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Radical and Ionic Reactions of Indolizin-1-ols: Synthesis of 3-Arylsulfanyl-, 3-(Tropon-2-yl)- and 3-(Tropolon-5-ylazo)-1-hydroxyindolizines from 3,3-Difluorocyclopropenes

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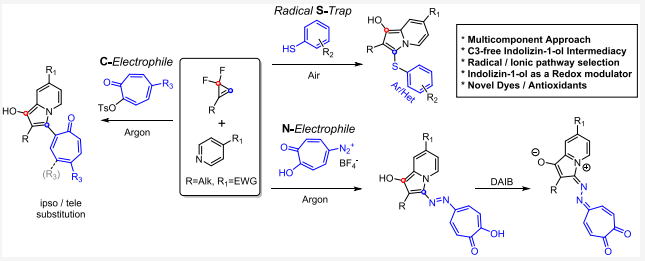
ABSTRACT: An aerobic multicomponent reaction between monoalkyl-3,3-difluorocyclopropenes, pyridines, and arylthiols has been discovered to afford 3-arylsulfanyl-1-hydroxyindolizines. This reaction proceeds via intermediate C3-free indolizin-1-ols, easily forming free radicals in air. In the presence of arylthiols, potent radical traps, incorporation of arylsulfanyl substituent occurs at the C3 position of indolizin-1-ols by radical recombination. On the contrary, in an inert atmosphere, intermediate 1-hydroxyindolizines react with C- and N-electrophiles in a one-pot fashion. Novel, intensively colored 3-(tropon-2-yl)-indolizin-1-ols and high absorption coefficient 3-(tropolon-5-ylazo)-indolizin-1-ol dyes were synthesized in a multicomponent manner in 50−80% yields. The presence of an O-uncapped indolizin-1-ol moiety modulates the redox properties of the whole molecule, facilitating free radical formation, which is susceptible to further transformations. Three such examples were demonstrated: oxidative recyclization of 3-(2-hydroxyphenylsulfanyl)-indolizin-1-ol, auto-oxidation of substituted 3,3′-biindolizine-1,1′-diol, and diacetoxyiodobenzene (DAIB)-mediated dehydrogenation of 3-(tropolon-5-ylazo)-indolizin-1-ol. The latter reaction affords 3-((4,5-dioxocyclohepta-2,6-dien-1-ylidene)hydrazono)-3*H*-indolizin-4-ium-1-olate, a mesomeric betaine, strongly absorbing light on the borders of the visible range and showing a solvatochromic effect.



INTRODUCTION

Indolizines are long-known aromatic heterocycles with bridgehead nitrogen, chemically remarkable for the electron-rich character of their pyrrole subunit. In general, indolizines, not stabilized by electron-withdrawing groups (EWGs), are light and air-sensitive. They are weakly basic and, analogously to indole and pyrrole, are susceptible to C-protonation, which occurs predominantly at C3 and in some cases at C1 position (Figure 1) but not at the nitrogen.[1] Being protonated, the indolizinium cation assembles the pyridinium substructure unit, conserving aromatic stabilization of the ion. Electrophilic attack also takes place at carbon C3 and at C1 to a less extent.

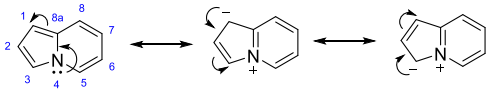


Figure 1. Numeration and resonance structures of indolizine.

In nature, indolizines are represented in their more or less saturated forms, for example, by swainsonine, monomorine, ipalbidine, harmicine, and other alkaloids possessing a broad spectrum of biological activities. Fully saturated indolizine core (azabicyclo[4.3.0]nonane) from the chemical point of view constitutes an ordinary tertiary amine and lacks all of the specific properties of the aromatic indolizine, which does not appear to occur in nature. Being a biostere for a widely common indole, indolizines are in the focus of medicinal chemistry. They show a variety of pharmacological activities[2] including anticancer, anti-inflammatory, antibacterial, antifungal, antioxidant, and analgesic, among others, but nevertheless none of the indolizine-based pharmaceuticals are available to date.[3] A significant segment of the studies on indolizines and their applications lies in the area of materials science such as photophysics and dyes,[4] including biological imaging[5] and dye-sensitized solar cell (DSSC) technology,[6] due to the unique electron distribution and therefore physicochemical properties of the indolizine heterocycle.

Indolizines with an additional π-electron donor in the pyrrole ring represent a special case and are less described due to a lack of developed synthetic methods or stability issues of the products. The notable contemporary works on the synthesis of O-substituted 1-hydroxyindolizines were reported

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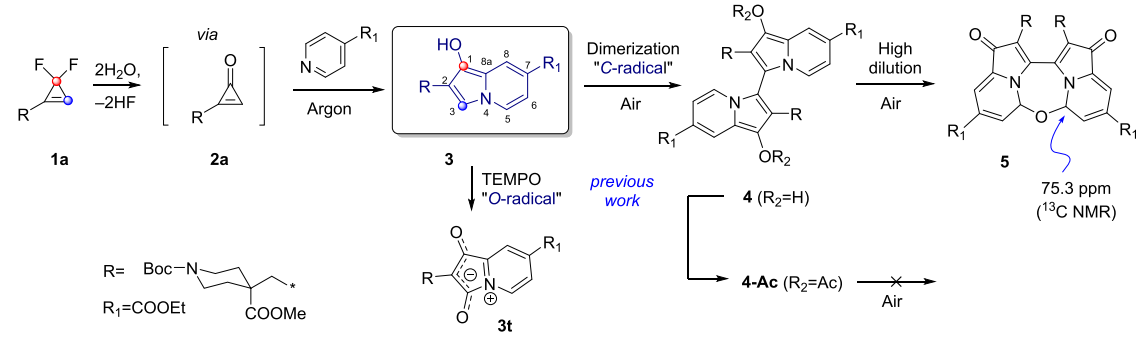
Scheme 1. In Situ Generation of the C3-Free 1-Hydroxyindolizines and Their Oxidative Transformations: Reactions with C- and O-Radicals



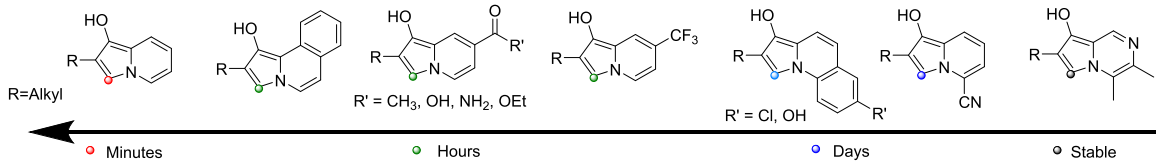


Figure 2. Estimated lifetime in air/C3 radical reactivity of 1-hydroxyindolizines in solution at room temperature (r.t.).

by Gevorgyan and Seregin,[7] and the multicomponent methodology in the field of 1- and 3-aminoindolizines was pioneered by Yan and Liu.[8] As was recognized since the early 1950s, specifically uncapped N*H* or O*H* groups in the pyrrole ring are responsible for heterocycle destabilization.[9] In 1964, in the light of research of diphenylcyclopropenone (first accessed in 1959), Breslow et al. synthesized 2,3-diphenyl-1-indolizinyl *cis*-1,2-diphenyl acrylate by the reaction of diphenylcyclopropenone with pyridine; however, the structure of the product was not elucidated. Years later, Lown and Matsumoto comprehensively studied[10] the reaction of diphenylcyclopropenone with heteroaromatic nitrogen compounds (including pyridines), and only in 1981, a regioisomer of the indolizinol products was reinvestigated and corrected by Wadsworth et al.[11] In 1989, the same authors extensively studied stable and isolable 1- and 3-oxoindolizinyl radicals, bearing two aryl substituents in the pyrrole ring. Remarkable reactivity of the C7 position, which is in conjugation with the OH group, was shown for diarylindolizinols.[12]

Not widely common, O-unprotected 1-hydroxyindolizines, without additional EWGs in the pyrrole ring, are delicate compounds due to high reduction potential and the ability for easy formation of cation radical species.[13] The study of the synthetic potential in hydroxyindolizine chemistry is important as it may open access to the derivatives, potentially interesting in the fields of materials science (*e.g.*, dyes) and medicinal chemistry.

RESULTS AND DISCUSSION

1-Hydroxyindolizines in Radical Reactions. Recently, we have shown that C3-free 1-hydrozyindolizines, generated in situ from 3,3-difluorocyclopropenes and pyridines, are prone to dimerization at the C3 position in air[14] (Scheme 1). This aerobic reaction, affording symmetric 3,3′-biindolizine-1,1′-diol **4**, was interpreted as the intermolecular recombination of 1-hydroxyindolizin-3-yl C-radicals. At the same time, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), being a stable aminoxyl O-radical, acts as a competitive radical trap, leading to a stable heterocyclic mesomeric betaine **3t**, after α,α'-tetramethylpiperidine part dissociation.[15]

We found that dimer **4**, a common unwanted product in the C3-free indolizin-1-ol chemistry, is poorly stable in air. For a better understanding of the yield decrease, associated with the initial dimerization at C3, we decided to track further aerobic transformations of dimer **4**. Its structure was previously determined indirectly, as the aromatic region in ^{1}H NMR spectra (in various conditions) was extremely broad to make reliable conclusions. First, we re-examined and proved the structure of 3,3′-biindolizine-1,1′-diol **4** by NMR spectroscopy of its O-acetylated derivative **4-Ac**. O-Capping completely resolves NMR broadening complications and makes indolizin-1-ols, dimer **4-Ac** in particular, completely air-stable. Noteworthily, such stability and NMR specificity depend on substituents and are more or less common for the class of O-uncapped indolizin-1-ols due to the easy formation of radical species. We discovered that 3,3′-biindolizine-1,1′-diol **4**, after standing in $CDCl_3$ at ambient conditions for a week, afforded an auto-oxidation product [1,3,6]oxadiazepine **5** with the loss of aromaticity in the pyridine rings. This oxadiazepine ring closure was effective only in diluted solutions, as a competing oxidative oligomerization of the starting dimer **4** prevailed at higher concentrations (>10 mg/mL). Being a hemiaminal ether with an interrupted conjugation, [1,3,6]-oxadiazepine **5** was found to be poorly stable and decomposed significantly upon an attempted high-performance liquid chromatography (HPLC) repurification but, nevertheless, was fully characterized in situ.

The aptitude of indolizin-1-ols to a variety of oxidative transformations allowed us to hypothesize that the C3-centered 1-hydroxyindolizin-3-yl radical can also be trapped by the reaction with thiols as a source of S-radicals in aerobic conditions. From structural positions, ease of formation of 1-hydroxyindolizin-3-yl radicals and their dimerization tendency in air depend on the pyridine ring substitution and follow Figure 2.

For example, 1-hydroxyindolizine with an unsubstituted pyridine ring is very reactive, showing the corresponding dimer (3,3′-biindolizine-1,1′-diol) as a major product after less than 20 min and auto-oxidizing further to [1,3,6]oxadiazepine in less than 20 h. On the contrary, pyrrolo[1,2-*a*]pyrazin-8-ol is a

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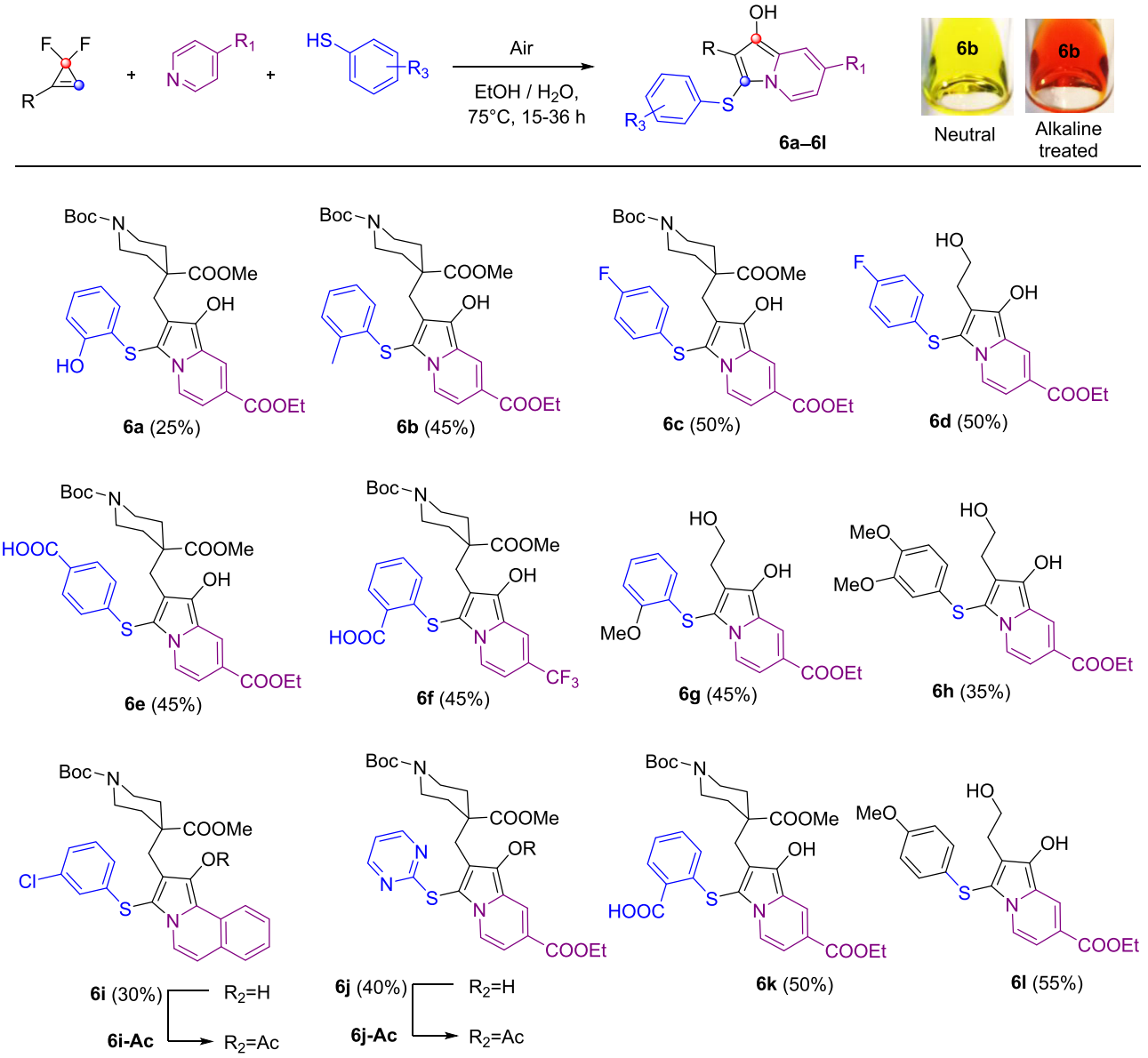

Figure 3. Three-component reaction of 3,3-difluorocyclopropenes, pyridines, and arylthiols.

bench stable compound. For our study, we selected 4-trifluoromethylpyridine, ethylisonicotinate, and isoquinoline as precursors for controllable and moderately C3-reactive indolizin-1-ols. When 1-hydroxyindolizine generation was performed in aerobic conditions in the presence of arylthiols, 3-arylsulfanyl-1-hydroxyindolizines **6a–l** were formed after 15–36 h in 25–55% yield (Figure 3). Experimentally, the synthetic procedure was simple mixing of 3,3-difluorocyclopropene, pyridine, and arylthiol reaction components in a near-stoichiometric ratio and heating the solution in wet ethanol at 70–80 °C in an open vessel. In this multicomponent reaction (MCR), we focused mostly on the variation of the arylthiol component and selected the examples covering electron-donating, electron-neutral, and electron-withdrawing groups at ortho-, meta-, and para-positions of the reagent. Hetero-aromatic pyrimidine-2-thione, existing preferably in the thione tautomeric form, worked analogously to thiophenols and yielded 3-(pyrimidin-2-ylsulfanyl)-1-hydroxyindolizine **6j**. The commonly observed side products, identified in this MCR, were symmetric disulfides (Ar–S–S–Ar), expectedly.

Except for almost colorless π-extended 1-hydroxypyrrolo-[2,1-*a*]isoquinoline **6i**, most of the 3-arylsulfanyl-1-hydroxyindolizines **6a–l** were yellow, showing an absorption band $\lambda \sim 415$ nm on the short-wave border of the visible spectral range. In aqueous (aq) alkali, a reversible bathochromic shift was observed due to the transition into the red-orange indolizin-1-olate anionic form. On the contrary, O-acetylation of **6j** shifted the absorption maximum ~35 nm hypsochromically, resulting in almost colorless 3-(pyrimidin-2-ylsulfanyl)-1-acetoxyindolizine **6j-Ac**.

NMR sample preparation was tedious and required optimization of the concentration of the *OH*-uncapped 3-arylsulfanyl-1-hydroxyindolizines **6a–l** to overcome signal broadening complication. Time after dissolution also played an important role, and sharper signals were observed after >15 h at room temperature (see the Supporting Information, pp S43 and S48). Typically, upon heating in dimethyl sulfoxide (DMSO)-d_6, ^{1}H NMR signals of indolizine ring and the closest to heterocycle exocyclic CH_2 groups' protons ($-CH_2-CH_2-$OH and $-COO-CH_2-CH_3$) showed strong and reversible

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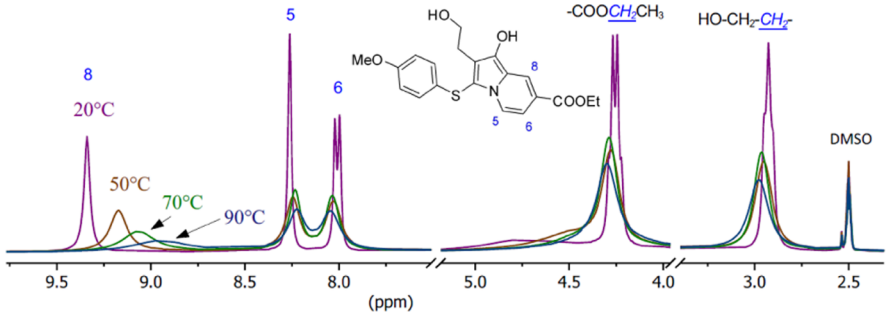
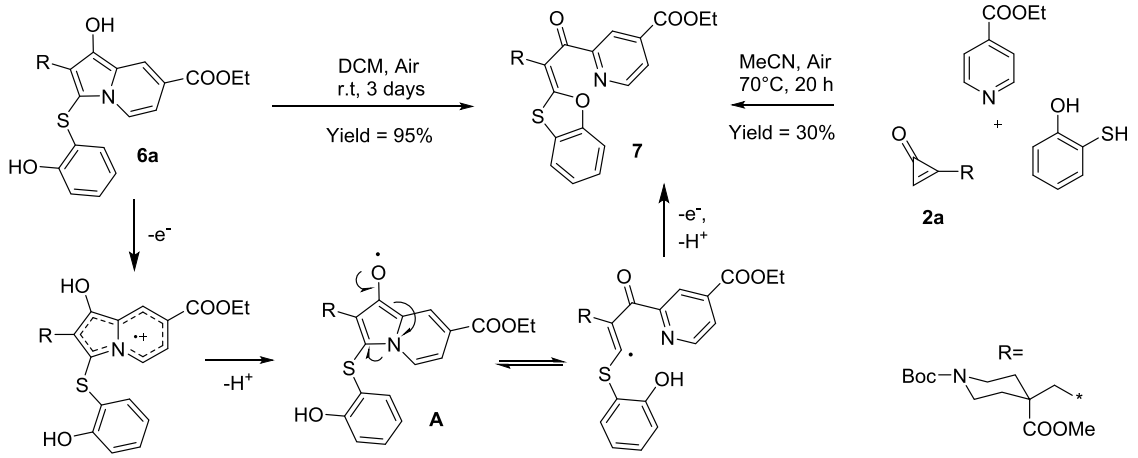
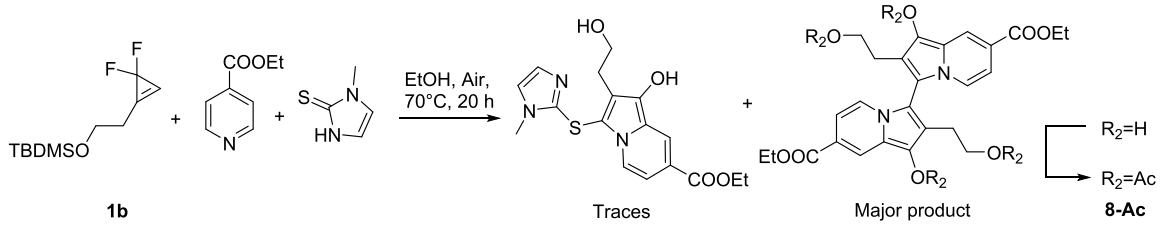


Figure 4. Influence of temperature on ^{1}H NMR of 3-(arylsulfanyl)-1-hydroxyindolizine **6l**. Only affected signals are shown.

Scheme 2. *E*/*Z*-Stereoselective Oxidative Recyclization of 3-(2-Hydroxyphenylsulfanyl)-1-hydroxyindolizine and a Plausible Mechanism



Scheme 3. Side Reaction in the Case of a Poorly Active Thio Component



signal broadening (Figure 4). For compounds **6i** and **6j** with stubbornly broad NMR spectra, we applied O-acetylation to resolve the signals. These NMR effects emerged due to the trace presence of paramagnetic oxyindolizinyl radical species, formed in subtle redox equilibrium; thus, minimization of the air exposure was important.

Stability of 3-Arylsulfanyl-1-hydroxyindolizines: Oxidative Recyclization. Modulation of redox properties, decreasing air stability of the whole molecule, is a common feature of the indolizin-1-ol moiety, as could be seen, for example, from the oxidation series **3** → **4** → **5** (Scheme 1) and our previous study.[15] We were curious about the potential oxidation of 3-arylsulfanyl-1-hydroxyindolizines **6a**–**l** and expected their further aerobic oxidation to form sulfoxides but found them quite stable in DMSO or solid state under ambient conditions. In chlorinated solvents upon heating, 3-arylsulfanyl-1-hydroxyindolizines gradually darkened without appreciable unambiguous chemical changes according to liquid chromatography–mass spectrometry (LC–MS). As exclusion, *ortho*-carboxylic acids **6f** and **6k** slowly oxidized in air, extruding hydrogen, according to LC–MS. Faster aerobic dehydrogenation was observed for *ortho*-phenol **6a**: after 3 days in dichloromethane (DCM) at room temperature, benzo[1,3]oxathiolylidene **7** was cleanly formed, despite starting **6a** showed air stability in solid state at least for 3 weeks (Scheme 2). This dehydrogenation was monitored by NMR and proceeded with high *E*/*Z* selectivity (see the Supporting Information, p S80); however, it was not possible to prove by NMR which isomer (*E* or *Z*) has been formed. Alternatively, benzo[1,3]oxathiolylidene **7** was obtained from cyclopropenone **2a**. In this experiment, corresponding indolizin-1-ol formed immediately after mixing of **2a** and ethylisonicotinate; however, an oxidative coupling/recyclization step required heating.

Mechanistically, we rationalized this transformation by one-electron oxidation of **6a** to form a cation radical, which after sequential deprotonation led to a free radical **A**. This radical intermediate is stabilized due to the delocalization, in which EWG in the pyridine ring is directly involved. Bond C3–N in the pyrrole ring of intermediate **A** becomes weakened and

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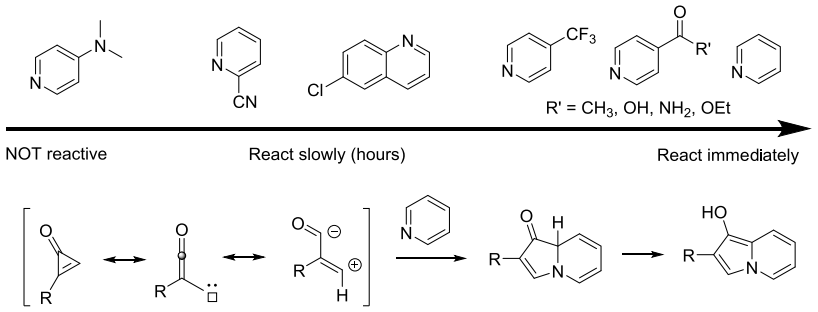

Figure 5. Reactivity of pyridines with cyclopropenone and plausible condensation mechanism.

cleaved. Next, conjugated addition, followed by one-electron oxidation/deprotonation, leads to oxidative recyclization product: benzo[1,3]oxathiolylidene **7**. Noteworthily, 3-arylsulfanyl-1-hydroxyindolizines (*e.g.*, **6h**, **6d**) potentially could form oxidative recyclization products of another type, with a hydroxyethyl side chain involved, but they were not observed. Interestingly, the type **A** free radicals were registered by LC-MS (atmospheric pressure chemical ionization (APCI)) as a separate chromatographic peak for 3-(arylsulfanyl)-indolizin-1-ols **6h** and **6d** after they were heated in dichloroethane (DCE) in air for 15 h.

Limitations. Certain limitations for the MCR of 3,3-difluorocyclopropenes, pyridines, and thiols have been met. For example, five-membered heterocyclic thiones such as 1-methylimidazole-2-thione, benzoxazole-2-thione, and aliphatic thiol (3-mercaptopropionic acid) reacted slowly and significant indolizin-1-ol dimerization took place, even when 3−4-fold excess of the thiol component was used (Scheme 3).

Pyridines' reactivity, with respect to the cyclopropenone **2a** reaction intermediate, depends on the substituents at the pyridine ring or its annulation (Figure 5). For example, ethylisonicotinate reacts immediately at the moment of addition, but the cyclopropenone could coexist with quinolines for hours at room temperature. 4-Dimethylaminopyridine (DMAP) did not react with the cyclopropenone even after 15 h: no corresponding indolizine (or its dimer) product was observed at all. Increased nucleophilicity of DMAP,[16] along with its inactivity toward cyclopropenone, indicates that the pyridine's nitrogen attack is not the only requirement for the successful condensation; hence, the pyridine C═N double bond should have suitable electronic properties. This may support a version that cyclopropenone participates in its carbene or 1,3-dipolar form in this formal [3 + 2] cycloaddition.

1-Hydroxyindolizines as a C3 Nucleophile. In continuation of the study and to expand the area of possible substituents at indolizin-1-ol C3 position, we prepared electrophilic tropones (Figure 6) from the common tropolone starting material (see the Supporting Information, p S3). *O*-Tosyltropolones are known for their facilitated reactivity with heteroatom- and C-nucleophiles.[17] 5-Pyrrol-1-yl-*O*-tosyltropolone **9f** was involved to estimate the ratio of ipso- and tele-substitution pathways, both common in chemistry of tropones,[18] and 5-tropolonediazonium tetrafluoroborate **9c**, easily obtained by diazotization of 5-aminotropolone, was included as an example of N-electrophile in a reaction with indolizin-1-ol in situ.

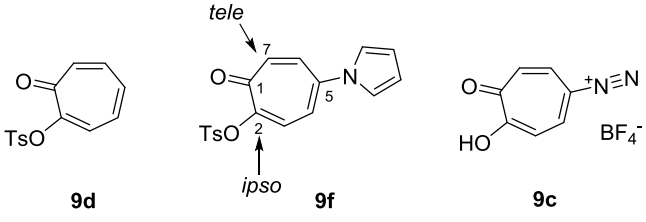

Figure 6. Tropone-based C- and N-electrophiles.

In the three-component reaction, involving 3,3-difluorocyclopropenes, ethylisonicotinate, and simple *O*-tosyltropolone **9d**, tropon-2-yl-1-hydroxyindolizines **10a** and **10b** were cleanly formed (Scheme 4).

Air stability of these red products has been evaluated: **10a** upon keeping in methanol in ambient conditions showed moderate stability and selectively extruded hydrogen along with the addition of methanol, according to MS spectra (30% conversion after 1 week). This product has not been isolated, however, due to its decomposition. An approach with the involvement of **10b** with hydroxyethyl side chain, borrowed from the example of 3-(2-hydroxyphenylsulfanyl)-indolizin-1-ol **6a** oxidative recyclization, did not work either: **10b** unselectively decomposed upon heating in MeCN in air overnight or being dried on SiO_2 at room temperature.

Pyrrole incorporation in the tropone residue decreased the air stability of 3-(7-oxo-4-pyrrol-1-yl-cyclohepta-1,3,5-trienyl)-indolizin-1-ol **11**, which was stabilized by O-acetylation accompanied by a notable hypsochromic shift. It turned out that O-acetylation favored separation of regioisomers **11a** and **11b** by chromatography on SiO_2. ^1H NMR spectra, too broad in the whole region for the isomers mixture **11**, became interpretable after O-capping to make a reliable structural conclusion. The ratio of the isomers showed that ipso-substitution is a major direction of the intermediate indolizin-1-ol attack; however, tele-substitution also took place to a less extent (28%; see the Supporting Information, p S107).

Next, we studied the interaction of indolizin-1-ol in situ with tropolonediazonium tetrafluoroborate **9c**, stable at room temperature. Reports based on the use of tropolones as the key motif of functional molecules are still limited, whereas metal complexes of tropolones are well known. The metal complexation ability of tropolone-based units has been explored, for example, in the design of metalloprotein inhibitors[19] or in DSSC technology.[20] We applied the "cold" conditions, generating C3-free indolizin-1-ols from 3,3-difluorocyclopropenes **1a** or **1b** and ethylisonicotinate in wet hexafluoroisopropanol (HFIP) in the presence of N-electrophile **9c**. After 2 h of being intensively colored, deep blue 3-(tropolon-5-ylazo)-indolizin-1-ols **12a** and **12b** were formed in the azo-coupling reaction. The presence of the acidic tropolone

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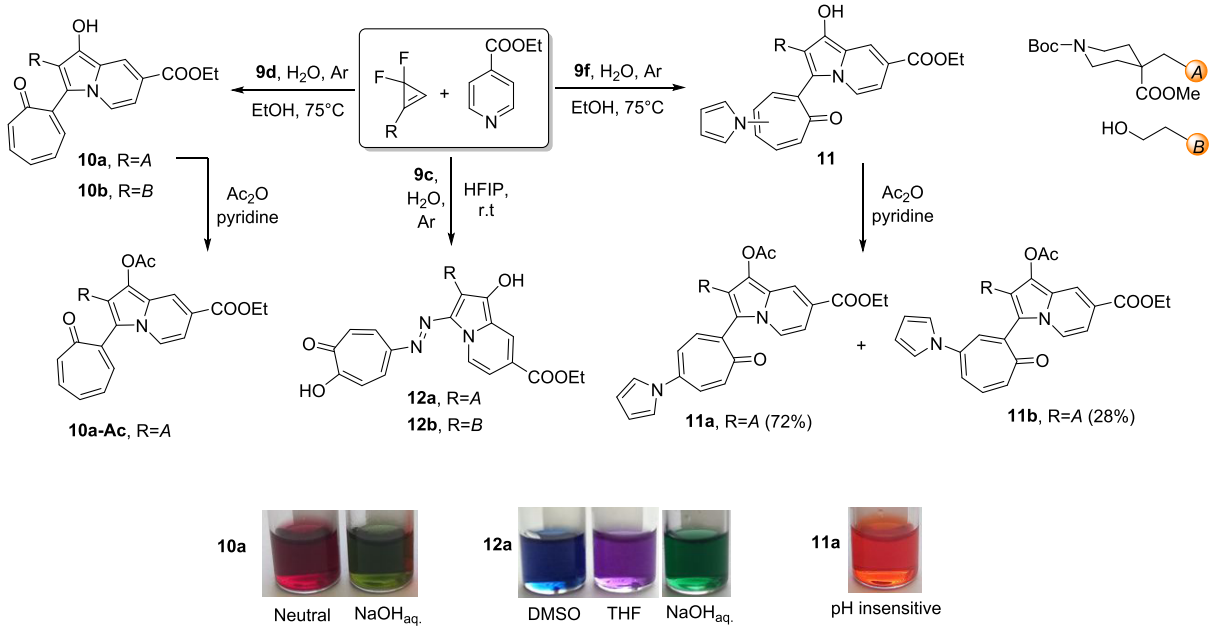
Scheme 4. Three-Component Reaction of 3,3-Difluorocyclopropenes, Ethylisonicotinate, and C/N-Electrophiles and Photographs of the Diluted Products' Solutions



fragment complicated the chromatographic purification of the products, and simple crystallization was more effective.

The red-purple tropon-2-yl-1-hydroxyindolizines **10a** and **10b**, possessing a developed conjugated system, showed an identical absorption band in the visible spectral range $\lambda \sim 520$ nm (Figure 7, red curve). Shifts of the visible spectrum band upon acetylation or deprotonation of the 1-hydroxyindolizine OH group were stronger and similar in direction, as was noted for 3-arylsulfanyl-1-hydroxyindolizines. For example, **10a** showed a reversible color change from red-purple to green in an alkaline solution, and its O-acetylation shifted the visible absorption band ~−60 nm hypsochromically, resulting in a red-orange acetyl derivative **10a-Ac**. The presence of the pyrrole substituent in 3-(7-oxo-4-pyrrol-1-yl-cyclohepta-1,3,5-trienyl)-indolizin-1-ols **11** did not much affect the absorption band in the visible region, and OH group deprotonation/acetylation color effects were quite similar to those for **10a** or **10b**.

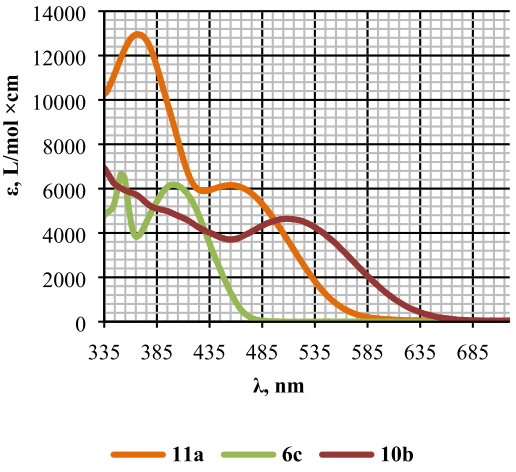


Figure 7. UV/vis spectra of indolizines **6c**, **10b**, and **11a** in MeCN.

For 3-(tropolon-5-ylazo)-indolizin-1-ols **12a** and **12b**, solvatochromism was observed with a color shift from blue in DMSO or methanol to turquoise in HFIP and violet in tetrahydrofuran (THF) or dioxane (Figure 8). In the biphasic system (NaOH aq/THF), azo-dye **12a** moved in the aqueous layer, forming a bright-green solution, which reversibly turned blue upon acidification with aqueous HCl.

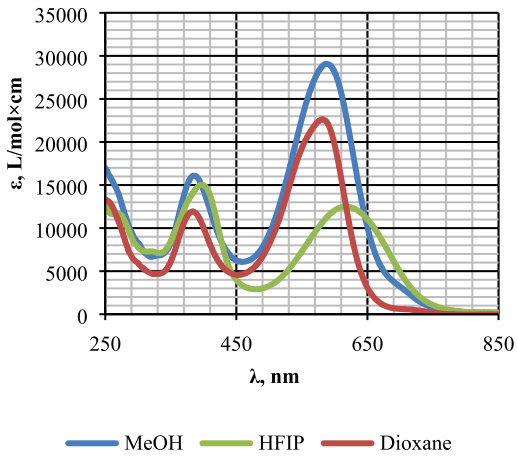


Figure 8. Solvatochromism for 3-(tropolon-5-ylazo)-indolizin-1-ol **12a**.

If the reaction mixtures containing products **12a** or **12b** were not properly degassed, partial dehydrogenation of the azo dyes was noticed. However, 3-(tropolon-5-ylazo)-indolizin-1-ols **12a** and **12b** were stable in DMSO in air, even after heating at 70 °C for 15 h. For the further study of this aerobic dehydrogenation, **12a** was used as it had better solubility in organic solvents than **12b**, bearing the additional polar OH group. We found that diacetoxyiodobenzene (DAIB) was an effective oxidizer to cleanly afford tropoquinoid betaine product 3-((4,5-dioxocyclohepta-2,6-dien-1-ylidene)-

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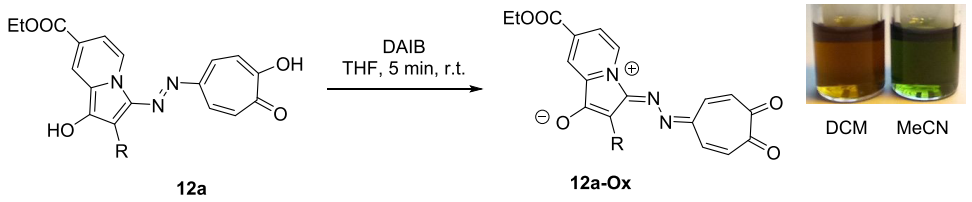
Scheme 5. Oxidative Transformation of 3-(Tropolon-5-ylazo)-1-hydroxyindolizine 12a and Solvatochromic Effect of 3-Hydrazono-3*H*-indolizin-4-ium-1-olate 12a-Ox



hydrazono)-3*H*-indolizin-4-ium-1-olate **12a-Ox** in less than 5 min at room temperature (Scheme 5).

According to the structure of **12a-Ox**, it allows a set of tautomeric forms. Normally, the tropoquinone ring was observed in NMR ($CDCl_3$, 25 or 50 °C) as a group of nonequivalent signals as it should. However, freshly purified (on SiO_2) and prepared sample showed signal coalescence of the tropoquinone fragment, slowly equilibrating back into the unsymmetrical form upon standing (see the Supporting Information, p S127). Two intense maxima on the borders of the visible spectral region were registered: $\lambda_{max}^{1} \sim 430$ nm and $\lambda_{max}^{2} \sim 730$ nm (Figure 9).

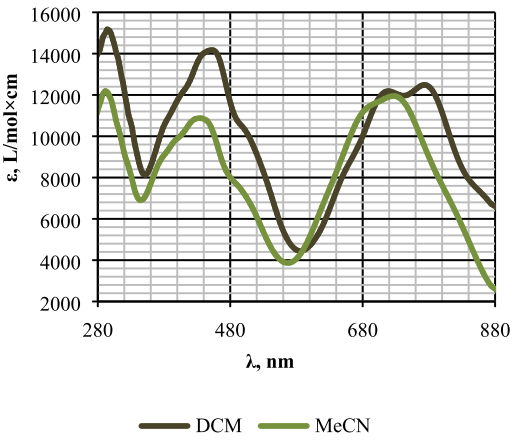


Figure 9. UV/vis spectra of 3-hydrazono-3*H*-indolizin-4-ium-1-olate **12a-Ox** mesomeric betaine in DCM and MeCN solutions.

Again, solvatochromism for **12a-Ox** was noticed, with a color change from green in polar solvents such as MeOH, DMSO, MeCN, or THF to brown-yellow in DCM. An interesting effect was observed in methanol: a green solution of **12A-Ox** turned violet upon sample dilution. This irreversible transition was associated with easy reduction of the tropoquinone back to tropolone **12a**.

As the NMR spectrum of 1-hydroxyindolizines, described in this study, was complicated in some cases, we tabulated the collected data, which can be useful guidance for further research in this field (Table 1).

CONCLUSIONS

A novel three-component reaction involving 3,3-difluorocyclopropenes, pyridines, and arylthiols to afford 3-(arylsulfanyl)-1-hydroxyindolizines has been studied. The reaction proceeds via a central intermediate, C3-free indolizin-1-ol, whose reactivity is directly affected by the substituents in the pyridine reaction component. Air and heating are essential to activate the radical pathway, so indolizin-1-ol could form a C3 radical, which is finally trapped with arylthiols present. In the case of the poorly reactive third component (either arylthiol or C/N-electrophile), intermediate 1-hydroxyindolizines dimerize on their own in air, yielding C−C-coupled [3,3′-biindolizine]-1,1′-diols. In an inert atmosphere, intermediate indolizin-1-ol behaves as a C3 nucleophile; thus, the ionic pathway is operating. Tropone-based C- and N-electrophiles were employed to afford novel, brightly colored 3-(tropon-2-yl)- and 3-(tropolon-5-ylazo)-indolizin-1-ols, respectively.

A common feature of the products containing 1-hydroxyindolizine moiety is the facilitated ability to oxidation. Three different types of such selective oxidations have been described: (1) auto-oxidation of 3,3′-biindolizine-1,1′-diol forming [1,3,6]oxadiazepine after oxygen incorporation at C5 positions of the 1-hydroxyindolizine units; (2) oxidative recyclization of 3-(2-hydroxyphenylsulfanyl)-indolizin-1-ol, accompanied by the pyrrole ring cleavage; and (3) dehydration of 3-(tropolon-5-ylazo)-indolizin-1-ol yielding 3-hydrazono-3*H*-indolizin-4-ium-1-olate mesomeric betaine.

This notable compound possesses interesting optical properties, showing a solvatochromic effect and strongly absorbing light on the borders of the visible spectral range and beyond (near-UV and near-IR). 3-(Arylsulfanyl)-1-hydroxyindolizines with the uncapped OH group are prone to oxidation and may comprise the basis for antioxidant development.

EXPERIMENTAL SECTION

General Information. Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. For the reactions that required heating, an oil bath was used as a heating source. Melting points were measured on a Sanyo Gallenkamp apparatus and were uncorrected. UV/vis spectra were recorded on a Specord M40 double-beam spectrometer.

HPLC chromatography was performed on a YMC-Pack Pro C18 150 × 20 mm2 reverse-phase preparative column (particle size, 10 μm; pore size, 12 nm) with gradient elution using H_2O/MeCN with 0.1% formic acid as a mobile phase. The elution time was 20 min at a flow rate of 15 mL/min; retention times (t_R) of the target compounds were given in the synthesis procedures below. Solvents from the HPLC fractions containing target products were removed using a Genevac HT-4X series II vacuum evaporator.

Analytical thin-layer chromatography (TLC) was performed using Sorbfil-A-UV TLC silica gel plates (IMID). Column chromatography was performed on a Teledyne Combiflash RF200 apparatus using Silica RediSep-R_f disposable columns.

^{1}H NMR (300 or 400 MHz), ^{13}C NMR (75 or 100 MHz), and ^{19}F NMR (282 MHz) spectra were recorded on a Bruker AVANCE II 300 MHz or a Varian MERCURY plus 400 MHz spectrometer with an internal deuterium lock. Chemical shifts (δ) were reported in ppm relative to the residual solvent signals: for DMSO-d_6: 2.50 ppm (^{1}H), 39.5 ppm (^{13}C); for $CDCl_3$: 7.26 ppm (^{1}H), 77.0 ppm (^{13}C); for CD_3OD: 3.25 ppm (^{1}H), 49.0 ppm (^{13}C). Fluorine chemical shifts were determined relative to $CFCl_3$ as an external standard. Structural assignments were made with additional information from the attached proton test (APT), gradient correlated spectroscopy (gCOSY),

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Table 1. Chemical Shifts of the Indolizin-1-ol Ring System in DMSO-d_6 at 25 °C (Carbon, ppm/Proton, ppm)[a]

cpd no./atom	1[b]	2[b]	3[b]	5	6	7[b]	8	9[b]
				3-(7-Oxocyclohepta-1,3,5-trienyl)-indolizines				
10b	137.9	114.0	122.9	123.0/7.2	107.3/6.7	114.1	120.1/8.2	118.7
10a-Ac	129.4	115.8	123.4	124.1/7.5	108.6/6.9	118.0	118.9/8.0	121.3
				1-Acetoxy-3-(7-oxo-4-pyrrol-1-yl-cyclohepta-1,3,5-trienyl)-indolizines				
11a	129.5	115.9	123.2	124.2/7.6	108.6/6.9	118.0	118.9/7.9	121.4
11b	129.3	115.9	122.6	123.6/7.6	108.3/6.9	118.2	118.5/8.0	121.3
				1-Hydroxy-3-(4-hydroxy-5-oxo-cyclohepta-1,3,6-trienylazo)-indolizines				
12a	141.8	112.6	132.9	124.6/9.4	112.7/7.2	121.7	119.2/8.4	
12b[c]	141.7	112.7	133.5	124.7/9.3	112.8/7.2	122.7	118.9/8.3	126.0
				Indolizin-4-ium-1-olates				
3t	178.5	86.0	147.4	133.7/9.0	127.5/8.4	142.3	114.7/8.0	164.7
12a-Ox[d]	176.1	97.9	159.4	133.6/9.4	125.6/8.3	143.9	118.3/8.4	147.9
				3-(Arylsulfanyl)-2-alkyl-indolizin-1-ols				
6a	137.9	118.7	107.9	122.1/7.9	108.8/6.9	115.8	120.4/8.3	121.3
6b	138.0	118.8	107.1	122.0/7.9	109.0/6.9	116.1	120.5/8.3	121.5
6c	137.9	118.5	108.1	121.9/8.0	109.1/6.9	116.3	120.4/8.3	121.4
6d	137.5	121.0	107.4	121.8/8.0	108.8/6.9	116.3	120.2/8.3	121.7
6e	138.0	118.8	106.3	122.0/7.9	109.2/6.9	116.5	120.5/8.4	121.8
6f	137.2	119.6	108.1	123.4/7.9	105.7/6.6	115.0	115.4/8.0	120.0
6g	137.4	121.2	105.9	122.0/7.9	108.6/6.9	116.0	120.1/8.3	121.9
6h	137.4	120.8	108.6	122.0/8.0	108.6/6.9	115.9	120.1/8.3	121.3
6i-Ac	129.5	122.7	106.8	121.1/8.1	111.6/6.0	121.7	123.5/n.a	127.1
6j-Ac	129.0	123.2	107.5	123.9/8.2	109.8/7.1	120.4	118.8/8.0	125.1
6k	138.1	118.9	108.9	121.9/7.8	109.1/6.8	116.2	120.5/8.4	121.5
6l	137.4	120.6	108.5	121.8/8.0	108.9/6.8	115.9	120.1/8.3	121.3
				[3,3′]Biindolizines				
8-Ac	128.8	120.5	110.5	122.6/7.3	110.0/7.0	119.2	119.3/8.1	123.2
4-Ac[d]	130.0	120.2	111.8	122.1/7.0	110.7/7.1	118.9	119.9/8.1	123.6

[a]Indolizine ring atoms are numbered according to IUPAC. [b]Quartenary carbons. [c]At 50 °C. [d]In $CDCl_3$.

gradient heteronuclear single quantum coherence (gHSQC), nuclear Overhauser enhancement spectroscopy (NOESY), total correlation spectroscopy (TOCSY), and gradient heteronuclear multiple bond correlation (gHMBC) (over ranges of two and three bonds: $^2J_{H-C-C}$, $^3J_{H-C-C-C}$) experiments.

LC-MS spectra were recorded on a Thermo Fisher Scientific Surveyor MSQ instrument equipped with a Phenomenex Onyx Monolithic C18 25 × 4.6 mm^2 column (at 25 °C) and detected by a photodiode array (PDA) detector at 200−800 nm, mass spectrometry (MS) APCI in positive and negative ions, and an evaporative light-scattering detector (ELSD) PL-ELS 2100. Mobile phase: A, 0.1% solution of formic acid in water; B, acetonitrile at 1.5 mL/min flow rate. High-resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF-Q II hybrid quadrupole time-of-flight mass spectrometer using electrospray ionization (ESI) in the positive ion mode.

Synthetic Procedures. *2,2′-Bis-(N-Boc-4-methoxycarbonylpiperidin-4-ylmethyl)-1,1′-dihydroxy-[3,3′]biindolizinyl-7,7′-dicarboxylic Acid Diethyl Ester (**4**).* 4-(3,3-Difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (330 mg, 1.0 mmol) and water (126 μL, 7.0 mmol, 7 equiv) were dissolved in hexafluoroisopropanol (HFIP) (7 mL), followed by ethylisonicotinate (155 mg, 1.0 mmol, 1 equiv) addition. The reaction mixture immediately became yellow, and the solvent was removed under reduced pressure. The residue was dissolved in MeCN (10 mL) and heated at 70 °C upon stirring in air for 4 h to complete dimerization. Then, the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC (40−85% MeCN for 20 min; t_R ∼ 13 min) to afford **4** as a dark yellow foam. Yield: 65%, 300 mg.

Characterization data corresponds to the previously reported.[14]

*1,1′-Diacetoxy-2,2′-bis-(N-Boc-4-methoxycarbonylpiperidin-4-ylmethyl)-[3,3′]biindolizinyl-7,7′-dicarboxylic Acid Diethyl Ester (**4-Ac**).* 2,2′-Bis-(*N*-Boc-4-methoxycarbonylpiperidin-4-ylmethyl)-1,1′-dihydroxy-[3,3′]biindolizinyl-7,7′-dicarboxylic acid diethyl ester **4** (92 mg, 0.1 mmol) was dissolved in DCM (3 mL), and pyridine (150 μL) was added at r.t. Then, Ac_2O (50 μL, 0.5 mmol, 5 equiv) was added and the reaction mixture was left stirring for next 15 h at r.t. in an argon atmosphere. Then, the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC (40−90% MeCN for 20 min; t_R ∼ 14 min) to afford **4-Ac** as a dark yellow amorphous solid. Yield: 70%, 70 mg.

TLC: R_f = 0.55 (EtOAc; brown spot (vis)). LC-MS: t_R ∼ 3.2 min. ^{1}H NMR (300 MHz, $CDCl_3$, 50 °C): δ 8.07 (dd, *J* = 1.8, 1.0 Hz, 2H), 7.11 (dd, *J* = 7.3, 1.8 Hz, 2H), 6.96 (dd, *J* = 7.4, 1.0 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 4H), 3.65 (m, 2H), 3.32 (m, 2H), 3.27 (s, 6H), 2.87 (d, *J* = 14.0 Hz, 2H), 2.67 (m, 2H), 2.62 (d, *J* = 14.0 Hz, 2H), 2.47 (m, 2H), 2.41 (s, 6H), 1.81 (m, 2H), 1.68 (m, 2H), 1.39 (t, *J* = 7.2 Hz, 6H), 1.36 (s, 18H), 1.21 (m, 2H), 0.86 (m, 2H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 50 °C): δ 174.6, 168.5, 165.3, 154.8, 130.0, 123.6, 122.1, 120.2, 119.9, 118.9, 111.8, 110.7, 79.4, 61.2, 51.6, 46.8, 41.2 (br.), 41.0 (br.), 34.4, 33.4, 32.6, 28.4, 20.7, 14.3.

HRMS (ESI-time-of-flight (TOF)) *m*/*z*: [M + H]$^+$ calcd for $C_{52}H_{67}N_4O_{16}$ 1003.4553; found: 1003.4561.

*4,4′-((4,8-Bis(ethoxycarbonyl)-2,10-dioxo-2,5a,6a,10-tetrahydro-[1,3,6]oxadiazepino[4,3,2-cd:5,6,7-c′d′]diindolizine-1,11-diyl)bis-(methylene))bis(N-Boc-4-methoxycarbonylpiperidine) (**5**)—Spectral Characterization.* 2,2′-Bis-(*N*-Boc-4-methoxycarbonylpiperidin-4-ylmethyl)-1,1′-dihydroxy-[3,3′]biindolizinyl-7,7′-dicarboxylic acid diethyl ester **4** (10 mg, 11 μmol) was dissolved in $CDCl_3$ (1 mL) and was left at r.t. for 1 week in air; then, NMR spectra were recorded. The solvent was removed under reduced pressure to afford **5** as a dark green-yellow amorphous solid, and MS spectra were recorded. Yield: 99%, 10 mg (crude).

TLC: R_f = 0.60 (EtOAc; orange spot (vis)). LC-MS: t_R ∼ 2.8 min. ^{1}H NMR (300 MHz, $CDCl_3$, 50 °C): δ 7.01 (m, 1H), 7.00 (m, 1H), 6.28 (d, *J* = 4.4 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.89 (m, 2H), 3.36 (s, 3H), 2.85 (d, *J* = 14.2 Hz, 1H), 2.71 (m, 1H), 2.63 (m, 1H),

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2.34 (d, J = 14.2 Hz, 1H), 2.03 (m, 1H), 2.88 (m, 1H), 1.44 (s, 9H), 1.43 (m, 2H), 1.37 (t, J = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, 50 °C): δ 184.6, 174.4, 163.4, 154.7, 149.9, 132.5, 130.4, 130.0, 114.1, 105.5, 79.6, 75.3, 62.0, 51.6, 47.3, 41.3 (br.), 34.4, 32.5, 32.3, 28.4, 14.1.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{48}H_{61}N_4O_{15}$ 933.4134; found: 933.4130.

Synthesis of 3-(Arylsulfanyl)-2-alkyl-1-hydroxyindolizines General Procedure. 3,3-Difluorocyclopropene **1a** or **1b** (1 equiv), substituted pyridine (or isoquinoline) (1 equiv), and aromatic thiol (1.2−1.5 equiv) were dissolved in EtOH (14 mL/mmol). Water (10 equiv) was added, and the flask was equipped with a Liebig condenser. The reaction mixture was heated at 70−80 °C for 18−36 h in air with periodic LC-MS monitoring. Then, the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC. Solvents from the appropriate HPLC fractions were removed in vacuo to afford 3-(arylsulfanyl)-2-alkyl-indolizin-1-ols **6a**−**l**.

*4-[7-Ethoxycarbonyl-1-hydroxy-3-(2-hydroxyphenylsulfanyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6a**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and 2-mercaptophenol (95 mg, 1.5 equiv) and isolated by HPLC (30−70% MeCN for 20 min; t_R ∼ 17 min) as yellow-green crystals (m.p. 212−214 °C). Yield: 25%, 73 mg.

TLC: R_f = 0.60 (EtOAc; UV (365 nm)). LC-MS: t_R ∼ 2.6 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 10.15 (s, 1H), 9.29 (s, 1H), 8.32 (dd, J = 1.9, 0.9 Hz, 1H), 7.86 (dd, J = 7.4, 0.9 Hz, 1H), 6.94 (ddd, J = 8.0, 7.2, 1.6 Hz, 1H), 6.86 (dd, J = 7.5, 1.8 Hz, 1H), 6.83 (dd, J = 8.0, 1.3 Hz, 1H), 6.54 (td, J = 7.5, 1.3 Hz, 1H), 5.81 (dd, J = 7.8, 1.6 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3,76 (br. m, 2H), 3.64 (s, 3H), 2.90 (s, 2H), 2.63 (br. m, 2H), 1.96 (br. m, 2H), 1.38 (m, 2H), 1.35 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.3, 165.1, 153.8, 153.8, 137.9, 126.7, 125.3, 122.1, 121.3, 120.9, 120.4, 119.8, 118.7, 115.8, 115.3, 108.8, 107.9, 78.6, 60.4, 51.9, 46.8, 41.2 (br.), 33.4, 32.7, 28.0, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{30}H_{37}N_2O_8S$ 585.2271; found: 585.2265.

*4-(7-Ethoxycarbonyl-1-hydroxy-3-o-tolylsulfanylindolizin-2-ylmethyl)-N-Boc-4-methoxycarbonylpiperidine (**6b**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and 2-thiocresol (93 mg, 1.5 equiv) and isolated by HPLC (30−70% MeCN for 20 min; t_R ∼ 17 min) as yellow crystals (m.p. 173−175 °C). Yield: 45%, 130 mg.

TLC: R_f = 0.63 (EtOAc; UV (365 nm), aq $KMnO_4$). LC-MS: t_R ∼ 3.0 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 9.35 (s, 1H [−O*H*]), 8.35 (br. s, 1H), 7.85 (br. d, J = 7.4 Hz, 1H), 7.22 (br. d, J = 7.6 Hz, 1H), 7.03 (br. t, J = 7.4 Hz, 1H), 6.92 (br. t, J = 7.6 Hz, 1H), 6.86 (br. d, J = 7.4 Hz, 1H), 5.84 (br. d, J = 7.9 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.75 (br. m, 2H), 3.65 (s, 3H), 2.88 (s, 2H), 2.63 (br. m, 2H), 2.41 (s, 3H), 1.96 (br. m, 2H), 1.39 (m, 2H), 1.35 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.3, 165.0, 153.9, 138.0, 134.2, 134.2, 130.7, 126.9, 125.6, 123.7, 122.0, 121.5, 120.5, 118.8, 116.1, 109.0, 107.1, 78.6, 60.5, 51.9, 46.9, 41.1, 33.4, 32.7, 28.0, 19.4, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{39}N_2O_7S$ 583.2478; found: 583.2481.

*4-[7-Ethoxycarbonyl-3-(4-fluorophenylsulfanyl)-1-hydroxyindolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6c**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and 4-fluorothiophenol (96 mg, 1.5 equiv) and isolated by HPLC (35−85% MeCN for 20 min; t_R ∼ 17 min) as light yellow crystals (m.p. 175−177 °C). Yield: 50%, 147 mg.

TLC: R_f = 0.67 (EtOAc; UV (365 nm), aq $KMnO_4$). LC-MS: t_R ∼ 2.9 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 9.34 (s, 1H), 8.33 (s, 1H), 7.96 (d, J = 7.4 Hz, 1H), 7.10 (m, 2H), 6.88 (d, J = 7.4 Hz, 1H), 6.82 (m, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.76 (br. m, 2H), 3.64 (s, 3H), 2.93 (br. s, 2H), 2.63 (br. m, 2H), 1.95 (m, 2H), 1.39 (m, 2H), 1.35 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

$^{19}F\{^1H\}$ NMR (282 MHz, DMSO-d_6, 25 °C): δ −116.43.

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.2, 164.9, 160.7 (d, $^1J_{C-F}$ = 240.7 Hz), 153.8, 137.9, 130.4, 127.7 (d, $^3J_{C-F}$ = 8.1 Hz), 121.9, 121.4, 120.4, 118.5, 116.6 (d, $^2J_{C-F}$ = 22.7 Hz), 116.3, 109.1, 108.1, 78.6, 60.4, 51.9, 46.8, 41.0 (br.), 33.4, 32.7, 28.0, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{30}H_{36}FN_2O_7S$ 587.2228; found: 587.2222.

*3-(4-Fluorophenylsulfanyl)-1-hydroxy-2-(2-hydroxyethyl)-indolizine-7-carboxylic Acid Ethyl Ester (**6d**).* The product was obtained from *tert*-butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg), ethylisonicotinate (75 mg, 1 equiv), and 4-fluorothiophenol (96 mg, 1.5 equiv) and isolated by HPLC (30−65% MeCN for 20 min; t_R ∼ 17 min) as a yellow amorphous solid. Yield: 50%, 94 mg.

TLC: R_f = 0.61 (EtOAc; UV (254 nm), aq $KMnO_4$). LC-MS: t_R ∼ 2.6 min.

^1H NMR (300 MHz, DMSO-d_6, 25 °C): 9.39 (s, 1H [−O*H*]), 8.28 (dd, J = 1.9, 0.9 Hz, 1H), 7.98 (dd, J = 7.5, 0.8 Hz, 1H), 6.86 (dd, J = 7.4, 1.8 Hz, 1H), 4.67 (br. s, 1H [−O*H*]), 4.26 (q, J = 7.1 Hz, 2H), 3.57 (t, J = 7.4 Hz, 2H), 2.89 (t, J = 7.4 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H).

^{19}F NMR (282 MHz, DMSO-d_6, 25 °C): δ −116.52 (tt, J = 8.8, 5.1 Hz).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 165.1, 160.8 (d, $^1J_{C-F}$ = 243.2 Hz), 137.5, 131.2 (d, $^4J_{C-F}$ = 3.1 Hz), 127.8 (d, $^3J_{C-F}$ = 8.0 Hz), 121.8, 121.7, 121.0, 120.2, 116.6 (d, $^2J_{C-F}$ = 22.4 Hz), 116.3, 108.8, 107.4, 60.9, 60.5, 27.8, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}FNO_4S$ 376.1019; found: 376.1026.

*4-[3-(4-Carboxyphenylsulfanyl)-7-ethoxycarbonyl-1-hydroxyindolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6e**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and 4-mercaptobenzoic acid (100 mg, 1.3 equiv) and isolated by HPLC (25−75% MeCN for 20 min; t_R ∼ 17 min) as yellow-green crystals (m.p. 226−228 °C). Yield: 45%, 137 mg.

TLC: R_f = 0.45 ((EtOAc/AcOH, 100:1); UV (365 nm), aq $KMnO_4$). LC-MS: t_R ∼ 2.6 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 12.72 (s, 1H [−COO*H*]), 9.28 (s, 1H [−O*H*]), 8.36 (br. s, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.78 (m, 2H), 6.89 (dd, J = 7.4, 1.8 Hz, 1H), 6.82 (m, 2H), 4.29 (q, J = 7.1 Hz, 2H), 3.74 (m, 2H), 3.64 (s, 3H), 2.93 (s, 2H), 2.66 (m, 2H), 1.97 (m, 2H), 1.39 (m, 2H), 1.35 (s, 9H), 1.32 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, 25 °C): δ 174.2, 166.7, 164.9, 153.8, 141.4, 138.0, 130.3, 128.2, 124.7, 122.0, 121.8, 120.5, 118.8, 116.5, 109.2, 106.3, 78.6, 60.4, 51.9, 46.8, 41.0 (br.), 33.4, 32.7, 28.0, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{37}N_2O_9S$ 613.2220; found: 613.2215.

*4-[3-(2-Carboxyphenylsulfanyl)-1-hydroxy-7-trifluoromethylindolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6f**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), 4-trifluoromethylpyridine (74 mg, 1 equiv), and thiosalicylic acid (100 mg, 1.3 equiv) and isolated by HPLC (25−75% MeCN for 20 min; t_R ∼ 17 min) as yellow-green crystals. Yield: 45%, 137 mg.

TLC: R_f = 0.45 ((EtOAc/AcOH, 100:1); UV (254 nm)). LC-MS: t_R ∼ 2.6 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 13.36 (s, 1H [−COO*H*]), 9.25 (s, 1H [−O*H*]), 7.99 (m, 1H + 1H), 7.89 (d, J = 7.4 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 6.60 (dd, J = 7.4, 1.8 Hz, 1H), 5.81 (d, J = 8.0 Hz, 1H), 3.75 (br. m, 2H),

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3.67 (s, 3H), 2.89 (s, 2H), 2.63 (br. m, 2H), 1.95 (br. m, 2H), 1.41 (m, 2H), 1.35 (s, 9H).

$^{19}F\{^1H\}$ NMR (282 MHz, DMSO-d_6, 25 °C): δ −61.51.

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.2, 167.3, 153.9, 139.7, 137.2, 133.1, 131.9, 127.2, 125.2, 124.5, 124.4 (q, $^1J_{C-F}$ = 271.0 Hz), 123.4, 120.0, 119.6, 115.4 (br.), 115.2 (q, $^2J_{C-F}$ = 32.7 Hz), 108.1, 105.7 (br.), 78.6, 51.9, 46.9, 41.1 (br.) 33.4, 32.7, 28.0.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{32}F_3N_2O_7S$ 609.1883; found: 609.1885.

*1-Hydroxy-2-(2-hydroxyethyl)-3-(2-methoxyphenylsulfanyl)-indolizine-7-carboxylic Acid Ethyl Ester (**6g**).* The product was obtained from *tert*-butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg), ethylisonicotinate (75 mg, 1 equiv), and 2-methoxythiophenol (105 mg, 1.5 equiv) and isolated by HPLC (35−70% MeCN for 20 min; t_R ∼ 13 min) as a dark yellow amorphous solid. Yield: 50%, 97 mg.

TLC: R_f = 0.63 (EtOAc; UV (365 nm)). LC-MS: t_R ∼ 2.6 min.

^1H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.36 (br. s, 1H [−O*H*]), 8.29 (br. s, 1H), 7.89 (br. d, J = 7.2 Hz, 1H), 7.11 (br. t, J ∼ 7.6 Hz, 1H), 7.02 (br. d, J = 8.5 Hz, 1H), 6.86 (br. d, J = 7.3 Hz, 1H), 6.70 (br. t, J = 7.6 Hz, 1H), 5.93 (br. d, J = 7.4 Hz, 1H), 4.90 (br. s, 1H [−O*H*]), 4.27 (br. q, J = 7.1 Hz, 2H), 3.89 (s, 3H), 3.52 (t, J = 7.8 Hz, 2H), 2.84 (br. t, J ∼ 7.8 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 165.1, 155.3, 137.5, 126.8, 124.6, 123.6, 122.0, 121.8, 121.3, 121.3, 120.1, 116.0, 111.3, 108.6, 105.9, 60.9, 60.4, 55.8, 27.8, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{22}NO_5S$ 388.1219; found: 388.1226.

*3-(3,4-Dimethoxyphenylsulfanyl)-1-hydroxy-2-(2-hydroxyethyl)-indolizine-7-carboxylic Acid Ethyl Ester (**6h**).* The product was obtained from *tert*-butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg), ethylisonicotinate (75 mg, 1 equiv), and 3,4-dimethoxythiophenol (128 mg, 1.5 equiv) and isolated by HPLC (35−65% MeCN for 20 min; t_R ∼ 12 min) as a dark yellow amorphous solid. Yield: 35%, 73 mg.

TLC: R_f = 0.63 (EtOAc; UV (365 nm)). LC-MS: t_R ∼ 2.6 min.

^1H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.33 (br. s, 1H [−O*H*]), 8.26 (br. s, 1H), 8.02 (br. s, 1H), 6.82 (br. s, 1H + 1H), 6.75 (br. s, 1H), 6.32 (br. d, J = 8.2 Hz, 1H), 4.94 (br. s, 1H [−O*H*]), 4.26 (br. s, 2H), 3.65 (s, 3H + 3H), 3.60 (br. s, 2H), 2.92 (br. s, 2H), 1.30 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 165.1, 149.4, 147.8, 137.4, 125.9, 121.9, 121.3, 120.7, 120.1, 118.8, 115.9, 112.8, 110.79, 108.6, 108.6 (overlapped), 60.9, 60.4, 55.5, 55.5 (overlapped), 27.8, 14.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{24}NO_6S$ 418.1325; found: 418.1332.

*4-[3-(3-Chlorophenylsulfanyl)-1-hydroxypyrrolo[2,1-a]-isoquinolin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6i**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), isoquinoline (65 mg, 1 equiv), and 3-chlorothiophenol (108 mg, 1.5 equiv) and isolated by HPLC (45−95% MeCN for 20 min; t_R ∼ 18 min) as a brown amorphous solid. Yield: 30%, 90 mg.

TLC: R_f = 0.63 (EtOAc; UV (254 nm), aq $KMnO_4$). LC-MS: t_R ∼ 3.1 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 9.00−6.25 (br. m, 10H), 8.64 (s, 1H [−O*H*]), 3.80 (br. m, 2H), 3.66 (br. s, 3H), 3.01 (br. s, 2H), 2.63 (br. m, 2H), 2.02 (br. m, 2H), 1.43 (br. m, 2H), 1.35 (br. s, 9H).

$^{13}C\{^1H\}$ NMR: noninformative due to strong signal broadening. For the characterization, compound **6i** was O-acylated (see compound **6i-Ac**).

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{34}ClN_2O_5S$ 581.1877; found: 581.1876.

*4-[1-Acetoxy-3-(3-chlorophenylsulfanyl)-pyrrolo[2,1-a]-isoquinolin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6i-Ac**).* 4-[3-(3-Chlorophenylsulfanyl)-1-hydroxypyrrolo[2,1-*a*]-isoquinolin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine **6i** (58 mg, 0.1 mmol) was dissolved in DCM (2 mL) and pyridine 80 μL was added at r.t. Then Ac_2O (20 μL, 2 equiv) was added and the reaction mixture was left stirring for 15 h at r.t. in argon atmosphere. Then the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC (60−90% MeCN for 20 min; t_R ∼ 15 min) to afford **6i-Ac** as an almost colorless foam. Yield: 95%, 60 mg.

TLC: R_f = 0.63 (EtOAc; UV (254 nm, blue spot), $KMnO_4$-inactive). LC-MS: t_R ∼ 3.2 min.

^1H NMR (400 MHz, DMSO-d_6, 25 °C): δ 8.08 (d, J = 7.4 Hz, 1H), 8.06 (d, J = 8.6 Hz, 1H), 7.75 (dd, J = 7.9, 1.2 Hz, 1H), 7.59 (ddd, J = 8.4, 7.3, 1.4 Hz, 1H), 7.50 (td, J = 7.5, 1.2 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 7.20 (ddd, J = 8.0, 2.1, 1.1 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.89 (t, J = 2.0 Hz, 1H), 6.74 (dt, J = 7.9, 1.4 Hz, 1H), 3.77 (br. m, 2H), 3.68 (s, 3H), 2.84 (br. s, 2H), 2.63 (br. m, 2H), 2.52 (s, 3H), 1.96 (br. m, 2H), 1.39 (m, 2H), 1.35 (s, 9H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 45 °C): δ 174.0, 168.5, 153.6, 138.3, 133.8, 130.6, 129.5, 127.8, 127.1, 126.7, 126.5, 125.6, 124.3, 123.5, 123.4, 122.7, 121.7, 121.6, 121.1, 111.6, 106.8, 78.2, 51.4, 46.3, 40.8, 33.9, 32.5, 27.7, 20.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{33}H_{36}ClN_2O_6S$ 623.1983; found: 623.1989.

*4-[7-Ethoxycarbonyl-1-hydroxy-3-(pyrimidin-2-ylsulfanyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6j**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and pyrimidine-2-thione (73 mg, 1.3 equiv) and isolated by HPLC (40−65% MeCN for 20 min; t_R ∼ 14 min) as a yellow-green foam. Yield: 40%, 114 mg.

TLC: R_f = 0.53 (EtOAc; UV (365 nm), aq $KMnO_4$). LC-MS: t_R ∼ 2.6 min.

^1H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.28 (s, 1H [−O*H*]), 8.56 (br. s, 2H), 8.33 (br. s, 1H), 7.95 (br. s, 1H), 7.27 (br. s, 1H), 6.86 (br. s, 1H), 4.29 (br. s, 2H), 3.71 (br. s, 2H), 3.64 (br. s, 3H), 2.87 (br. s, 2H), 1.92 (br. s, 2H), 1.34 (br. s, 2H + 9H + 3H).

$^{13}C\{^1H\}$ NMR: noninformative due to strong signal broadening. For characterization, compound **6j** was O-acylated (see compound **6j-Ac**).

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{35}N_4O_7S$ 571.2227; found: 571.2221.

*4-[1-Acetoxy-7-ethoxycarbonyl-3-(pyrimidin-2-ylsulfanyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6j-Ac**).* 4-[7-Ethoxycarbonyl-1-hydroxy-3-(pyrimidin-2-ylsulfanyl)-indolizin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine **6j** (57 mg, 0.1 mmol) was dissolved in DCM (2 mL), and 80 μL of pyridine was added. Then, Ac_2O (20 μL, 0.2 mmol, 2 equiv) was added and the reaction mixture was left stirring for 15 h at r.t. Then, the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC (35−70% MeCN for 20 min; t_R ∼ 17 min) to afford **6j-Ac** as a colorless foam. Yield: 95%, 58 mg.

TLC: R_f = 0.60 (EtOAc; UV (365, 245 nm)). LC-MS: t_R ∼ 2.7 min.

^1H NMR (300 MHz, DMSO-d_6, 25 °C): δ 8.60 (d, J = 4.9 Hz, 2H), 8.20 (d, J = 7.4 Hz, 1H), 8.03 (s, 1H), 7.30 (t, J = 4.9 Hz, 1H), 7.09 (dd, J = 7.4, 1.8 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 3.67 (br. m, 2H), 3.65 (s, 3H), 2.89 (br. m, 2H), 2.57 (br. m, 2H), 2.40 (s, 3H), 1.88 (m, 2H), 1.33 (br. m, 2H), 1.33 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.4, 168.9, 168.9 (overlapped), 164.7, 158.6, 153.8, 129.0, 125.1, 123.9, 123.2, 120.4, 118.8, 118.7, 109.8, 107.5, 78.6, 60.9, 52.1, 46.7, 40.9 (br.), 34.0, 32.5 (br.), 28.0, 20.6, 14.2.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{30}H_{37}N_4O_8S$ 613.2333; found: 613.2337.

*4-[3-(2-Carboxyphenylsulfanyl)-7-ethoxycarbonyl-1-hydroxyindolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**6k**).* The product was obtained from 4-(3,3-difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 1 equiv), and thiosalicylic acid (100 mg, 1.3 equiv) and isolated by HPLC (40−75% MeCN for 20 min; t_R ∼ 12 min) as yellow crystals (m.p. 235−237 °C). Yield: 50%, 153 mg.

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TLC: R_f = 0.45 (EtOAc/AcOH, 100:1; UV (365 nm), aq $KMnO_4$). LC-MS: t_R ~ 2.7 min.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 13.34 (br. s, 1H [−COO*H*]), 9.37 (br. s, 1H [−O*H*]), 8.36 (s, 1H), 7.98 (d, J = 7.5 Hz, 1H), 7.78 (d, J = 7.4 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 7.4 Hz, 1H), 5.80 (d, J = 7.9 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.75 (br. m, 2H), 3.67 (s, 3H), 2.87 (s, 2H), 2.62 (br. m, 2H), 1.95 (br. m, 2H), 1.39 (m, 2H), 1.35 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.2, 167.4, 165.1, 153.9, 139.7, 138.1, 132.9, 131.8, 127.4, 125.1, 124.6, 121.9, 121.5, 120.5, 118.9, 116.2, 109.1, 108.9, 78.6, 60.4, 51.9, 46.9, 41.0 (br.), 33.3, 32.7, 28.1, 14.3.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{31}H_{37}N_2O_9S$ 613.2220; found: 613.2216.

*3-(4-Methoxyphenylsulfanyl)-1-hydroxy-2-(2-hydroxyethyl)-indolizine-7-carboxylic Acid Ethyl Ester (**6l**).* The product was obtained from *tert*-butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg), ethylisonicotinate (75 mg, 1 equiv), and 4-methoxythiophenol (105 mg, 1.5 equiv) and isolated by HPLC (35−70% MeCN for 20 min; t_R ~ 13 min) as a yellow amorphous solid. Yield: 55%, 107 mg.

TLC: R_f = 0.65 (EtOAc; UV (365 nm)). LC-MS: t_R ~ 2.6 min.

^{1}H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.33 (s, 1H [−O*H*]), 8.26 (br. s, 1H), 8.01 (d, J = 7.5 Hz, 1H), 6.91 (m, 2H), 6.83 (br. m, 2H + 1H), 4.76 (br. s, 1H [−O*H*]), 4.26 (br. q, J = 7.1 Hz, 2H), 3.66 (s, 3H), 3.59 (t, J = 7.3 Hz, 2H), 2.93 (br. t, J = 7.4 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 165.1, 158.2, 137.4, 128.3, 125.6, 121.7, 121.3, 120.6, 120.1, 115.9, 115.2, 108.9, 108.6, 61.0, 60.4, 55.2, 27.8, 14.3.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{22}NO_5S$ 388.1219; found: 388.1213.

*4-[2-Benzo[1,3]oxathiol-(2E)-ylidene-3-(4-ethoxycarbonylpyridin-2-yl)-3-oxopropyl]-N-Boc-4-methoxycarbonylpiperidine (**7**).* *Method A.* 4-[7-Ethoxycarbonyl-1-hydroxy-3-(2-hydroxyphenylsulfanyl)-indolizin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine **6a** (58 mg, 0.1 mmol) was dissolved in DCM (2 mL) and left stirring at r.t. for 3 days in air. Then, LC-MS indicated clean formation of the product and the mixture was concentrated under reduced pressure. The crude product was additionally purified by HPLC (40−80% MeCN for 20 min; t_R ~ 15 min) to afford **7** as a light brown foam. Yield 95%, 55 mg.

Method B. 4-(3-Oxocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **2a** (155 mg, 0.5 mmol) was dissolved in MeCN (5 mL), and ethylisonicotinate (76 mg, 1 equiv) was added to the solution in an argon atmosphere at r.t. Lemon-yellow colorization was observed, indicating the formation of 4-(7-ethoxycarbonyl-1-hydroxy-indolizin-2-ylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine (MW = 460, TLC R_f = 0.5 (EtOAc)). 2-Mercaptophenol (70 mg, 1.1 equiv) was added at r.t. (No reaction was observed after 1 h at r.t. in air.) Then, the reaction flask was equipped with a Liebig condenser and the mixture was heated at 70 °C for 15 h in air. Then, it was concentrated under reduced pressure and the product was isolated by HPLC (40−80% MeCN for 20 min; t_R ~ 15 min) to afford **7** as a light brown foam. Yield 30%, 87 mg.

TLC: R_f = 0.62 (EtOAc). LC-MS: t_R ~ 2.9 min.

^{1}H NMR (300 MHz, DMSO-d_6, 25 °C): δ 8.84 (d, J = 5.0 Hz, 1H), 8.19 (dd, J = 1.7, 0.9 Hz, 1H), 7.98 (dd, J = 5.0, 1.8 Hz, 1H), 7.86 (dd, J = 7.7, 1.4 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.45 (td, J = 7.8, 1.4 Hz, 1H), 7.36 (td, J = 7.5, 1.1 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.66 (br. m, 2H), 3.55 (s, 2H), 3.28 (s, 3H), 2.45 (br. m, 2H), 1.86 (br. m, 2H), 1.36 (t, J = 7.1 Hz, 3H), 1.30 (s, 9H), 1.05 (br. m, 2H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 187.8, 174.2, 172.0, 164.1, 157.7, 154.0, 151.1, 149.2, 138.5, 127.9, 125.5, 124.1, 123.2, 122.7, 111.6, 105.5, 78.6, 61.9, 51.5, 46.9, 41.1, 35.4, 32.8, 28.0, 14.0.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{30}H_{35}N_2O_8S$ 583.2115; found: 583.2110.

*1′-Acetoxy-2,2′-bis-(2-acetoxyethyl)-1-isopropenyloxy-[3,3′]-biindolizinyl-7,7′-dicarboxylic Acid Diethyl Ester (**8-Ac**).* *tert*-Butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg), *N*-methyl-1,3-dihydro-imidazole-2-thione (228 mg, 4.0 equiv), ethylisonicotinate (76 mg, 1 equiv), and water (90 μL, 10 equiv) were dissolved in EtOH (10 mL), and the mixture was heated at 70 °C for 24 h. After that time, the reaction mixture contained a dimer of *N*-methyl-1,3-dihydro-imidazole-2-thione and dimerized (at C3 position) indolizin-1-ol: (1,1′-dihydroxy-2,2′-bis-(2-hydroxyethyl)-[3,3′]biindolizinyl-7,7′-dicarboxylic acid diethyl ester, MW = 496). The latter was roughly isolated by flash chromatography on SiO_2, using EtOAc as an eluent, the solvent was removed in vacuo, and the residue was redissolved in pyridine (1 mL). To this solution, acetic anhydride (0.3 mL) was added slowly upon stirring and the reaction mixture was left at r.t. for 72 h. After full acetylation was reached, the mixture was concentrated in vacuo and the crude product was purified by HPLC (40−70% MeCN for 20 min; t_R ~ 15 min) to afford **8-Ac** as a light yellow amorphous solid. Yield: 30%, 50 mg.

TLC: R_f = 0.63 (EtOAc; UV (365 nm)). LC-MS: t_R ~ 2.7 min.

^{1}H NMR (400 MHz, DMSO-d_6, 50 °C): δ 8.08 (dd, J = 1.9, 1.0 Hz, 2H), 7.34 (dd, J = 7.4, 1.0 Hz, 2H), 7.00 (dd, J = 7.4, 1.9 Hz, 2H), 4.33 (q, J = 7.1 Hz, 4H), 4.01 (m, 2H), 3.92 (m, 2H), 2.45 (s, 6H), 2.74 (m, 4H), 1.73 (s, 6H), 1.32 (t, J = 7.1 Hz, 6H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 170.2, 169.3, 164.8, 128.8, 123.2, 122.6, 120.5, 119.3, 119.2, 110.5, 110.0, 62.4, 60.9, 23.4, 20.6, 20.3, 14.3.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{34}H_{37}N_2O_{12}$ 665.2347; found: 665.2351.

*4-Hydroxy-5-oxo-cyclohepta-1,3,6-trienediazonium Tetrafluoroborate (**9c**).* 5-Aminotropolone (CAS# 7021-46-7) (274 mg, 2 mmol) was dissolved in EtOH (10 mL), and tetrafluoroboric acid (HBF_4 45% in water) (2 mL) was added in one portion. The reaction mixture was cooled in an ice/water bath, and $NaNO_2$ (276 mg, 2 equiv) in water (0.4 mL) was added within 15 min. The mixture was stirred for 0.5 h and then diluted with diethyl ether (120 mL). After stirring with ether for the next 15 min, the formed precipitate was filtered to afford **9c** as light brown crystals. Yield: 95%, 448 mg.

Characterization data corresponds to the previously reported.[21]

*2-Hydroxy-5-pyrrol-1-yl-cyclohepta-2,4,6-trienone (5-pyrrol-1-yl-tropolone) (**9e**).* 5-Aminotropolone (CAS# 7021-46-7) (274 mg, 2 mmol) was dissolved in dioxane (4 mL), and 2,5-dimethoxytetrahydrofuran (265 mg, 1.2 equiv) was added. Then, water (180 μL) and Amberlyst-15 (100 mg) were added, the reaction vessel was sealed, and the mixture was heated at 90 °C for 5 h. Then, the amberlyst beads were filtered off and the filtrate was concentrated under reduced pressure. The crude product was crystallized from MeCN/Et_2O to afford **9e** as a dark yellow solid. Yield: 65%, 243 mg.

Characterization data corresponds to the previously reported.[22]

*Toluene-4-sulfonic Acid 7-Oxo-4-pyrrol-1-ylcyclohepta-1,3,5-trienyl Ester (**9f**).* 2-Hydroxy-5-pyrrol-1-yl-cyclohepta-2,4,6-trienone (5-pyrrol-1-yl-tropolone) **9e** (187 mg, 1 mmol) was dissolved in DCM (1 mL) and pyridine (1 mL). To this solution, 4-toluenesulfonyl chloride (250 mg, 1.3 equiv) was added and the reaction was stirred for 72 h with periodic LC-MS monitoring. After the reaction completion, the mixture was diluted with 2 M HCl (5 mL) and extracted with DCM (20 mL). The organic layer was separated, and volatiles were removed under reduced pressure. The crude product was recrystallized from MeCN/Et_2O to afford **9f** as dark yellow crystals (m.p. 174−176 °C). Yield: 60%, 205 mg.

LC-MS: t_R ~ 2.4 min.

^{1}H NMR (400 MHz, DMSO-d_6, 50 °C): δ 7.85 (m, 2H), 7.78 (dd, J = 13.1, 2.5 Hz, 1H), 7.48 (m, 2H), 7.40 (d, J = 10.5 Hz, 1H), 7.36 (m, 2H), 7.24 (dd, J = 10.5, 2.5 Hz, 1H), 7.20 (d, J = 13.0 Hz, 1H), 6.36 (m, 2H), 2.44 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 50 °C): δ 177.0, 150.7, 145.4, 144.2, 141.0, 133.0, 132.7, 129.8, 129.8 (overlapped), 127.9, 120.0, 118.1, 112.1, 20.9.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{16}NO_4S$ 342.0800; found: 342.0810.

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*4-[7-Ethoxycarbonyl-1-hydroxy-3-(7-oxocyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**10a**).* 4-(3,3-Difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 0.5 mmol, 1 equiv), tropolone tosylate **9d** (CAS 38768-08-0) (152 mg, 1.1 equiv), and water (90 μL, 10 equiv) were dissolved in EtOH (7 mL). The reaction mixture was heated at 70 °C in an argon atmosphere for 24 h. Volatiles were removed under reduced pressure, and the residue was dissolved in DCM (5 mL). Saturated aq $NaHCO_3$ (1 mL) was added, followed by Boc_2O (65 mg, 0.3 mmol, 0.6 equiv) addition, and the mixture was stirred for 10 min at r.t. in an argon atmosphere. Then, the organic layer was separated and concentrated under reduced pressure, and the crude product was purified by HPLC (25−65% MeCN for 20 min; t_R ∼ 17 min) to afford **10a** as a red-purple foam. Yield: 50%, 140 mg.

TLC: R_f = 0.50 (EtOAc; red spot (vis), aq $KMnO_4$). LC-MS: t_R ∼ 2.4 min.

^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ 8.50−6.00 (br. m-s, 8H), 4.3 (br. m, 2H), 3.71 (br. m, 2H), 3.48 (br. s, 3H), 2.64 (br. m, 2H), 1.93 (br. m, 2H), 1.33 (s, 9H), 1.29 (br. t, *J* = 7.0 Hz, 3H), 1.28 (br. m, 2H).

^{13}C{^{1}H} NMR: noninformative due to strong signal broadening. For characterization, compound **10a** was O-acetylated (see compound **10a-Ac**).

HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{31}H_{37}N_2O_8$ 565.2550; found: 565.2552.

*4-[7-Ethoxycarbonyl-1-acetoxy-3-(7-oxocyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**10a-Ac**).* 4-[7-Ethoxycarbonyl-1-hydroxy-3-(7-oxocyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine **10a** (113 mg, 0.2 mmol) was dissolved in THF (4 mL), and 150 μL of pyridine was added at r.t. Then, Ac_2O (80 μL, 0.8 mmol, 4 equiv) was added and the reaction mixture was left stirring for 7 h at r.t. Then, the mixture was concentrated under reduced pressure, and the crude product was purified by HPLC (35−70% MeCN for 20 min; t_R ∼ 14 min) to afford **10a-Ac** as a red-orange foam. Yield: 80%, 97 mg.

TLC: R_f = 0.50 (EtOAc; red-orange spot (vis), aq $KMnO_4$). LC-MS: t_R ∼ 2.5 min.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 7.94 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.60 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.51 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.42 (ddd, *J* = 12.0, 7.9, 1.5 Hz, 1H), 7.29 (m, 1H), 7.23 (m, 1H), 7.15 (d, *J* = 12.3 Hz, 1H), 6.92 (dd, *J* = 7.5, 1.9 Hz, 1H), 4.31 (q, *J* = 7.0 Hz, 2H), 3.58 (br. m, 2H), 3.53 (s, 3H), 2.80 (br. m, 2H), 2.56 (br. m, 2H), 2.40 (s, 3H), 1.76 (br. m, 2H), 1.32 (s, 9H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.22 (br. m, 1H), 1.00 (br. m, 1H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 184.4, 174.3, 169.1, 164.9, 153.9, 141.7, 141.5, 141.4, 136.6, 136.1, 133.9, 129.4, 124.1, 123.4, 121.3, 118.9, 118.0, 115.8, 108.6, 78.7, 60.7, 52.0, 46.8, 41.0 (br.), 33.0, 31.6, 28.0, 20.6, 14.3.

HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{33}H_{39}N_2O_9$ 607.2656; found: 607.2649.

*1-Hydroxy-2-(2-hydroxyethyl)-3-(7-oxocyclohepta-1,3,5-trienyl)-indolizine-7-carboxylic Acid Ethyl Ester (**10b**).* *tert*-Butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (1.5 mmol, 350 mg), ethylisonicotinate (228 mg, 1 equiv), and water (270 μL, 10 equiv) were dissolved in EtOH (15 mL), and tropolone tosylate **9d** (CAS 38768-08-0) (415 mg, 1.0 equiv) was added. The reaction mixture was heated at 70 °C in an argon atmosphere for 24 h. Then, the solvent was removed under reduced pressure and the crude product was purified by HPLC (20−60% MeCN for 20 min; t_R ∼ 10 min) to afford **10b** as a red-purple foam. Yield: 80%, 423 mg.

TLC: R_f = 0.29 (EtOAc; red spot (vis)). LC-MS: t_R ∼ 2.1 min.

^{1}H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.20 (s, 1H [−O*H*]), 8.23 (br. m, 1H), 7.68 (br. m, 1H), 7.38 (br. m, 1H), 7.25 (br. m, 3H), 7.11 (br. m, 1H), 6.68 (br. m, 1H), 4.86 (br. s, 1H [−O*H*]), 4.27 (br. q, 2H), 3.52 (br. t, 2H), 2.66 (br. t, 2H), 1.31 (br. t, 3H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 184.4, 165.3, 141.4, 140.9, 140.4, 137.9, 136.3, 135.3, 133.7, 122.9, 122.8, 120.1, 118.7, 114.4, 113.8, 107.3, 60.7, 60.2, 27.3, 14.4.

HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{20}H_{20}NO_5$ 354.1342; found: 354.1338.

*4-[7-Ethoxycarbonyl-1-hydroxy-3-(7-oxo-4/3-pyrrol-1-ylcyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**11**), 75/25% Mixture of Regioisomers.* 4-(3,3-Difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (166 mg, 0.5 mmol), ethylisonicotinate (75 mg, 0.5 mmol, 1 equiv), toluene-4-sulfonic acid 7-oxo-4-pyrrol-1-ylcyclohepta-1,3,5-trienyl ester **9f** (171 mg, 1.0 equiv), and water (90 μL, 10 equiv) were dissolved in EtOH (7 mL). The reaction mixture was heated at 70 °C in an argon atmosphere for 36 h. Volatiles were removed under reduced pressure, and the residue was dissolved in DCM (5 mL). Saturated aq $NaHCO_3$ (1 mL) was added, followed by Boc_2O (65 mg, 0.3 mmol, 0.6 equiv) addition, and the mixture was stirred for 10 min at r.t. in an argon atmosphere. Then, the organic layer was separated and concentrated under reduced pressure, and the crude product was purified by HPLC (35−75% MeCN for 20 min; t_R ∼ 16 min) to afford mixture **11** as a red-purple foam. Yield: 70%, 220 mg.

TLC: R_f = 0.56 (EtOAc; red spot (vis), fades quickly).

^{1}H NMR and ^{13}C{^{1}H} NMR: noninformative due to strong signal broadening. For characterization and isomers separation, mixture **11** was O-acetylated (see compounds **11a** and **11b**).

*4-[1-Acetoxy-7-ethoxycarbonyl-3-(7-oxo-4-pyrrol-1-ylcyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**11a**) and 4-[1-Acetoxy-7-ethoxycarbonyl-3-(7-oxo-3-pyrrol-1-ylcyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonylpiperidine (**11b**).* The mixture of regioisomers **11** 4-[7-Ethoxycarbonyl-1-hydroxy-3-(7-oxo-4/3-pyrrol-1-ylcyclohepta-1,3,5-trienyl)-indolizin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine (72/28%) (189 mg, 0.3 mmol) was dissolved in THF (4 mL), and 450 μL of pyridine was added. Then, Ac_2O (120 μL, 1.2 mmol, 4 equiv) was added and the reaction mixture was left stirring for 7 h at r.t. in an argon atmosphere. Then, it was concentrated under reduced pressure, and the crude was purified by HPLC (40−70% MeCN for 20 min; t_R ∼ 16 min) to afford a pure mixture of **11a** and **11b** as a red-orange solid. Yield (both isomers): 80%, 161 mg. Then, regioisomers were separated by column chromatography on SiO_2 using EtOAc/hexane (7:3) as an eluent to afford **11a** and **11b** as red-orange foams. Yield (**8a**) = 58%, 116 mg; Yield (**11b**) = 22%, 45 mg.

***11a**, Major Regioisomer (72%).* TLC: R_f = 0.60 (EtOAc/hexane 7:3); orange spot (vis). LC-MS: t_R ∼ 2.7 min.

^{1}H NMR (400 MHz, DMSO-d_6, 50 °C): δ 7.94 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.85 (dd, *J* = 13.0, 2.7 Hz, 1H), 7.59 (d, *J* = 10.0 Hz, 0H), 7.56 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.44 (m, 2H), 7.37 (dd, *J* = 10.1, 2.7 Hz, 1H), 7.26 (d, *J* = 13.0 Hz, 1H), 6.93 (dd, *J* = 7.4, 1.9 Hz, 1H), 6.39 (m, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.61 (br. m, 2H), 3.55 (s, 3H), 2.84 (br. s, 2H), 2.60 (m, 2H), 2.41 (s, 3H), 1.81 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.31 (s, 9H), 1.21 (br. m, 2H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 182.9, 174.3, 169.1, 164.9, 154.0, 144.7, 141.8, 141.4, 137.4, 132.1, 129.5, 124.2, 123.2, 121.4, 120.6, 120.1, 118.9, 118.0, 115.9, 112.5, 108.6, 78.6, 60.7, 52.0, 46.9, 41.1 (br.), 33.1, 31.5, 28.0, 20.6, 14.3.

HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{37}H_{42}N_3O_9$ 672.2922; found: 672.2924.

***11b**, Minor Regioisomer (28%).* TLC: R_f = 0.49 (EtOAc/hexane 7:3); orange spot (vis). LC-MS: t_R ∼ 2.7 min.

^{1}H NMR (400 MHz, DMSO-d_6, 50 °C): δ 7.93 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.80 (d, *J* = 2.2 Hz, 1H), 7.64 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.46 (dd, *J* = 11.4, 9.2 Hz, 1H), 7.41 (dt, *J* = 9.3, 1.7 Hz, 1H), 7.32 (m, 2H), 7.04 (dd, *J* = 11.3, 1.5 Hz, 1H), 6.93 (dd, *J* = 7.4, 1.9 Hz, 1H), 6.32 (m, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.62 (br. m, 2H), 3.50 (s, 3H), 2.82 (br. s, 2H), 2.58 (m, 2H), 2.40 (s, 3H), 1.80 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.33 (s, 9H), 1.20 (br. m, 2H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 70 °C): δ 182.9, 174.1, 168.3, 164.5, 153.6, 142.7, 141.0, 137.5, 137.1, 135.4, 129.3, 124.1, 123.6, 122.6, 121.3, 120.0, 118.5, 118.2, 115.9, 111.4, 108.3, 78.3, 60.2, 51.3, 46.4, 40.7, 32.9, 32.2, 27.7, 20.1, 13.8.

HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{37}H_{42}N_3O_9$ 672.2922; found: 672.2931.

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*4-[7-Ethoxycarbonyl-1-hydroxy-3-(4-hydroxy-5-oxocyclohepta-1,3,6-trienylazo)-indolizin-2-ylmethyl]-N-Boc-4-methoxycarbonyl-piperidine (**12a**).* 4-(3,3-Difluorocycloprop-1-enylmethyl)-*N*-Boc-4-methoxycarbonylpiperidine **1a** (100 mg, 0.3 mmol) and 4-hydroxy-5-oxocyclohepta-1,3,6-trienediazonium tetrafluoroborate **9c** (85 mg, 1.2 equiv) were placed in a reaction vial. Ethylisonicotinate (46 mg, 1 equiv) and water (54 μL, 10 equiv) were dissolved in hexafluoroisopropanol (HFIP) (2 mL) in a separate vial. Then, the solution of ethylisonicotinate was added in the reaction vial under an argon atmosphere at r.t. upon stirring. After 2 h, the solvent was removed under reduced pressure and the residue was washed with diethyl ether (5 mL) and water (1 mL) and crystallized from diethyl ether/MeCN to afford **12a** as a deep blue dye. The product was insoluble in CCl_4. Yield: 65%, 119 mg.

TLC: R_f = 0.40 ((EtOAc/MeOH/DCM/AcOH 60:20:20:1); blue spot (vis)). LC-MS: $t_R \sim 2.5$ min.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 10.20 (br. s, 1H [−O*H*]), 9.85 (br. s, 1H [−O*H*]), 9.40 (br. s, 1H), 8.39 (s, 1H), 7.96 (m, $^3J \sim 11.6$ Hz, 2H), 7.30 (m, $^3J \sim 11.6$ Hz, 2H), 7.20 (d, J = 7.4 Hz, 1H), 4.33 (q, J = 7.0 Hz, 2H), 3.78 (br. m, 2H), 3.43 (s, 3H), 3.19 (s, 2H), 2.63 (br. m, 2H), 2.01 (br. m, 2H), 1.49 (br. m, 2H), 1.35 (t, J = 7.0 Hz, 3H), 1.35 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 174.3, 170.8, 164.3, 154.0, 152.2, 141.8, 132.9, 130.4, 124.8, 124.4, 121.7, 119.2, 112.7, 112.7 (overlapped), 78.6, 61.1, 51.8, 47.2, 41.1 (br.), 32.8, 32.5, 28.0, 14.2.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{31}H_{37}N_4O_9$ 609.2561; found: 609.2550.

*1-Hydroxy-2-(2-hydroxyethyl)-3-(4-hydroxy-5-oxocyclohepta-1,3,6-trienylazo)-indolizine-7-carboxylic Acid Ethyl Ester (**12b**).* *tert*-Butyl-[2-(3,3-difluorocycloprop-1-enyl)-ethoxy]-dimethylsilane **1b** (0.5 mmol, 117 mg) and 4-hydroxy-5-oxocyclohepta-1,3,6-trienediazonium tetrafluoroborate **9c** (118 mg, 1.0 equiv) were placed in a reaction vial. Ethylisonicotinate (76 mg, 1 equiv) and water (90 μL, 10 equiv) were dissolved in hexafluoroisopropanol (HFIP) (2 mL) in a separate vial. Then, the solution of ethylisonicotinate was added in the reaction vial under an argon atmosphere at r.t. upon stirring. After 2 h, the solvent was removed under reduced pressure and the residue was diluted with EtOAc (4 mL). The precipitated product was collected by filtration and additionally washed on a filter with $CHCl_3$ (2 mL), water (1 mL), and diethyl ether (2 mL) to afford **12b** as a deep blue dye. The product was soluble in THF. Yield: 55%, 110 mg.

TLC: R_f = 0.40 (MeOH; blue spot (vis)). LC-MS: $t_R \sim 2.4$ min.

^{1}H NMR (300 MHz, DMSO-d_6, 50 °C): δ 9.87 (br. s, 1H [−O*H*]—observed at 25 °C), 9.33 (d, J = 7.2 Hz, 1H), 8.30 (d, J = 1.7 Hz, 1H), 8.02 (m, $^3J \sim 11.8$ Hz, 2H), 7.34 (m, $^3J \sim 11.8$ Hz, 2H), 7.22 (dd, J = 7.3, 1.7 Hz, 1H), 4.35 (q, J = 7.0 Hz, 2H), 3.70 (t, J = 7.0 Hz, 2H), 3.14 (t, J = 7.0 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 50 °C): δ 170.3, 164.5, 153.0, 141.7, 133.5, 130.54 126.0, 124.7, 124.7 (overlapped), 122.7, 118.9, 112.7, 112.7 (overlapped), 61.2, 60.8, 27.3, 14.3.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{20}N_3O_6$ 398.1352; found: 398.1350.

*(E)-2-((N-Boc-4-(methoxycarbonyl)piperidin-4-yl)methyl)-3-((4,5-dioxocyclohepta-2,6-dien-1-ylidene)hydrazono)-7-(ethoxycarbonyl)-3H-indolizin-4-ium-1-olate (**12a-Ox**).* 4-[7-Ethoxycarbonyl-1-hydroxy-3-(4-hydroxy-5-oxocyclohepta-1,3,6-trienylazo)-indolizin-2-ylmethyl]-*N*-Boc-4-methoxycarbonylpiperidine **12a** (0.2 mmol, 122 mg) was dissolved in THF (15 mL), and diacetoxyiodobenzene (DAIB) (64 mg, 1 equiv) was added portionally as a solution in THF (5 mL) at r.t. upon stirring. After 5 min, the characteristic deep blue color of the starting **12a** disappeared and the solvent was removed under reduced pressure. The residue was suspended in water (0.2 mL) and diethyl ether (3 mL), and the solids were collected by filtration to afford **12a-Ox** as a black amorphous solid. Yield: 65%, 80 mg.

TLC: R_f = 0.27 (EtOAc; dark green spot (vis)). LC-MS: $t_R \sim 2.4$ min.

^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 9.42 (d, J = 5.9 Hz, 1H), 8.44 (d, J = 1.4 Hz, 1H), 8.32 (dd, J = 6.1, 1.4 Hz, 1H), 8.16 (dd, J = 13.0, 1.8 Hz, 1H), 7.39 (dd, J = 12.8, 1.8 Hz, 1H), 6.75 (d, J = 12.8 Hz, 1H), 6.65 (d, J = 13.0 Hz, 1H), 4.56 (q, J = 7.2 Hz, 2H), 3.96 (m, 2H), 3.60 (s, 3H), 3.11 (s, 2H), 2.73 (m, 2H), 2.16 (m, 2H), 1.56 (m, 2H), 1.49 (t, J = 7.1 Hz, 3H), 1.44 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C): δ 186.0, 184.1, 176.1, 175.1, 161.4, 159.4, 155.2, 154.8, 147.9, 143.9, 142.5, 133.6 (br.), 129.4, 128.71, 125.6, 125.6 (overlapped), 118.3, 97.9, 79.4, 63.9, 51.8, 47.9, 41.5 (br.), 33.4, 32.2, 28.4, 14.1.

HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{31}H_{35}N_4O_9$ 607.2405; found: 607.2412.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00747.

Copies of assigned ^{1}H, ^{13}C{^{1}H} NMR, 2D NMR, and LC-MS spectral data (PDF)

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Notes

The authors declare no competing financial interest.

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