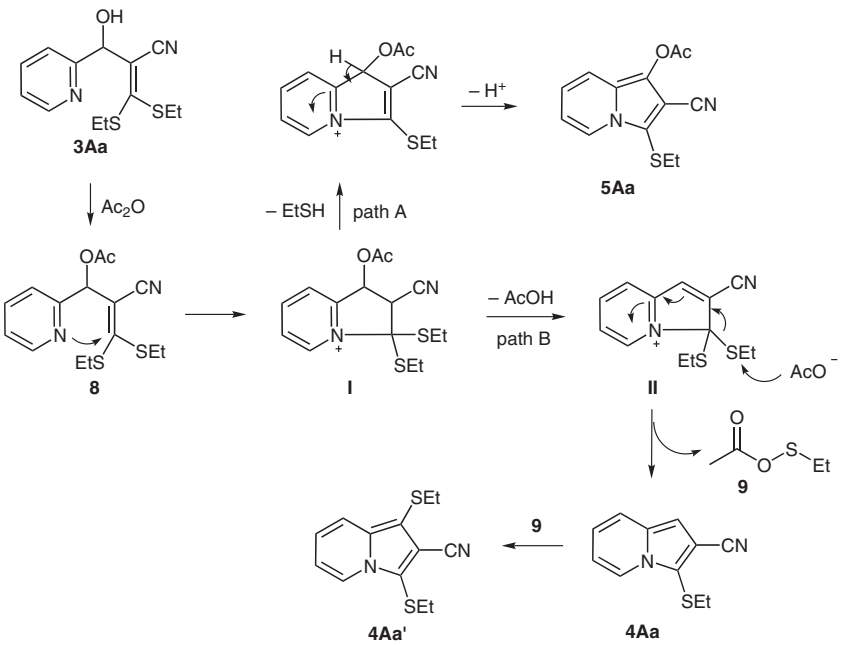
[a] Isolated yields after silica column chromatography.
[b] **3Aa** (1.0 mmol), Ac_2O (0.4 mL), DMF (4.0 mL), 120 °C.
[c] **3** (1.0 mmol), Ac_2O (1.0 mL), 50 °C for 2 h, then heating to 120 °C.
[d] **3** (1.0 mmol), Ac_2O (1.0 mL), 50 °C for 1 h, then heating to 80 °C.

stituent with 2-pyridinecarbaldehyde afforded the 2-substituted indolizine derivatives via an intramolecular Michael-type addition and elimination of acetic acid sequence.[12a,b] Interestingly, in our experiment, when the BH adduct **3Aa** bearing β,β-dialkylthio groups was treated with acetic anhydride at 120 °C in DMF for six hours, three indolizine derivatives, namely 3-(ethylthio)indolizine-2-carbonitrile (**4Aa**), 1,3-bis(ethylthio)indolizine-2-carbonitrile (**4Aa′**), and 2-cyano-3-(ethylthio)indolizin-1-yl acetate (**5Aa**), were obtained in 31%, 47%, and 5% isolated yields, respectively (Table 2, entry 1). Of these products, the minor product **5Aa** should be reasonably explained to have formed via an intramolecular aza-Michael addition of the pyridine nitrogen on the ketene dithioacetal moiety of **3Aa** and subsequent elimination of ethanethiol. However, the favorable formation of **4Aa** and **4Aa′** seemed unexpected. It was found that the products of this reaction strongly depended on the reaction time. By prolonging the reaction time, the yield of **4Aa′** was increased along with the decrease of **4Aa**. By optimizing the reaction conditions, **4Aa** could be obtained in 88% yield as the sole product when the reaction was performed in neat acetic anhydride first at 50 °C for two hours to allow the complete acetylation of **3Aa** and then at 120 °C for an additional four hours (entry 2).

Subsequently, the annulation reactions of other BH adducts **3** obtained in our work were carried out under the optimized reaction conditions (entry 2). As shown in Table 2, all the reactions proceeded smoothly to afford two kinds of substituted indolizine derivatives **4** and **5** depending on the substrates. 2,3-Disubstituted indolizines **4Ab** and **4Ac** were obtained in high yields from **3Ab** and **3Ac** (entries 3 and 4). Thiopyrano-fused indolizines **4Ae** and **4Af** were also formed from the corresponding BH adducts **3Ae** and **3Af** (entries 5 and 6). In contrast, lower temperature was enough to complete the reaction for the substrates **3Ba–Bc** and **3Be** derived from 2-quinolinecarbaldehyde. Thus, heating a mixture of **3** and acetic anhydride under 80 °C furnished 1,2,3-trisubstituted indolizine derivatives **5Ba–Bc** in 79–87% yields (entries 7–9), while 2,3-disubstituted product **4Be** was formed in the case of **3Be** as substrate (entry 10).

On the basis of the above results, a possible mechanism for the formations of **4**, **4′**, and **5** is proposed as depicted in Scheme 2 using annulation of **3Aa** as an example. This pathway begins with the formation of **8** by acetylation of **3Aa** in the presence of acetic anhydride. An intramolecular aza-Michael addition of the pyridine nitrogen on the ketene dithioacetal moiety gives intermediate **I**. Then, two different elimination pathways (Path A and Path B) would lead to the formation of two kinds of indolizine derivatives **4Aa** and **5Aa**. Path A involves an elimination of ethanethiol from **I** followed by deprotonation to afford **5Aa**. Correspondingly, in the path B, the elimination of acetic acid from **I** first provides intermediate **II**. Subsequently, desulfenylation of **II** assisted by acetic acid in the aromatization step yields **4Aa** along with the formation of unstable ethanesulfenyl acetate (**9**) (a potent sulfenylating agent). Thus, the formation of **4Aa′** should be due to the electrophilic substitution at the 1-position of **4Aa** by **9**. In 1993, Hamel and co-workers reported a nonreductive method for the desulfenylation of 3-indolyl sulfides using trifluoroacetic acid as catalyst.[22] Compared to their work, the desulfenylation of **II** is believed to be assisted by acetic acid in our experiment.

As presented above, we have found a novel method to rapidly synthesize 1,2-di- and 1,2,3-trisubstituted indolizine derivatives **4** and **5** via formal [3+2] annulation of α-EWG ketene dithioacetals and 2-pyridine-/2-quinolinecarbaldehyde. With the readily available 2,3-disubstituted indoliz-



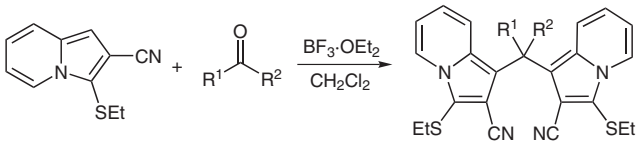
Scheme 2 Proposed mechanism for the construction of indolizines **4** and **5** from **3**

ine derivatives **4** in hand, we then explored their utility in the synthesis of bis(1-indolizinyl)methanes.

Bis- and tris(heteroaryl)methanes and analogues are often present as natural compounds in foods and beverages,[23] and are broadly used in cyanine dyes[24] and in the synthesis of various heterocyclic macromolecules.[25] Despite the fact that indolizine is one of the basic nitrogen heterocyclic compounds with 10π electron system, the synthesis and utility of triheteroarylmethanes based on indolizine are much less recognized in comparison to its isomer indole, which has found extensive application in triheteroarylmethane synthesis.[26] In 2001, Tominaga et al. synthesized bis(1-indolizinyl)methane derivatives by the condensation of 3,7-di- or 2,3,7-trisubstituted indolizines with aldehydes in the presence of excess trifluoroacetic acid to be used as the precursors of oxidative chromogenic reagents in clinical analysis.[27] In our work, indolizines **4** bearing 2,3-disustituted groups provide a novel subject for the regiospecific synthesis of bis(1-indolizinyl)methanes.

Initially, the condensation of indolizine **4Aa** with piperonaldehyde (**6a**) was tried in the presence of $BF_3{\cdot}OEt_2$ at room temperature in dichloromethane. To our delight, the reaction produced bis(1-indolizinyl)piperonylmethane (**7a**) in quantitative isolated yield within two hours. Interestingly, when a catalytic amount of $BF_3{\cdot}OEt_2$ (10 mol%) was used, the desired product **7a** was also obtained in 99% yield (Table 3, entry 1).

Table 3 Condensation Reaction between Indolizine **4Aa** with Aldehydes/Ketone **6**



4Aa **6** **7**

Entry[a]	6	R^1	R^2	Time (h)	Product 7	Yield (%)[b]
1	**6a**	3,4-$(OCH_2O)C_6H_3$	H	2	**7a**	99
2	**6b**	4-$MeOC_6H_4$	H	4	**7b**	96
3	**6c**	Ph	H	8	**7c**	95
4	**6d**	4-ClC_6H_4	H	10	**7d**	93
5	**6e**	4-$CHOC_6H_4$	H	12	**7e1**	87
6	**6e**	4-$CHOC_6H_4$	H	18	**7e2**	92[c]
7	**6f**	2-furyl	H	4	**7f**	96
8	**6g**	2-thienyl	H	6	**7g**	99
9	**6h**	Et	H	5	**7h**	89
10	**6i**	Me	Me	24	**7i**	75[d]

[a] $BF_3{\cdot}OEt_2$ (10 mol%), r.t.
[b] Isolated yield after silica gel chromatography.
[c] **4Aa**:**6e** = 2:1.
[d] Large excess of **6i** was used.

Encouraged by the above results, we then investigated the scope of the reaction. A variety of aldehydes and ketones were thus selected as electrophiles to react with **4Aa** under the identical conditions and the experimental results are listed in Table 3. All aldehydes tested, including arylaldehydes with electron-donating groups (entries 1 and 2) and electron-withdrawing groups (entries 4 and 5), heteroaromatic aldehydes (entries 7 and 8), and aliphatic aldehydes (entry 9) could readily react with **4Aa** to afford the condensation products, bis(1-indolizinyl)arylmethanes **7a**–**e1**, bis(1-indolizinyl)heteroarylmethanes **7f** and **7g**, and bis(1-indolizinyl)alkanes **7h**, respectively, in excellent yields. Notably, 2-fold excess of **4Aa** with respect to phthalaldehyde (**6e**) was enough to afford the double-condensation adduct **7e2** in 92% yield (entry 6). In comparison to the reactions with aldehydes (entries 1–9), the reaction with ketone (entry 10) afforded the corresponding bis(1-indolizinyl)alkane **7i** in slightly lower yield. The structure of **7** was further established by X-ray diffraction studies of **7d** (Figure 1).[28] All the above results indicated the extraordinarily high reactivity of **4Aa** toward carbonyl electrophiles. It is noteworthy that the alkylthio group at the 3-position of indolizines **4** can act as either an activating group to promote the C–C coupling reaction as mentioned or as a protecting group[29] (easily displaced[30] or removed by Raney Ni desulfurization) to make the electrophilic substitution reaction occur only at the 1-position of the indolizine core. Thus, an efficient and regiospecific synthesis of bis(1-indolizinyl)methanes has been provided.

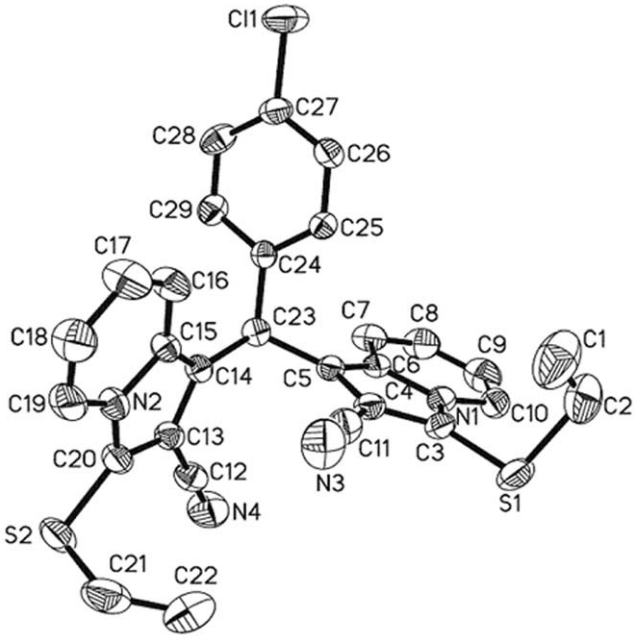


Figure 1 Molecular structure of **7d**

In summary, we have demonstrated an easy and practical method for the synthesis of 2,3-disubstituted indolizines **4** and 1,2,3-trisubstituted indolizines **5** via formal [3+2] annulation of α-EWG ketene dithioacetals and 2-pyridine-/

2-quinolinecarbaldehyde. The formation of indolizines **4** and **5** involve two pathways: 1) an intramolecular aza-Michael addition of the pyridine nitrogen and elimination of acetic acid, followed by a desulfenylation with the assistance of acetate acid to afford **4**; and 2) a similar aza-Michael addition followed by the elimination of alkanethiol to give **5**. Indolizines **4** and **5**, including their thiopyrano-fused analogues, are expected to be useful building blocks in organic synthesis. Thus, **4Aa** has been successfully applied to the synthesis of bis(1-indolizinyl)methanes **7** by the condensation of **4Aa** with a broad range of aldehydes and ketones in the presence of catalytic amount of $BF_3{\cdot}OEt_2$.

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. Petroleum ether (PE) used refers to the fraction boiling in the range 60–90 °C. The products were purified by column chromatography over silica gel (300–400 mesh). All reactions were monitored by TLC, which was performed on precoated aluminum sheets of silica gel 60 (F_{254}). Melting points were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at r.t. on a Varian spectrometer operating at 500 MHz and 125 MHz, respectively, using TMS as internal standard. Chemical shifts are in δ (ppm). IR spectra (KBr) were recorded on a Magna-560 FTIR spectrophotometer in the range of 400–4000 cm^{-1}. Mass spectra were measured on an Agilient 1100 LCMsD spectrometer. Elemental analyses were obtained on a VarioEL analyzer. X-ray diffraction was measured on a Siemens P4 diffractometer. Compounds **1** were prepared according to our previous reports.[16g,h]

3,3-Bis(ethylthio)-2-[hydroxy(pyridin-2-yl)methyl]acrylonitrile (3Aa); Typical Procedure

To a solution of 3,3-bis(ethylthio)acrylonitrile (**1a**; 692 mg, 4.0 mmol) and 2-pyridinecarbaldehyde (**2A**; 471 mg, 4.4 mmol) in MeCN (10.0 mL) was added $TiCl_4$ (0.49 mL, 4.4 mmol) at 0 °C. The reaction was allowed to proceed at 0 °C and was complete in 4 h. The above mixture was quenched with sat. aq $NaHCO_3$ (10 mL). After filtration, the filtrate was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with H_2O (20 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography on silica gel to give **3Aa** (952 mg, 85%) as colorless crystals (eluent: Et_2O–PE, 1:3); mp 96–98 °C.

IR (KBr): 3197, 2985, 2208, 1521, 1418 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.0 Hz, 3 H), 1.35 (t, *J* = 7.0 Hz, 3 H), 2.93–3.14 (m, 4 H), 5.62 (d, *J* = 5.0 Hz, 1 H), 6.14 (d, *J* = 5.0 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.30 (dd, *J* = 5.0, 7.0 Hz, 1 H), 7.73 (dd, *J* = 8.0, 7.0 Hz, 1 H), 8.60 (d, *J* = 5.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.0, 15.5, 29.5, 29.9, 70.8, 116.3, 120.9, 122.0, 123.6, 137.6, 148.4, 154.9, 156.8.

ES-MS: *m*/*z* = 281 [M + 1]$^+$.

Anal. Calcd for $C_{13}H_{16}N_2OS_2$: C, 55.68; H, 5.75; N, 9.99. Found: C, 55.82; H, 5.61; N, 10.01.

3,3-Bis(butylthio)-2-[hydroxy(pyridin-2-yl)methyl]acrylonitrile (3Ab)

Colorless oil.

IR (KBr): 3417, 2960, 2209, 1484, 1592 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.94 (t, *J* = 7.5 Hz, 3 H), 1.39–1.46 (m, 4 H), 1.56–1.65 (m, 4 H), 2.89–3.12 (m, 4 H), 6.12 (s, 1 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 7.27 (dd, *J* = 7.5, 5.0 Hz, 1 H), 7.71 (t, *J* = 7.5 Hz, 1 H), 8.57 (d, *J* = 5.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.3 (2 C), 20.4, 20.5, 30.4, 30.8, 33.3, 33.8, 69.4, 108.5, 114.7, 119.9, 122.1, 136.0, 146.9, 154.4, 155.4.

ES-MS: *m*/*z* = 337 [M + 1]$^+$.

Anal. Calcd for $C_{17}H_{24}N_2OS_2$: C, 60.68; H, 7.19; N, 8.32. Found: C, 60.92; H, 7.44; N, 8.12.

3,3-Bis(benzylthio)-2-[hydroxy(pyridin-2-yl)methyl]acrylonitrile (3Ac)

Colorless crystals; mp 80–82 °C.

IR (KBr): 2923, 2227, 1484, 1234 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.14–4.25 (m, 4 H), 5.36 (br s, 1 H), 5.90 (s, 1 H), 6.48 (d, *J* = 7.5 Hz, 1 H), 7.21 (dd, *J* = 7.5, 5.5 Hz, 1 H), 7.24–7.35 (m, 10 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 8.51 (d, *J* = 5.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 39.5, 39.9, 70.9, 115.8, 120.9, 123.4, 123.9, 128.0, 128.1, 128.9 (2 C), 129.2 (4 C), 129.5 (2 C), 136.3, 136.8, 137.4, 148.2, 153.4, 156.3.

ES-MS: *m*/*z* = 405 [M + 1]$^+$.

Anal. Calcd for $C_{23}H_{20}N_2OS_2$: C, 68.29; H, 4.98; N, 6.92. Found: C, 68.39; H, 4.90; N, 6.95.

6-(Ethylthio)-5-[hydroxy(pyridin-2-yl)methyl]-2-(*p*-tolyl)-2,3-dihydrothiopyran-4-one (3Ae)

Yellow crystals; 100 °C (dec.).

IR (KBr): 3346, 2924, 1659, 1471 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.0 Hz, 3 H), 2.35 (s, 3 H), 2.88 (dd, *J* = 16.5, 3.0 Hz, 1 H), 3.04–3.10 (m, 2 H), 3.16 (d, *J* = 14.0 Hz, 1 H), 4.64 (dd, *J* = 14.0, 3.0 Hz, 1 H), 5.08 (br s, 1 H), 6.16 (s, 1 H), 7.14 (t, *J* = 6.5 Hz, 1 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 7.48 (d, *J* = 8.0 Hz, 1 H), 7.66 (t, *J* = 7.0 Hz, 1 H), 8.53 (d, *J* = 4.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 20.4, 26.8, 44.2, 45.3, 70.6, 119.3, 121.0, 126.7 (2 C), 129.0 (2C), 130.6, 133.2, 135.7, 135.8, 137.9, 147.3, 161.0, 191.4.

ES-MS: *m*/*z* = 372 [M + 1]$^+$.

Anal. Calcd for $C_{20}H_{21}NO_2S_2$: C, 64.66; H, 5.70; N, 3.77. Found: C, 64.96; H, 5.91; N, 3.65.

2-(4-Chlorophenyl)-6-(ethylthio)-5-[hydroxyl(pyridin-2-yl)methyl]-2,3-dihydrothiopyran-4-one (3Af)

Yellow crystals; 130 °C (dec.).

IR (KBr): 3347, 2922, 1655, 1470 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.0 Hz, 3 H), 2.89 (d, *J* = 13.5 Hz, 1 H), 2.97–3.15 (m, 3 H), 4.62 (d, *J* = 13.5 Hz, 1 H), 5.06 (br s, 1 H), 6.14 (s, 1 H), 7.08 (t, *J* = 6.5 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 6.5 Hz, 1 H), 7.65 (t, *J* = 7.0 Hz, 1 H), 8.52 (d, *J* = 4.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.9, 27.9, 44.9, 45.7, 71.2, 120.2, 121.5, 122.1, 129.2 (2 C), 129.5 (2 C), 134.8, 135.8, 136.4, 148.0, 148.5, 161.7, 191.9.

ES-MS: *m*/*z* = 392 [M + 1]$^+$.

Anal. Calcd for $C_{19}H_{18}ClNO_2S_2$: C, 58.22; H, 4.63; N, 3.57. Found: C, 58.51; H, 4.71; N, 3.56.

3,3-Bis(ethylthio)-2-[hydroxy(quinolin-2-yl)methyl]acrylonitrile (3Ba)

Yellow crystals; mp 92–94 °C.

IR (KBr): 3147, 2925, 2229 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.5 Hz, 3 H), 1.38 (t, *J* = 7.5 Hz, 3 H), 1.59 (br s, 1 H), 2.95–3.14 (m, 3 H), 3.16–3.18 (m, 1 H), 6.29 (s, 1 H), 7.27 (d, *J* = 8.5 Hz, 1 H), 7.59 (t, *J* = 8.0 Hz, 1 H), 7.77 (t, *J* = 8.0 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 8.14 (d, *J* = 8.0 Hz, 1 H), 8.19 (d, *J* = 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.0, 15.5, 29.7, 30.0, 71.2, 116.2, 118.2, 121.7, 127.3, 127.8, 128.2, 129.3, 130.5, 138.1, 146.4, 155.3, 156.5.

ES-MS: *m*/*z* = 331 [M + 1]$^+$.

Anal. Calcd for $C_{17}H_{18}N_2OS_2$: C, 61.79; H, 5.49; N, 8.48. Found: C, 61.93; H, 5.66; N, 8.44.

3,3-Bis(butylthio)-2-[hydroxy(quinolin-2-yl)methyl]acrylonitrile (3Bb)

Colorless oil.

IR (KBr): 3420, 2953, 2220, 1480 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.5 Hz, 3 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 1.41–1.50 (m, 4 H), 1.59–1.69 (m, 4 H), 2.91–3.15 (m, 4 H), 6.15 (br s, 1 H), 6.28 (s, 1 H), 7.25 (d, *J* = 8.5 Hz, 1 H), 7.57 (t, *J* = 6.5 Hz, 1 H), 7.73–7.76 (m, 1 H), 7.83 (d, *J* = 7.5 Hz, 1 H), 8.11 (d, *J* = 8.5 Hz, 1 H), 8.17 (d, *J* = 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8 (2 C), 21.8, 22.0, 31.9, 32.3, 35.0, 35.3, 71.2, 116.2, 118.2, 121.0, 127.2, 127.8, 128.1, 129.1, 130.4, 138.0, 146.3, 156.3, 156.5.

ES-MS: *m*/*z* = 387 [M + 1]$^+$.

Anal. Calcd for $C_{21}H_{26}N_2OS_2$: C, 65.25; H, 6.78; N, 7.25. Found: C, 65.49; H, 6.92; N, 7.35.

3,3-Bis(benzylthio)-2-[hydroxy(quinolin-2-yl)methyl]acrylonitrile (3Bc)

Light yellow crystals; mp 92–94 °C.

IR (KBr): 3360, 2920, 2227, 1480 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.15–4.28 (m, 4 H), 6.01 (br s, 1 H), 6.42 (d, *J* = 8.5 Hz, 1 H), 7.24–7.36 (m, 11 H), 7.55 (t, *J* = 8.0, 6.0 Hz, 1 H), 7.71 (t, *J* = 8.0, 6.0 Hz, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.93 (d, *J* = 8.5 Hz, 1 H), 8.05 (d, *J* = 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 39.6. 39.9, 71.2, 115.9, 118.2, 123.3, 127.3, 127.8, 128.0, 128.1, 128.2, 129.0, 129.2, 129.5 (2 C), 129.7 (4 C), 130.4 (2 C), 136.3, 136.8, 137.9, 146.2, 154.2, 155.9.

ES-MS: *m*/*z* = 455 [M + 1]$^+$.

Anal. Calcd for $C_{27}H_{22}N_2OS_2$: C, 71.33; H, 4.88; N, 6.16. Found: C, 71.49; H, 4.85; N, 6.14.

6-(Ethylthio)-5-[hydroxy(quinolin-2-yl)methyl]-2-(*p*-tolyl)-2,3-dihydrothiopyran-4-one (3Be)

Yellow crystals; mp 115 °C (dec.).

IR (KBr): 3141, 2928, 1670, 1451 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 8.0 Hz, 3 H), 2.37 (s, 3 H), 2.94 (t, *J* = 17.0, 2.0 Hz, 1 H), 2.98–3.11 (m, 2 H), 3.21 (t, *J* = 17.0 Hz, 1 H), 4.65 (d, *J* = 14.0 Hz, 1 H), 5.65 (d, *J* = 6.5 Hz, 1 H), 6.38 (d, *J* = 6.5 Hz, 1 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 7.52 (t, *J* = 6.5, 2.5 Hz, 1 H), 7.70 (t, *J* = 8.5, 7.0 Hz, 1 H), 7.80 (d, *J* = 8.5 Hz, 1 H), 8.10 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8, 20.2, 26.6, 43.9, 45.2, 69.6, 117.2, 125.1, 126.3, 126.5 (2 C), 128.0 (2 C), 128.4 (2 C), 128.7 (2 C), 130.0, 133.0, 135.6, 137.7, 145.4, 160.0, 190.7.

ES-MS: *m*/*z* = 422 [M + 1]$^+$.

Anal. Calcd for $C_{24}H_{23}NO_2S_2$: C, 68.38; H, 5.50; N, 3.32. Found: C, 68.69; H, 5.78; N, 3.29.

2-Cyano-3,3-bis(ethylthio)-1-(pyridin-2-yl)allyl Acetate (8)

A solution of **3Aa** (280 mg, 1.0 mmol) in Ac_2O (2 mL) was stirred at 50 °C for 2.0 h. The resulting mixture was poured into ice-water, basified with aq K_2CO_3, and extracted with CH_2Cl_2 (2 × 5 mL). The combined organic extracts were washed with H_2O (10 mL), dried (Na_2SO_4), filtered, and concentrated to give **8** (318 mg, 99%) as colorless crystals; mp 80–81 °C.

IR (KBr): 2974, 2212, 1736, 1565, 1219 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.5 Hz, 3 H), 1.32 (t, *J* = 7.5 Hz, 3 H), 2.22 (s, 3 H), 2.88–3.00 (m, 2 H), 3.02–3.11 (m, 2 H), 7.11 (s, 1 H), 7.23–7.25 (m, 1 H), 7.51 (d, *J* = 8.0 Hz, 1 H), 7.71–7.75 (m, 1 H), 8.59 (d, *J* = 4.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.9, 15.5, 21.2, 29.8, 30.1, 74.1, 116.2, 116.5, 121.2, 123.6, 137.2, 149.9, 156.3, 158.5, 169.7.

ES-MS: *m*/*z* = 323 [M + 1]$^+$.

Anal. Calcd for $C_{15}H_{18}N_2O_2S_2$: C, 55.87; H, 5.63; N, 8.69. Found: C, 55.99; H, 5.76; N, 8.65.

Compounds 4 and 5; Typical Procedures

Conditions A; 3-(Ethylthio)indolizine-2-carbonitrile (4Aa)

A solution of **3Aa** (2.8 g, 10 mmol) in Ac_2O (10 mL) was stirred at 50 °C for 2 h to allow the complete acetylation of **3Aa** (TLC monitoring). Then, the above mixture was heated to 120 °C for an additional 4 h. The mixture was poured into ice-water, basified with aq K_2CO_3, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with H_2O (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel to give **4Aa** (1.78 g, 88%) as a light yellow oil (eluent: Et_2O–PE, 1:40).

IR (KBr): 2957, 2231, 1463 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 3 H,), 2.75 (q, *J* = 7.5 Hz, 2 H), 6.76 (s, 1 H), 6.77 (d, *J* = 7.0 Hz, 1 H), 6.90 (dd, *J* = 9.0, 7.0 Hz, 1 H), 7.39 (d, *J* = 9.0 Hz, 1 H), 8.37 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4, 30.6, 103.7, 106.3, 113.7, 116.3, 118.3, 120.1, 120.8, 124.1, 135.0.

ES-MS: *m*/*z* = 203 [M + 1]$^+$.

Anal. Calcd for $C_{11}H_{10}N_2S$: C, 65.32; H, 4.98; N, 13.85. Found: C, 65.59; H, 4.89; N, 13.84.

1,3-Bis(ethylthio)indolizine-2-carbonitrile (4Aa′)

Light yellow oil.

IR (KBr): 2957, 2231, 1500 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17–1.24 (m, 6 H), 2.75–2.82 (m, 4 H), 6.84 (t, *J* = 7.0 Hz, 1 H), 7.01–7.04 (m, 1 H), 7.69 (d, *J* = 9.0 Hz, 1 H), 8.42 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4 (2 C), 30.7, 31.5, 106.2, 112.7, 114.3, 115.2, 119.0, 119.2, 122.0, 124.4, 138.2.

ES-MS: *m*/*z* = 263 [M + 1]$^+$.

Anal. Calcd for $C_{13}H_{14}N_2S_2$: C, 59.51; H, 5.38; N, 10.68. Found: C, 60.39; H, 5.06; N, 10.74.

3-(Butylthio)indolizine-2-carbonitrile (4Ab)

Light yellow oil.

IR (KBr): 2957, 2231, 1464 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.5 Hz, 3 H), 1.40–1.53 (m, 4 H), 2.73 (t, *J* = 7.5 Hz, 2 H), 6.76 (s, 1 H), 6.78 (d, *J* = 7.0 Hz, 1 H), 6.90 (dd, *J* = 9.0, 7.0 Hz, 1 H), 7.40 (d, *J* = 9.0 Hz, 1 H), 8.36 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9, 21.9, 32.1, 36.1, 103.7, 106.1, 113.6, 116.3, 118.8, 120.1, 120.8, 124.0, 135.0.

ES-MS: *m*/*z* = 231 $[M + 1]^+$.

Anal. Calcd for $C_{13}H_{14}N_2S$: C, 67.79; H, 6.13; N, 12.16. Found: C, 67.93; H, 6.29; N, 12.10.

3-(Benzylthio)indolizine-2-carbonitrile (4Ac)
Light yellow crystals; mp 78–80 °C.

IR (KBr): 2958, 2232, 1334 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92 (s, 2 H), 6.55 (t, *J* = 7.0 Hz, 1 H), 6.72 (s, 1 H), 6.82 (t, *J* = 7.5 Hz, 1 H), 6.95 (d, *J* = 7.5 Hz, 2 H), 7.11–7.16 (m, 3 H), 7.32 (d, *J* = 9.0 Hz, 1 H), 7.97 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.3, 103.6, 106.3, 109.7, 113.0, 115.6, 117.3, 119.5, 120.6, 123.6, 127.5, 128.5, 128.7, 128.9, 134.8, 137.0.

ES-MS: *m*/*z* = 265 $[M + 1]^+$.

Anal. Calcd for $C_{16}H_{12}N_2S$: C, 72.70; H, 4.58; N, 10.60. Found: C, 72.86; H, 4.50; N, 10.64.

2-(*p*-Tolyl)-2,3-dihydrothiopyrano[3,2-*b*]indolizin-4-one (4Ae)
Yellow crystals; mp 118–120 °C.

IR (KBr): 2926, 1670, 1451 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 3.09 (d, *J* = 16.0 Hz, 1 H), 3.36 (dd, *J* = 16.0, 13.0 Hz, 1 H), 4.89 (d, *J* = 13.0 Hz, 1 H), 6.57–6.59 (m, 1 H), 6.64–6.66 (m, 1 H), 6.93 (s, 1 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 7.0 Hz, 1 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 7.52 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.1, 46.1, 48.6, 96.8, 111.5, 117.1, 119.9, 120.9, 122.2, 123.8, 126.3 (2 C), 128.6 (2 C), 132.6, 134.1, 137.6, 190.7.

ES-MS: *m*/*z* = 292 $[M + 1]^+$.

Anal. Calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77. Found: C, 74.25; H, 4.96; N, 4.86.

2-(4-Chlorophenyl)-2,3-dihydrothiopyrano[3,2-*b*]indolizin-4-one (4Af)
Yellow crystals; mp 187–189 °C.

IR (KBr): 2927, 1658, 1451 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.10 (d, *J* = 17.0 Hz, 1 H), 3.32 (dd, *J* = 17.0, 13.0 Hz, 1 H), 4.88 (d, *J* = 12.0 Hz, 1 H), 6.59 (t, *J* = 7.0 Hz, 1 H), 6.67 (t, *J* = 6.5 Hz, 1 H), 6.92 (s, 1 H), 7.35–7.43 (m, 5 H), 7.52 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 45.9, 47.9, 96.9, 111.7, 117.3 (2 C), 119.9, 120.9, 122.1, 127.8 (2 C), 128.1 (2 C), 132.7, 133.5, 135.6, 190.1.

ES-MS: *m*/*z* = 314 $[M + 1]^+$.

Anal. Calcd for $C_{17}H_{12}ClNOS$: C, 65.07; H, 3.85; N, 4.46. Found: C, 65.33; H, 3.72; N, 4.45.

Conditions B; 2-Cyano-1-(ethylthio)pyrrolo[1,2-*a*]quinolin-3-yl Acetate (5Ba)
A solution of **3Ba** (1.65 g, 5.0 mmol) in Ac_2O (5 mL) was stirred at 50 °C for 1 h to allow the complete acetylation of **3Ba** monitored by TLC. Then, the above mixture was heated to 80 °C for an additional 6 h. The mixture was poured into ice-water, basified with aq K_2CO_3, and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with H_2O (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel to give **5Ba** (1.35 g, 87%) as colorless crystals (eluent: Et_2O–PE, 1:40); mp 88–90 °C.

IR (KBr): 2924, 2227, 1753, 1200 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.0 Hz, 3 H), 2.43 (s, 3 H), 2.93 (q, *J* = 7.0 Hz, 2 H), 7.11 (d, *J* = 9.0 Hz, 1 H), 7.14 (d, *J* = 9.0 Hz, 1 H), 7.45 (t, *J* = 7.0 Hz, 1 H), 7.58 (t, *J* = 7.0 Hz, 1 H), 7.66 (d, *J* = 7.0 Hz, 1 H), 9.90 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.5, 20.6, 32.0, 103.4, 110.0, 113.6, 114.9, 118.0, 121.1, 122.9, 125.9, 126.0 (2C), 128.7, 129.4, 135.3, 168.6.

ES-MS: *m*/*z* = 311 $[M + 1]^+$.

Anal. Calcd for $C_{17}H_{14}N_2O_2S$: C, 65.79; H, 4.55; N, 9.03. Found: C, 65.93; H, 4.48; N, 9.09.

2-Cyano-3-(ethylthio)indolizin-1-yl Acetate (5Aa)
Colorless crystals; mp 116–118 °C.

IR (KBr): 2961, 2926, 2361, 1774, 1368 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.5 Hz, 3 H), 2.41 (s, 3 H), 2.79 (q, *J* = 7.5 Hz, 2 H), 6.74 (t, *J* = 7.0 Hz, 1 H), 6.86 (dd, *J* = 9.5 Hz, 1 H), 7.25 (dd, *J* = 9.5, 4.5 Hz, 1 H), 8.33 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4, 20.6, 30.8, 100.2, 113.5, 113.9, 115.4, 117.1, 120.3, 123.4, 125.9, 127.7, 168.7.

ES-MS: *m*/*z* = 261 $[M + 1]^+$.

Anal. Calcd for $C_{13}H_{12}N_2O_2S$: C, 59.98; H, 4.65; N, 10.76. Found: C, 60.32; H, 4.79; N, 10.70.

1-(Butylthio)-2-cyanopyrrolo[1,2-*a*]quinolin-3-yl Acetate (5Bb)
Colorless crystals; mp 67–69 °C.

IR (KBr): 2957, 2924, 2856, 2231, 1774, 1194 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.42–1.48 (m, 2 H), 1.56–1.62 (m, 2 H), 2.43 (s, 3 H), 2.89 (t, *J* = 7.0 Hz, 2 H), 7.10 (d, *J* = 10.0 Hz, 1 H), 7.13 (d, *J* = 9.0 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.57 (dd, *J* = 8.5, 7.0 Hz, 1 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 9.89 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8, 20.7, 22.0, 31.2, 37.7, 103.0, 113.6, 114.9, 117.9, 121.6, 122.9, 125.8, 125.9, 126.0, 128.7, 129.4 (2 C), 135.3, 168.6.

ES-MS: *m*/*z* = 339 $[M + 1]^+$.

Anal. Calcd for $C_{19}H_{18}N_2O_2S$: C, 67.43; H, 5.36; N, 8.28. Found: C, 67.29; H, 5.41; N, 8.33.

1-(Benzoylthio)-2-cyanopyrrolo[1,2-*a*]quinolin-3-yl Acetate (5Bc)
Light yellow crystals; mp 127–129 °C.

IR (KBr): 2925, 2226, 1745, 1484, 1201 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 4.07 (s, 2 H), 7.03–7.13 (m, 7 H), 7.43 (t, *J* = 7.5 Hz, 1 H), 7.53 (dd, *J* = 8.5, 7.5 Hz, 1 H), 7.63 (d, *J* = 7.5 Hz, 1 H), 9.83 (d, *J* = 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.7, 42.9, 103.5, 113.2, 114.8, 118.0, 123.0, 125.7, 125.9 (2 C), 127.9, 128.7 (4 C), 129.3 (4 C), 135.0, 135.7, 168.6.

ES-MS: *m*/*z* = 373 $[M + 1]^+$.

Anal. Calcd for $C_{22}H_{16}N_2O_2S$: C, 70.95; H, 4.33; N, 7.52. Found: C, 70.63; H, 4.49; N, 7.50.

2-(*p*-Tolyl)-4*H*-thiopyrano[3,2-*b*]benzindolizin-4-one (4Be)
Light yellow crystals; mp 168–170 °C.

IR (KBr): 2923, 2223, 1665, 1460 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 3.10 (d, *J* = 17.0 Hz, 1 H), 3.39 (dd, *J* = 17.0, 14.0 Hz, 1 H), 4.90 (d, *J* = 14.0 Hz, 1 H),

6.94 (d, *J* = 9.5 Hz, 1 H), 7.05 (s, 1 H), 7.20–7.26 (m, 3 H), 7.34 (t, *J* = 7.0 Hz, 1 H), 7.41 (d, *J* = 8.0 Hz, 3 H), 7.58 (d, *J* = 7.0 Hz, 1 H), 8.45 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 46.0, 50.5, 102.1, 117.6 (2 C), 119.8, 121.0, 125.1, 126.2, 127.4, 127.7 (3 C), 128.6, 129.9 (2 C), 133.3, 134.7, 135.1, 139.0, 191.3.

ES-MS: *m*/*z* = 344 $[M + 1]^+$.

Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 76.72; H, 4.81; N, 4.12.

1,1′-[(Benzo[*d*][1,3]dioxol-5-yl)methylene]bis[3-(ethylthio)indolizine-2-carbonitrile] (7a)
Colorless crystals; mp 110 °C (dec.).

IR (KBr): 2923, 2227, 1484, 1234 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 6 H), 2.76 (q, *J* = 7.5 Hz, 4 H), 5.98 (s, 2 H), 6.21 (s, 1 H), 6.72–6.78 (m, 7 H), 6.93 (dd, *J* = 7.5, 2.0 Hz, 2 H), 8.39 (d, *J* = 6.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.3 (2 C), 30.6 (2 C), 40.3, 101.4, 107.0, 108.6, 109.5, 113.7, 115.1 (3 C), 118.1, 118.6 (2 C), 119.0 (3 C), 120.6 (3 C), 122.1, 124.2 (3 C), 133.0, 134.7, 147.1, 148.4.

ES-MS: *m*/*z* = 537 $[M + 1]^+$.

Anal. Calcd for $C_{30}H_{24}N_4O_2S_2$: C, 67.14; H, 4.51; N, 10.44. Found: C, 67.29; H, 4.42; N, 10.39.

1,1′-[(4-Methoxyphenyl)methylene]bis[3-(ethylthio)indolizine-2-carbonitrile] (7b)
Colorless crystals; mp 130 °C (dec.).

IR (KBr): 2920, 2225, 1507 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (t, *J* = 7.0 Hz, 6 H), 2.76 (q, *J* = 7.0 Hz, 4 H), 3.81 (s, 3 H), 6.24 (s, 1 H), 6.71–6.73 (m, 4 H), 6.87 (dd, *J* = 8.0, 4.0 Hz, 4 H), 7.16 (d, *J* = 8.5 Hz, 2 H), 8.39 (dd, *J* = 5.0, 3.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 15.3 (2 C), 30.6 (2 C), 40.0, 55.5, 107.1, 113.6 (2 C), 114.4 (2 C), 115.1 (2 C), 118.5 (4 C), 119.1 (2 C), 120.4 (2 C), 124.1 (2 C), 129.9 (2 C), 132.9 (2 C), 133.1 (2 C), 159.1.

ES-MS: *m*/*z* = 523 $[M + 1]^+$.

Anal. Calcd for $C_{30}H_{26}N_4OS_2$: C, 68.94; H, 5.01; N, 10.72. Found: C, 69.26; H, 5.49; N, 10.78.

1,1′-(Phenylmethylene)bis[3-(ethylthio)indolizine-2-carbonitrile] (7c)
Colorless crystals; 140 °C (dec.).

IR (KBr): 2923, 2227, 1484, 1234 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 6 H), 2.76 (q, *J* = 7.5 Hz, 4 H), 6.30 (s, 1 H), 6.72 (dd, *J* = 6.0, 9.0 Hz, 4 H), 6.84 (dd, *J* = 4.0, 10.0 Hz, 2 H), 7.25–7.27 (m, 2 H), 7.32–7.36 (m, 3 H), 8.39 (dd, *J* = 4.5, 7.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.3 (2 C), 30.6 (2 C), 40.7, 107.1 (2 C), 113.7 (2 C), 115.1 (2 C), 118.1 (2 C), 118.6, 119.0 (2 C), 120.5 (2 C), 124.2 (2 C), 127.7 (2 C), 128.9 (2 C), 129.0 (2 C), 133.1 (2 C), 140.8.

ES-MS: *m*/*z* = 493 $[M + 1]^+$.

Anal. Calcd for $C_{29}H_{24}N_4S_2$: C, 70.70; H, 4.91; N, 11.37. Found: C, 70.99; H, 5.12; N, 11.30.

1,1′-[(4-Chlorophenyl)methylene]bis[3-(ethylthio)indolizine-2-carbonitrile] (7d)
Yellowish crystals; mp 130 °C (dec.).

IR (KBr): 2924, 2227, 1520, 1360 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.0 Hz, 6 H), 2.76 (q, *J* = 7.5 Hz, 4 H), 6.26 (s, 1 H), 6.75–6.77 (m, 4 H), 6.89 (d, *J* = 7.5 Hz, 2 H), 7.18 (d, *J* = 8.5 Hz, 2 H), 7.31 (d, *J* = 8.5 Hz, 2 H), 8.40 (d, *J* = 5.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.3 (2 C), 30.6 (2 C), 40.1, 107.1 (2 C), 113.8 (2 C), 115.1 (2 C), 117.3 (2 C), 118.8 (4 C), 120.8 (2 C), 124.3 (2 C), 129.2 (2 C), 130.3 (2 C), 133.0 (2 C), 133.4, 139.3.

ES-MS: *m*/*z* = 527 $[M + 1]^+$.

Anal. Calcd for $C_{29}H_{23}ClN_4S_2$: C, 66.08; H, 4.40; N, 10.63. Found: C, 66.49; H, 4.58; N, 10.58.

1,1′-[(4-Formylphenyl)methylene]bis[3-(ethylthio)indolizine-2-carbonitrile] (7e1)
Light yellow crystals; mp 156–158 °C.

IR (KBr): 2925, 2227, 1670, 1521 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.5 Hz, 6 H), 2.77 (q, *J* = 7.5 Hz, 4 H), 6.35 (s, 1 H), 6.76 (t, *J* = 8.0, 3.5 Hz, 4 H), 6.91 (t, *J* = 6.0, 4.5 Hz, 2 H), 7.43 (d, *J* = 8.0 Hz, 2 H), 7.86 (d, *J* = 8.0 Hz, 2 H), 8.41 (t, *J* = 7.5, 3.0 Hz, 2 H), 10.03 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4 (2 C), 30.6 (2 C), 40.7, 107.1 (2 C), 113.9 (2 C), 115.0 (2 C), 116.6 (2 C), 118.6 (2 C), 119.1 (2 C), 121.0 (2 C), 124.4 (2 C), 129.7 (2 C), 130.5 (2 C), 133.1 (2 C), 135.7, 147.7, 192.0.

ES-MS: *m*/*z* = 521 $[M + 1]^+$.

Anal. Calcd for $C_{30}H_{24}N_4OS_2$: C, 69.20; H, 4.65; N, 10.76. Found: C, 69.46; H, 4.57; N, 10.72.

1,1′,1″,1‴-[1,4-Phenylenebis(methanetriyl)]tetrakis[3-(ethylthio)indolizine-2-carbonitrile] (7e2)
Colorless crystals; mp 202–204 °C.

IR (KBr): 2926, 2226, 1440, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.0 Hz, 12 H), 2.75 (q, *J* = 7.0 Hz, 8 H), 6.31 (s, 2 H), 6.72–6.78 (m, 8 H), 6.99 (d, *J* = 9.5 Hz, 4 H), 7.22 (s, 4 H), 8.39 (d, *J* = 6.5 Hz, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.3 (4 C), 30.6 (4 C), 40.3 (2 C), 107.1 (4 C), 113.7 (4 C), 115.2 (4 C), 117.7 (4 C), 118.6 (4 C), 119.2 (4 C), 120.7 (4 C), 124.2 (4 C), 129.4 (4 C), 133.1 (4 C), 139.9 (2 C).

ES-MS: *m*/*z* = 907 $[M + 1]^+$.

Anal. Calcd for $C_{52}H_{42}N_8S_4$: C, 68.84; H, 4.67; N, 12.35. Found: C, 69.13; H, 4.79; N, 12.27.

1,1′-(2-Furylmethylene)bis[3-(ethylthio)indolizine-2-carbonitrile] (7f)
Yellowish crystals; mp 130 °C (dec.).

IR (KBr): 2974, 2224, 1330 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 7.0 Hz, 6 H), 2.74 (q, *J* = 7.0 Hz, 4 H), 6.07 (s, 1 H), 6.23 (s, 1 H), 6.40 (s, 1 H), 6.75 (t, *J* = 7.0 Hz, 2 H), 6.81 (dd, *J* = 9.0, 7.0 Hz, 2 H), 7.04 (d, *J* = 9.0 Hz, 2 H), 7.46 (s, 1 H), 8.38 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.6 (2 C), 30.6, 34.6 (2 C), 106.5 (2 C), 109.23 (2 C), 111.0 (2 C), 113.8 (2 C), 115.1, 116.2, 118.5, 118.9 (2 C), 120.9 (2 C), 124.1 (2 C), 132.9 (2 C), 142.5 (2 C), 153.2.

ES-MS: *m*/*z* = 483 $[M + 1]^+$.

Anal. Calcd for $C_{27}H_{22}N_4OS_2$: C, 67.19; H, 4.59; N, 11.61. Found: C, 67.33; H, 4.48; N, 11.66.

1,1′-(2-Thienylmethylene)bis[3-(ethylthio)indolizine-2-carbonitrile] (7g)
Yellowish crystals; 120 °C (dec.).

IR (KBr): 2969, 2226, 1516, 1235 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.0 Hz, 6 H), 2.76 (q, *J* = 7.0 Hz, 4 H), 6.49 (s, 1 H), 6.75–6.89 (m, 5 H), 6.99 (dd, *J* = 5.0, 4.0 Hz, 1 H), 7.06 (d, *J* = 9.0 Hz, 2 H), 2.28 (t, *J* = 5.0 Hz, 1 H), 8.39 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1 (2 C), 29.3 (2 C), 34.8, 105.3, 112.6 (2 C), 113.8, 116.7 (2 C), 117.4, 117.8 (2 C), 119.5 (2 C), 122.9 (2 C), 124.3 (2 C), 125.6 (2 C), 126.0 (2 C), 131.6 (2 C), 143.7.

ES-MS: *m*/*z* = 499 $[M + 1]^+$.

Anal. Calcd for $C_{27}H_{22}N_4S_3$: C, 65.03; H, 4.45; N, 11.23. Found: C, 65.39; H, 4.38; N, 11.32.

1,1′-(Propane-1,1-diyl)bis[3-(ethylthio)indolizine-2-carbonitrile] (7h)

Colorless crystals; 80 °C (dec.).

IR (KBr): 2924, 2226, 1507, 1361 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.0 Hz, 3 H), 1.17 (t, *J* = 7.5 Hz, 6 H), 2.60 (q, *J* = 7.0 Hz, 2 H), 2.73 (q, *J* = 7.5 Hz, 4 H), 4.66 (t, *J* = 8.0 Hz, 1 H), 6.71 (t, *J* = 6.0, 7.5 Hz, 2 H), 6.83–6.85 (m, 2 H), 7.58 (d, *J* = 9.5 Hz, 2 H), 8.32 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.4, 15.3 (2 C), 27.2, 30.5 (2 C), 37.4, 105.7 (2 C), 113.8 (2 C), 116.7 (2 C), 117.5 (2 C), 119.0 (2 C), 119.3 (2 C), 120.3 (2 C), 124.04 (2 C), 132.5 (2 C).

ES-MS: *m*/*z* = 445 $[M + 1]^+$.

Anal. Calcd for $C_{25}H_{24}N_4S_2$: C, 67.53; H, 5.44; N, 12.60. Found: C, 67.32; H, 5.31; N, 12.55.

1,1′-(Propane-2,2-diyl)bis[3-(ethylthio)indolizine-2-carbonitrile] (7i)

Colorless crystals; mp 70–72 °C.

IR (KBr): 2923, 2227, 1484, 1234 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 6 H), 2.15 (s, 6 H), 2.77 (q, *J* = 7.5 Hz, 4 H), 6.63 (d, *J* = 8.5 Hz, 2 H), 6.66 (d, *J* = 6.5 Hz, 2 H), 6.97 (d, *J* = 7.0 Hz, 2 H), 8.38 (d, *J* = 6.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2 (2 C), 30.5 (2 C), 31.7 (2 C), 38.0, 104.9 (2 C), 110.0 (2 C), 113.3 (2 C), 116.6 (2 C), 119.6 (2 C), 119.9 (2 C), 124.3 (2 C), 125.0 (2 C), 131.9 (2 C).

ES-MS: *m*/*z* = 445 $[M + 1]^+$.

Anal. Calcd for $C_{25}H_{24}N_4S_2$: C, 67.53; H, 5.44; N, 12.60. Found: C, 67.81; H, 5.59; N, 12.49.

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