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# Lewis Acid Catalyzed Annulation of Donor−Acceptor Cyclopropane and *N*-Tosylaziridinedicarboxylate: One-Step Synthesis of Functionalized 2*H*-Furo[2,3-*c*]pyrroles

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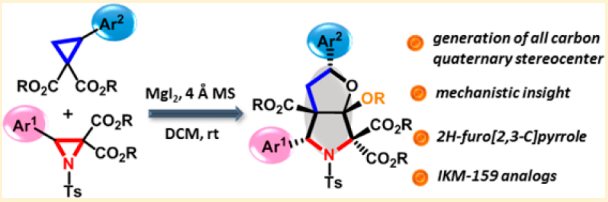
Supporting Information

**ABSTRACT:** An efficient $MgI_2$-catalyzed annulation between donor−acceptor cyclopropane and *N*-tosylaziridinedicarboxylate to access highly substituted 2*H*-furo[2,3-*c*]pyrrole bearing two rings and four stereocenters, including one quaternary carbon stereocenter, has been developed. This methodology can be used for the synthesis of biologically active compounds like IKM-159. This work also offers an insight into the mechanism of the annulation process.




Nitrogen-containing heterocycles have occupied a unique position in naturally derived and pharmaceutically relevant molecules for many years.[1] The 2*H*-furo[2,3-*c*]-pyrroles, in particular, constitute the cyclic core structure present in a class of heterocyclic glutamate analogous known as IKM compounds (Figure 1).[2] Among this class of compounds,

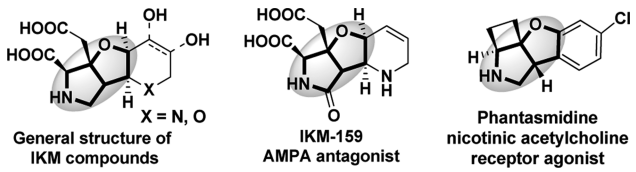


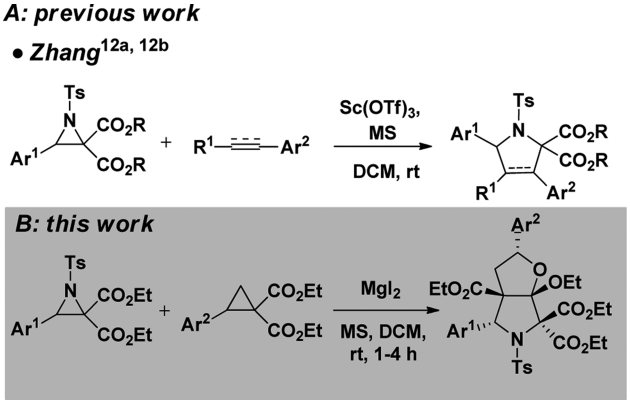

**Figure 1.** Natural products containing 2*H*-furo[2,3-*c*]pyrrole ring.

IKM-159 is most potent and acts as an α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA)[3] receptor-selective antagonist with no inhibitory action on kainate (KA) receptors.[4] In addition, the 2*H*-furo[2,3-*c*]pyrroles provide synthetic access to phantasmidine,[5] a potent nicotinic acetylcholine receptor agonist. Consequently, there is immense interest in the development of novel synthetic methodology for facile access to these moieties.

In general, three-membered rings offer a unique combination of reactivity, synthetic flexibility, and atom economy. Because of their reactivity and ease of preparation, donor−acceptor cyclopropanes (DACs) are currently one of the most versatile three-carbon synthone in organic synthesis. Earlier investigations by several groups revealed its reactivity as a 1,3-dipole for the construction of five-, six-, and seven-membered heterocycles.[6] Nevertheless, it was also found that the 1,3-dipolar nature of DAC makes it vulnerable to undergo dimerization following variety of mechanisms. Tomilov and co-workers reported an interesting cyclodimerization of DAC for the synthesis of substituted 2-oxabicyclo[3.3.0]octanes where the organocatalyst (tetrasubstituted 1-pyrazolines) played a crucial role in stabilizing the reactive open chain intermediate generated from the cyclopropane and also for selective annulation.[7] On the other hand, aziridines are multifaceted building blocks for the synthesis of numerous nitrogen-containing biologically active compounds of contemporary interest.[8] One of the most widely encountered reactions of aziridines is nucleophilic opening of the heterocyclic ring due to the reactivity of the strained C−N bonds.[9] However, C−C bond heterolysis of aziridines[10] is largely unexplored in the literature due to the relatively high energy barrier which is calculated by Huisgen to be ca. 29 kcal $mol^{-1}$.[11]

A recent work by Zhang and co-workers disclosed that metal-catalyzed C−C bond cleavage of *N*-tosylaziridinedicarboxylate leads to [3 + 2] cycloaddition with alkynes/olefins for the synthesis of functionalized 3-pyrrolines/pyrolidines[12a,b] (Scheme 1A).

**Scheme 1. Annulation of *N*-tosylaziridinedicarboxylate**

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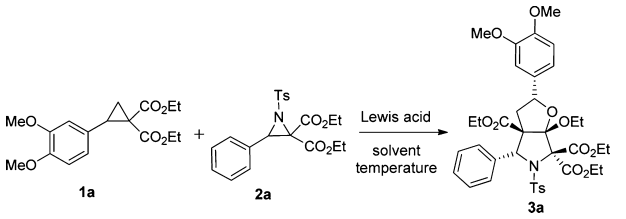
Recently, we explored the possibility of intermolecular cycloaddition reaction between DAC and another strained ring (epoxide) for the synthesis of functionalized tetrahydrofurans.[13] These results encouraged us to investigate the annulations of DAC with *N*-tosylaziridinedicarboxylate which has not been reported in the literature. From the previous reports by the Carreira group[14] and then by Lautens' group,[15] we were concerned about the role of $MgI_2$ for activation as well as ring opening of DAC in making $MgI_2$ the first choice of Lewis acid for the proposed transformation. Gratifyingly, in our study, we found that $MgI_2$ catalyzes the annulation between *N*-tosylaziridinedicarboxylate and DAC under mild conditions (Scheme 1B). The pathway follows selective C−C bond cleavage in situ, providing a highly diastereoselective and facile route to access functionalized 2*H*-furo[2,3-*c*]pyrrole. Furthermore, this protocol gives one-step access to valuable IKM analogues with the generation of a quaternary carbon stereogenic center.

We initiated our investigation with activated cyclopropane **1a** (1 equiv) and 3-phenyl-*N*-tosylaziridinedicarboxylate **2a** (1 equiv) to afford 2*H*-furo[2,3-*c*]pyrrole **3a** (Table 1). In order to optimize the reaction between **1a** and **2a** to give **3a**, various Lewis acids were employed, and $MgI_2$ was found to be the most effective (Table 1). The structure of **3a** was confirmed unambiguously by single-crystal X-ray diffraction analysis (Table 3; also see the Supporting Information).[16] To enhance the product yield, the amount of catalyst was also screened, and the highest yield was obtained when 20 mol % of $MgI_2$ was loaded (Table 1, entry 3). No further enhancement in yield was achieved with higher loading of magnesium iodide (Table 1, entry 4), and in fact, in the case of 100 mol % catalyst loading, rapid decomposition of DAC occurs, leading to a complex mixture (Table 1, entry 5). The other commercially available Lewis acids such as $Mg(OTf)_2$, $Sc(OTf)_3$, $InCl_3$, $Yb(OTf)_3$, $Zn(OTf)_2$, $MgBr_2$, and $ZnI_2$ did not lead to **3a** (Table 1, entries 6−9 and 12−14). In the case of $BF_3{\cdot}OEt_2$, early decomposition of DAC was observed (Table 1, entry 11), and use of $GaCl_3$ produced **3a** in trace amounts (Table 1, entry 10).

Solvents were also optimized to check the reaction feasibility as well as yield, and it was observed that reaction proceeded well with $CCl_4$, toluene, and acetonitrile at the expense of longer reaction time (Table 2).

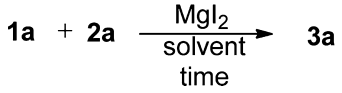
**Table 1. Optimization of Reaction Conditions between 1a and 2a**[a]




| entry | Lewis acid | LA (mol %) | *T* (°C) | solvent | isolated yield (%) |
|---|---|---|---|---|---|
| 1 | $MgI_2$ | 5 | 25 | $CH_2Cl_2$ | 25 |
| 2 | $MgI_2$ | 10 | 25 | $CH_2Cl_2$ | 40 |
| **3** | **$MgI_2$** | **20** | **25** | **$CH_2Cl_2$** | **65** |
| 4 | $MgI_2$ | 50 | 25 | $CH_2Cl_2$ | 65 |
| 5 | $MgI_2$ | 100 | 25 | $CH_2Cl_2$ | c.m.[c] |
| 6 | $Mg(OTf)_2$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 7 | $Sc(OTf)_3$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 8 | $InCl_3$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 9 | $Yb(OTf)_3$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 10 | $GaCl_3$ | 20 | 25 | $CH_2Cl_2$ | 20 |
| 11 | $BF_3OEt_2$ | 20 | 25 | $CH_2Cl_2$ | c.m.[c] |
| 12 | $Zn(OTf)_2$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 13 | $MgBr_2$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 14 | $ZnI_2$ | 20 | 25 | $CH_2Cl_2$ | n.r.[b] |
| 15 | $MgBr_2$ + KI | (20 + 20) | 25 | $CH_2Cl_2$ | 60 |

[a]Reactions were carried out with 1 equiv of **1a** and 1 equiv of **2a** in the presence of molecular sieves (4 Å) in DCM. [b]n.r. = no reaction. [c]c.m. = complex mixture.

**Table 2. Solvent Variation**[a]




| entry | $MgI_2$ (mol %) | solvent | time (h) | isolated yield (%) |
|---|---|---|---|---|
| 1 | 20 | $CH_2Cl_2$ | 2 | 65 |
| 2 | 20 | $ClCH_2CH_2Cl$ | 2 | 65 |
| 3 | 20 | $CCl_4$ | 3 | 60 |
| 4 | 20 | THF | 6 | n.r.[b] |
| 5 | 20 | $CH_3CN$ | 8 | 50 |
| 6 | 20 | toluene | 5 | 60 |

[a]Reactions were carried out with 1 equiv of **1a** and 1 equiv of **2a** in the presence of molecular sieves (4 Å) in DCM. [b]No reaction.

With the optimized reaction conditions (Table 1, entry 3), the scope and limitations of the methodology to access 2*H*-furo[2,3-*c*]pyrrole were explored with various DACs and *N*-tosylaziridinedicarboxylates, and the results are shown in Table 3. Initially, we employed relatively more activated DAC bearing electron-donating functionality in the vicinal phenyl ring and obtained the desired product in good isolated yield (Table 3, **3a−e**). It is noteworthy that with the increase of electron-donating substituents, on one end of DAC, reaction rates were significantly increased (Table 3, **3b−d**). 2-Furyl-substituted DAC was the first to produce the annulated product (in 1 h, Table 3, **3d**). Interestingly, with either 2,4,6-trimethoxyphenyl-substituted or mesityl-substituted DAC, the desired annulated product was not formed. This may be due to steric hindrance by ortho substituents present in the phenyl ring. We next investigated less electronically enriched cyclopropane to assess their effects on the annulation process. Not surprisingly, they showed less efficiency. Phenyl-substituted DAC failed to undergo annulations at room temperature, only yielding the desired product when the reaction was carried out at 80 °C in DCE (Table 3, **3f**). *p*-Tolyl-substituted DAC also only yielded the desired product at elevated temperature (Table 3, **3g**).

Next, we examined the substrate scope of *N*-tosylaziridine-dicarboxylate to form 2*H*-furo[2,3-*c*]pyrrole (Table 3). Encouraged by the results obtained in the case of cyclopropane bearing electron-donating substituents, we preferentially used electronically enriched *N*-tosylaziridinedicarboxylate as the first variant in the annulation and obtained the desired products in good isolated yield (Table 3, **3h** and **3i**). This was not the case with diethyl 3-(4-nitrophenyl)-1-tosylaziridine-2,2-dicarboxylate, which failed to give the desired product. Likewise, we obtained our product in the case of 3-(4-chlorophenyl)-1-tosylaziridine-2,2-dicarboxylate (Table 3, **3j**). The annulation also proceeded well with naphthyl substituent (Table 3, **3k**). In both cases of substrate variation, the product was formed in


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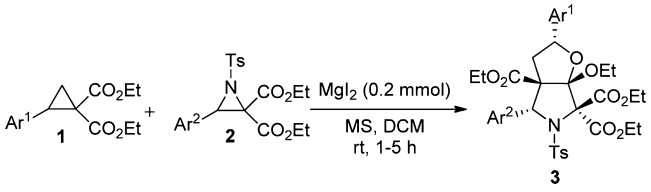
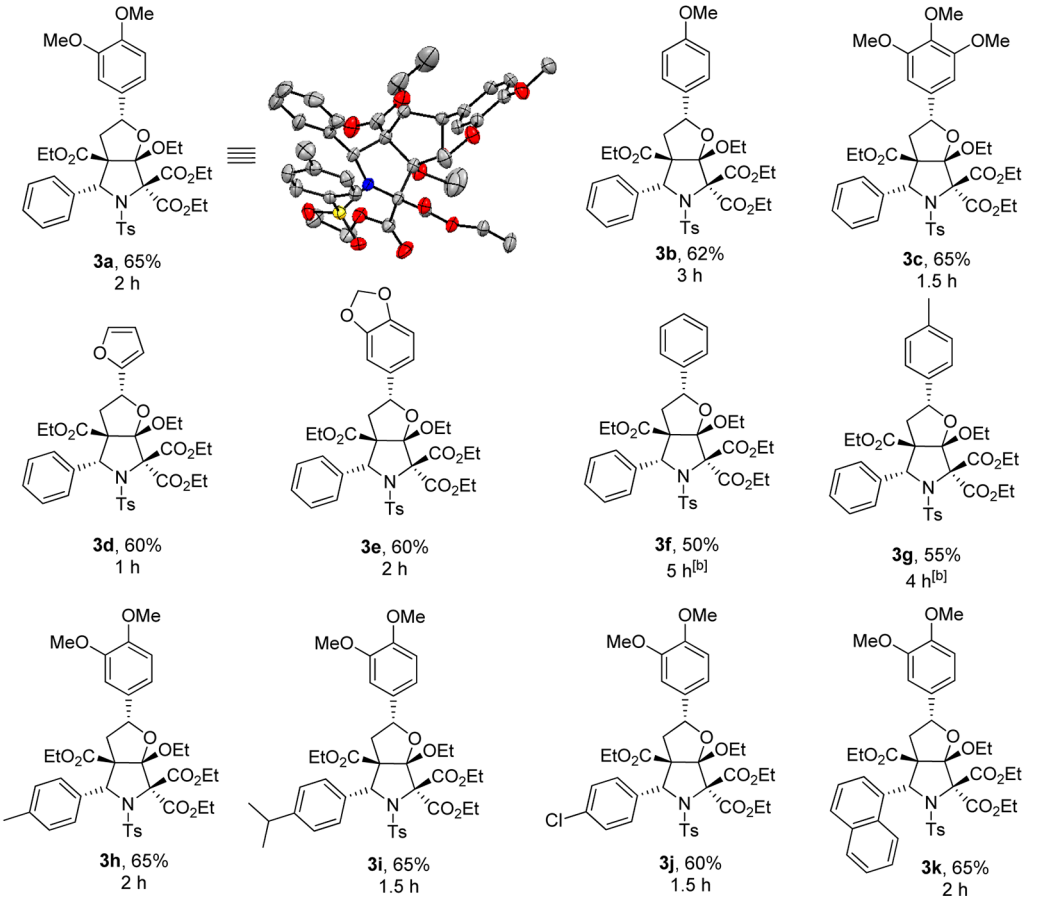
**Table 3. Scope of the Annulation Reaction**[a]



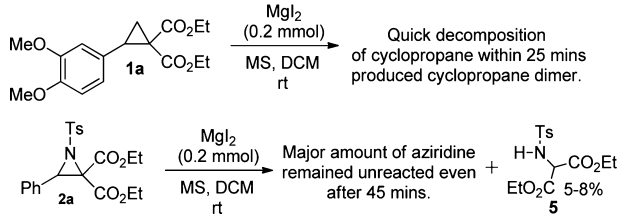




[a]Unless otherwise specified, all reactions were carried out in DCM at 25 °C with 1 equiv of both DAC and *N*-Ts-aziridinedicarboxylate in the presence of $MgI_2$ (20 mol %) and 4 Å MS; isolated yields are reported. [b]Reactions were carried out in DCE in 80 °C while the other conditions remained the same.

good yields (50%−65%) along with recovered starting cyclopropane (5−10%).

Though it is very difficult at this stage to state the actual mechanism of this unique annulation, to ascertain a plausible mechanism several experiments were carried out as described. The reaction proceeds quite well with $MgI_2$ (Table 1, entry 3) but fails with $MgBr_2$ (Table 1, entry 13), clearly suggesting that iodide plays a crucial role in the initiation of the reaction. With the use of another metal iodide, $ZnI_2$ instead of $MgI_2$, the annulation reaction did not proceed (Table 1, entry 14). This result prompted us to investigate the annulation process with $MgBr_2$ and KI in combination as catalysts. Under these conditions, we found that the annulated product was formed in good yield (Table 1, entry 15). Accordingly, it can be stated that both $Mg^{2+}$ and $I^-$ are essential in the initiation step. We further proceeded to identify any of the key intermediates generated during the reaction. Both DAC and *N*-tosylaziridinedicarboxylate were separately treated with $MgI_2$ (Scheme 2). Rapid decomposition of DAC was noticed while *N*-tosylaziridinedicarboxylate remained largely unreacted, producing only a trace amount of open-chain product **5**[12b] (caused by nucleophilic attack of $H_2O$). This indicates that the reaction is initiated by DAC.

**Scheme 2. Experiments in Support of Mechanism**




On the basis of our investigation, a plausible mechanism is proposed (as shown in Scheme 3).

Initially, DAC undergoes rapid nucleophilic ring opening assisted by iodide to form open-chain intermediate **I**. The open-chain intermediate **I** is highly unstable and interacts with



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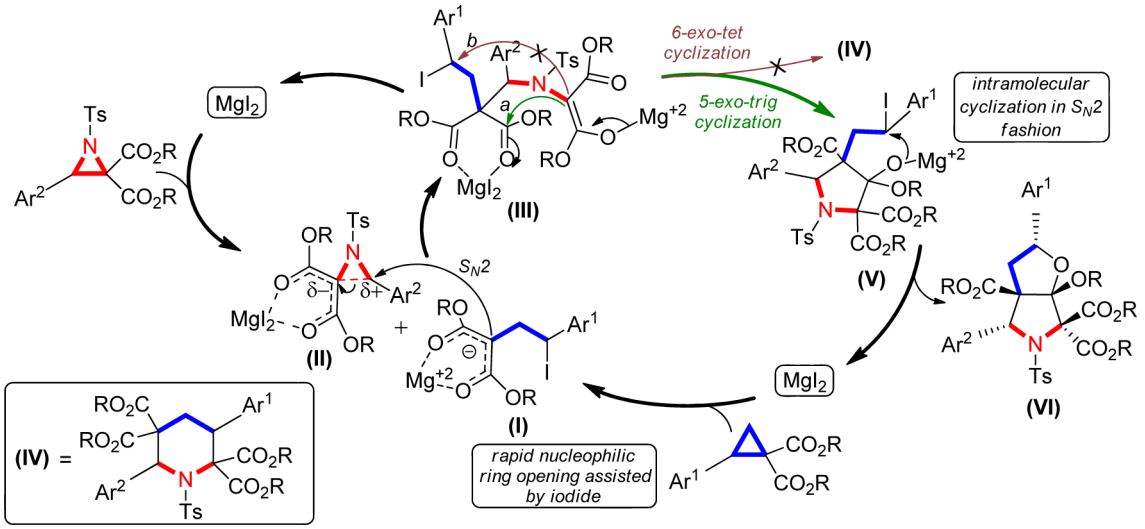
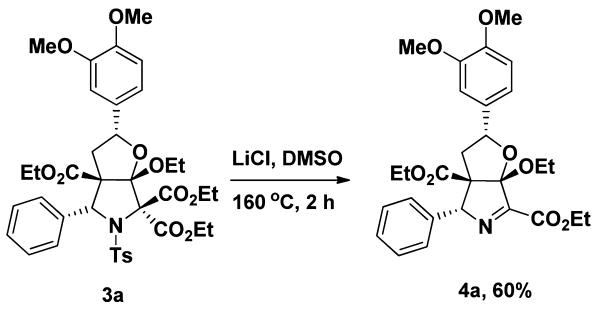
**Scheme 3. Plausible Mechanism**




simultaneously activated aziridine **II** in $S_N2$ fashion to give the key intermediate **III**. Consequently, two possible pathways open for cyclization according to Baldwin's rule[17] from intermediate **III**. However, pathway b (*6-exo-tet* cyclization) is likely to be disfavored due to faster formation of the five-membered ring. Subsequently, it follows pathway a (*5-exo-trig* cyclization route) to attack one of the carboxylate electrophilic centers of DAC positioned in proximity. As soon the aziridine ester anion attacks the carbonyl, it achieves a more favorable conformation (intermediate **V**) to undergo intramolecular cyclization in $S_N2$ fashion, leading to the formation of 2*H*-furo[2,3-*c*]pyrrole (**VI**).

The susceptibility of 2*H*-furo[2,3-*c*]pyrrole for further synthetic application is assessed next, for which we have checked the decarboxylation reaction. In the presence of LiCl at 160 °C, 2*H*-furo[2,3-*c*]pyrrole easily gave **4a** in good isolated yield (60%) after the selective mono-decarboxylation and tosyl group deprotection[18] (Scheme 4).

**Scheme 4. Mono-decarboxylation and Tosyl Deprotection**



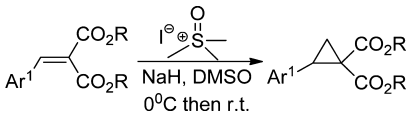

## CONCLUSION

In conclusion, we have developed a novel annulation reaction that employs intramolecular cyclization between donor–acceptor cyclopropane and *N*-tosylaziridinedicarboxylate to obtain 2*H*-furo[2,3-*c*]pyrrole in high yield. In this process, a new kind of reactivity of *N*-tosylaziridinedicarboxylate is demonstrated that follows intramolecular cyclization rather than formal [3 + 3]-cycloaddition. The one-step, highly diastereoselective synthetic protocol reported here will be of immense application in the synthesis of biologically active compounds like IKM-159.

## EXPERIMENTAL SECTION

**General Information.** All reactions were carried out under nitrogen atmosphere in oven-dried glassware. All solvents and reagents were obtained from commercial sources and were purified using the standard procedure prior to use. Powdered molecular sieves 4 Å (MS 4 Å) were dried at 200 °C under vacuum prior to use. The developed chromatogram was analyzed by UV lamp (254 nm) or *p*-anisaldehyde solution. Products were purified by flash chromatography on silica gel (mesh size 230–400). The $^1$H NMR and $^{13}$C NMR spectra were recorded in $CDCl_3$. Chemical shifts of $^1$H and $^{13}$C NMR spectra are expressed in parts per million (ppm). All coupling constants are absolute values and are expressed in hertz. The description of the signals includes the following: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, dt = doublet of triplet, q = quartet, br = broad, and m = multiplet.

**General Procedure for Synthesis of Cyclopropane 1,1-Diester Derivatives.**[19]




Sodium hydride (2.5 equiv) was taken in a two-neck, round-bottom flask and washed three to four times with dry hexane. Trimethylsulfoxonium iodide (2.5 equiv) was added and the mixture suspended in anhydrous DMSO under nitrogen atmosphere. The mixture was cooled to 0 °C and stirred for 30 min. A solution of the appropriate benzylidene malonate (1 equiv) in anhydrous DMSO was added, and the reaction mixture was allowed to stir at room temperature. Upon completion of the reaction (as determined by TLC analysis), the solution was poured onto ice and extracted with diethyl ether. The combined organic layers were washed once with brine, dried over sodium sulfate, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column chromatography with EtOAc/hexane as eluent.

*Diethyl 2-(3,4-Dimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**1a**).*[19d] Diethyl 2-(3,4-dimethoxybenzylidene)malonate (0.5 g, 1.62 mmol), NaH (0.1 g, 4.06 mmol), trimethylsulfoxonium iodide (0.9 g, 4.06 mmol), dry DMSO (10 mL), reaction time = 6 h, **1a** (0.37 g, yield 72%), colorless oil. $^1$H NMR: $\delta$ 6.76 (m, 3H), 4.23 (q, $J$ = 7.12 Hz, 2H), 3.89 (q, $J$ = 7.12 Hz, 2H), 3.86 (s, 3H), 3.84(s, 3H), 3.18 (m, 1H), 2.13 (m, 1H), 1.68 (m, 1H), 1.3 (t, $J$ = 7.12 Hz, 3H), 0.93 (t, $J$ = 7.12 Hz, 3H).



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*Diethyl 2-(4-Methoxyphenyl)cyclopropane-1,1-dicarboxylate (**1b**).*[19d] Diethyl 2-(4-methoxybenzylidene)malonate (0.5 g, 1.80 mmol), NaH (0.1 g, 4.50 mmol), trimethylsulfoxonium iodide (1.0 g, 4.50 mmol), dry DMSO (11 mL), reaction time = 5 h, **1b** (0.39 g, yield 74%), colorless oil. $^1$H NMR: $\delta$ 7.14 (d, $J$ = 8.64 Hz, 2H), 6.79 (d, $J$ = 8.64 Hz, 2H), 4.04 (q, $J$ = 7.12 Hz, 2H), 3.87 (q, $J$ = 7.12 Hz, 2H), 3.72 (s, 3H), 3.33−3.37 (m, 1H), 2.29−2.32 (m, 1H), 2.24−2.27 (m, 1H), 1.11 (t, $J$ = 7.12 Hz, 3H), 0.72 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-(3,4,5-Trimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**1c**).*[19d] Diethyl 2-(3,4,5-trimethoxybenzylidene)malonate (0.5 g, 1.47 mmol), NaH (0.09 g, 3.67 mmol), trimethylsulfoxonium iodide (0.8 g, 3.67 mmol), dry DMSO (9 mL), reaction time = 5h, **1c** (0.36 g, yield 70%), colorless oil. $^1$H NMR: $\delta$ 6.43 (s, 2H), 4.13 (q, $J$ = 7.12 Hz, 2H), 3.89 (q, $J$ = 7.12 Hz, 2H), 3.83(s, 6H), 3.81 (s, 3H), 3.34−3.36 (m, 1H), 2.22−2.25 (m, 1H), 1.66−1.69 (m, 1H), 1.28 (t, $J$ = 7.12 Hz, 3H), 0.92 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-(2,4,6-Trimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**1d**).*[19d] Diethyl 2-(2,4,6-trimethoxybenzylidene)malonate (0.5 g, 1.47 mmol), NaH (0.09 g, 3.67 mmol), trimethylsulfoxonium iodide (0.8 g, 3.67 mmol), dry DMSO (9 mL), reaction time =7 h, **1d** (0.34 g, yield 65%), colorless oil. $^1$H NMR: $\delta$ 6.04 (s, 2H), 4.22 (q, $J$ = 7.12 Hz, 2H), 3.84 (q, $J$ = 7.12 Hz, 2H), 3.76 (s, 3H), 3.74(s, 6H), 2.81−2.83 (m, 1H), 2.35−2.37 (m, 1H), 1.74−1.77 (m, 1H), 1.28 (t, $J$ = 7.12 Hz, 3H), 0.95 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-(Furan-2-yl)cyclopropane-1,1-dicarboxylate (**1e**).*[19] Diethyl 2-(furan-2-ylmethylene)malonate (0.5 g, 2.09 mmol), NaH (0.12 g, 5.22 mmol),trimethylsulfoxonium iodide (1.18 g, 5.22 mmol), dry DMSO (12 mL), reaction time = 5 h, **1e** (0.36 g, yield 69%), colorless oil. $^1$H NMR: $\delta$ 7.27−7.29 (m, 1H), 6.27−6.28 (m, 1H), 6.11−6.12 (m, 1H), 4.24 (q, $J$ = 7.12 Hz, 2H), 4.02 (q, $J$ = 7.12 Hz, 2H), 3.06−3.10 (m, 1H), 2.04−2.07 (m, 1H), 1.73−1.76 (m, 1H), 1.28 (t, $J$ = 7.12 Hz, 3H), 1.07 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-Mesitylcyclopropane-1,1-dicarboxylate (**1f**).*[19] Diethyl 2-(2,4,6-trimethylbenzylidene)malonate (0.5 g, 1.72 mmol), NaH (0.1 g, 4.30 mmol), trimethylsulfoxonium iodide (0.94 g, 4.30 mmol), dry DMSO (10 mL), reaction time = 5 h, **1f** (0.36 g, yield 70%), colorless oil. $^1$H NMR: $\delta$ 6.76 (s, 2H), 4.27 (q, $J$ = 7.12 Hz, 2H), 3.79−3.82 (m, 2H), 3.02−3.04 (m, 1H), 2.37−2.39 (m, 1H), 2.32 (s, 6H), 2.21 (s, 3H), 1.90−1.92 (m, 1H), 1.31 (t, $J$ = 7.12 Hz, 3H), 0.87 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-(Benzo[1−2]dioxol-5-yl)cyclopropane-1,1-dicarboxylate (**1g**).*[19] Diethyl 2-(benzo[*d*][1,3]dioxol-5-ylmethylene)malonate (0.5 g, 1.71 mmol), NaH (0.1 g, 4.27 mmol), trimethylsulfoxonium iodide (0.93 g, 4.27 mmol), dry DMSO (10 mL), reaction time = 5 h, **1g** (0.38 g, yield 73%), colorless oil. $^1$H NMR: $\delta$ 6.65−6.67 (m, 3H), 5.9 (s, 2H), 4.19 (q, $J$ = 7.12 Hz, 2H), 3.87−3.90 (m, 2H), 3.10−3.13 (m, 1H), 2.07−2.11 (m, 1H), 1.62−1.66 (m, 1H), 1.27 (t, $J$ = 7.12 Hz, 3H), 0.95 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-Phenylcyclopropane-1,1-dicarboxylate (**1h**).*[19d] Diethyl 2-benzylidenemalonate (0.5 g, 2.01 mmol), NaH (0.12 g, 5.02 mmol), trimethylsulfoxonium iodide (1.1 g, 5.02 mmol), dry DMSO (12 mL), reaction time = 4 h, **1h** (0.35 g, yield 67%), colorless oil. $^1$H NMR: $\delta$ 7.19−7.31 (m, 5H), 4.12 (q, $J$ = 7.12 Hz, 2H), 3.81 (q, $J$ = 7.12 Hz, 2H), 3.11−3.20 (m, 1H), 2.16−2.19 (m, 1H), 1.66−1.73 (m, 1H), 1.27 (t, $J$ = 7.12 Hz, 3H), 0.84 (t, $J$ = 7.12 Hz, 3H).

*Diethyl 2-(p-Tolyl)cyclopropane-1,1-dicarboxylate (**1i**).*[19d] Diethyl 2-(4-methylbenzylidene)malonate (0.5 g, 1.90 mmol), NaH (0.11 g, 4.75 mmol), trimethylsulfoxonium iodide (1.04 g, 4.75 mmol), dry DMSO (12 mL), reaction time = 4 h, **1i** (0.36 g, yield 70%), colorless oil. $^1$H NMR: $\delta$ 7.10−7.16 (m, 4H), 4.02 (q, $J$ = 7.12 Hz, 2H), 3.83 (q, $J$ = 7.12 Hz, 2H), 3.34−3.38 (m, 1H), 2.36−2.38 (m, 1H), 2.32 (s, 3H), 2.24−2.27 (m, 1H), 1.12 (t, $J$ = 7.12 Hz, 3H), 0.72 (t, $J$ = 7.12 Hz, 3H).

**General Procedure for Synthesis of *N*-Tosylaziridine-2,2-dicarboxylate.**[20] Aziridines were prepared according to the literature.[20]

*Diethyl 3-Phenyl-1-tosylaziridine-2,2-dicarboxylate (**2a**).*[20] *N*-Benzylidene-4-methylbenzenesulfonamide (0.5 g, 1.92 mmol), 2-bromomalonate (0.5 g, 2.11 mmol), NaH (0.05 g, 2.11 mmol), dry $CH_3CN$ (19 mL), reaction time = 12 min, **2a** (0.67 g, yield 83%), colorless oil. $^1$H NMR: $\delta$ 7.96 (d, $J$ = 7.6 Hz, 2H), 7.34 (d, $J$ = 7.6 Hz, 2H), 7.20−7.27 (m, 5H), 4.89 (s, 1H), 4.36−4.42 (m, 2H), 3.86−4.00 (m, 2H), 2.43 (s, 3H), 1.36 (t, $J$ = 7.0 Hz, 3H), 0.87 (t, $J$ = 6.8 Hz, 3H).

*Diethyl 3-(p-Tolyl)-1-tosylaziridine-2,2-dicarboxylate (**2b**).*[20] 4-Methyl-*N*-(4-methylbenzylidene)benzenesulfonamide (0.5 g, 1.82 mmol), 2-bromomalonate (0.47 g, 2.0 mmol), NaH (0.05 g, 2.0 mmol), dry $CH_3CN$ (18 mL), reaction time = 10 min, **2b** (0.6 g, yield 77%), colorless oil $^1$H NMR: $\delta$ 7.95 (d, $J$ = 8.0 Hz, 2H), 7.34 (d, $J$ = 8.0 Hz, 2H), 7.12 (d, $J$ = 8.0 Hz, 2H), 7.05 (d, $J$ = 8.0 Hz, 2H), 4.85 (s, 1 H), 4.32−4.44 (m, 2H), 3.97 (q, $J$ = 7.0 Hz, 2H), 2.45 (s, 3H), 2.28 (s, 3H), 1.37 (t, $J$ = 7.0 Hz, 3H), 0.93 (t, $J$ = 7.0 Hz, 3H).

*Diethyl 3-(4-Isopropylphenyl)-1-tosylaziridine-2,2-dicarboxylate (**2c**).*[20] *N*-(4-Isopropylbenzylidene)-4-methylbenzenesulfonamide (0.5 g, 1.65 mmol), 2-bromomalonate (0.43 g, 1.81 mmol), NaH (0.04 g, 1.81 mmol), dry $CH_3CN$ (16 mL), reaction time = 10 min, **2c** (0.6 g, yield 79%), colorless oil. $^1$H NMR: $\delta$ 7.96 (d, $J$ = 7.6 Hz, 2H), 7.34 (d, $J$ = 7.6 Hz, 2H), 7.15 (d, $J$ = 7.6 Hz, 2H), 7.10 (d, $J$ = 7.6 Hz, 2H), 4.87 (s, 1H), 4.36−4.43 (m, 2H), 4.07−4.17 (m, 1H), 3.89−4.01 (m, 2H), 2.44 (s, 3H), 1.36 (t, $J$ = 6.8 Hz, 3H), 1.17 (d, $J$ = 6.4 Hz, 6H), 0.84 (t, $J$ = 6.8 Hz, 3H).

*Diethyl 3-(4-Nitrophenyl)-1-tosylaziridine-2,2-dicarboxylate (**2d**).*[20] 4-Methyl-*N*-(4-nitrobenzylidene)benzenesulfonamide (0.5 g, 1.64 mmol), 2-bromomalonate (0.43 g, 1.80 mmol), NaH (0.04 g, 1.80 mmol), dry $CH_3CN$ (16 mL), reaction time = 17 min, **2d** (0.63 g, yield 84%), colorless oil. $^1$H NMR: $\delta$ 8.14 (d, $J$ = 7.6 Hz, 2H), 7.95 (d, $J$ = 7.6 Hz, 2H), 7.45 (d, $J$ = 7.6 Hz, 2H), 7.38 (d, $J$ = 7.6 Hz, 2H), 4.92 (s, 1H), 4.35−4.47 (m, 2H), 3.90−4.04 (m, 2H), 2.47 (s, 3H), 1.38 (t, $J$ = 6.6 Hz, 3H), 0.95 (t, $J$ = 6.6 Hz, 3H).

*Diethyl 3-(4-Chlorophenyl)-1-tosylaziridine-2,2-dicarboxylate (**2e**).*[20] *N*-(4-Chlorobenzylidene)-4-methylbenzenesulfonamide (0.5 g, 1.70 mmol), 2-bromomalonate (0.44 g, 1.87 mmol), NaH (0.04 g, 1.87 mmol), dry $CH_3CN$ (17 mL), reaction time = 15 min, **2e** (0.62 g, yield 80%), colorless oil. $^1$H NMR (400 MHz): $\delta$ 7.94 (d, $J$ = 8.0 Hz, 2H), 7.36 (d, $J$ = 8.0 Hz, 2H), 7.24 (d, $J$ = 8.4 Hz, 2H), 7.19 (d, $J$ = 8.4 Hz, 2H), 4.83 (s, 1H), 4.32−4.42 (m, 2H), 3.94−4.11 (m, 2H), 2.45 (s, 3H), 1.37 (t, $J$ = 7.0 Hz, 3H), 0.95 (t, $J$ = 7.2 Hz, 3H).

*Diethyl 3-(Naphthalen-1-yl)-1-tosylaziridine-2,2-dicarboxylate (**2f**).*[20] 4-Methyl-*N*-(naphthalen-1-ylmethylene)benzenesulfonamide (0.5 g, 1.61 mmol), 2-bromomalonate (0.43 g, 1.77 mmol), NaH (0.04 g, 1.77 mmol), dry $CH_3CN$ (16 mL), reaction time = 10 min, **2f** (0.61 g, yield 82%), colorless oil. $^1$H NMR: $\delta$ 8.24 (d, $J$ = 8.0 Hz, 1H), 8.03 (d, $J$ = 8.4 Hz, 2H), 7.83 (d, $J$ = 8.0 Hz, 1H), 7.74−7.78 (m, 1H), 7.55−7.60 (m, 1H), 7.48−7.52 (m, 1 H), 7.39 (d, $J$ = 8.0 Hz, 2H), 7.28−7.33 (m, 2H), 5.30 (s, 1H), 4.48 (q, $J$ = 7.2 Hz, 2H), 3.70 (q, $J$ = 7.2 Hz, 2H), 2.47 (s, 3H), 1.42 (t, $J$ = 7.2 Hz, 3H), 0.45 (t, $J$ = 7.2 Hz, 3H).

**Representative Procedure for Cycloaddition Reaction of DAC and *N*-Tosylaziridine-2,2-dicarboxylate.** To a round-bottom flask equipped with a magnetic stir bar were added with donor−acceptor cyclopropane (1 equiv), *N*-tosylaziridine-2,2-dicarboxylate (1 equiv), activated 4 Å MS (200 mol %), and $MgI_2$ (0.2 equiv) under nitrogen atmosphere. DCM was added as a solvent to the reaction mixture and stirred at room temperature until completion of the reaction (as monitored by TLC). The reaction mixture was passed through a small pad of Celite, and solvent was evaporated on a rotary evaporator. The crude mixture was further purified by flash column chromatography on silica gel with EtOAc/hexane as eluent.

*Triethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-phenyl-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3a**).* Reaction time: 2 h, **1a** (0.25 g, 0.77 mmol), **2a** (0.32 g, 0.77 mmol), white solid, mp 127 °C, 0.37 g, yield 65%, $R_f$ value 0.25 (EtOAc/Hexane) = 2:10 (v/v).

***3a**:* $^1$H NMR (400 MHz): $\delta$ 7.52 (d, $J$ = 8.2 Hz, 2H), 7.26 (s, 1H). 7.07−6.99 (m, $J$ = 8.5, 7.4, 6.9 Hz, 6H), 6.77 (s, 3H), 6.56 (s, 1H), 5.22 (dd, $J$ = 10.5, 4.1 Hz, 1H), 4.43−4.37 (m, $J$ = 7.3, 6.9, 3.2 Hz, 4H), 4.29−4.22 (m, $J$ = 5.9, 4.7, 3.6 Hz, 2H), 4.04−3.99 (m, $J$ = 6.8, 3.0 Hz, 1H), 3.98 (s, 3H), 3.86 (s, 3H), 3.83−3.77 (m, $J$ = 7.0, 2.8 Hz, 1H), 2.37 (s, 3H), 2.08 (dd, $J$ = 13.3, 2.1 Hz, 1H), 1.92 (dd, $J$ = 13.1, 4.2 Hz, 1H), 1.50 (t, $J$ = 7.5 Hz, 3H), 1.35 (t, $J$ = 7.2 Hz, 3H), 1.30 (t,



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$J$ = 7.1 Hz, 3H), 1.10 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.5, 166.2, 165.9 (3 −C═O, C-18, C-19, C-20), 149.3, 148.9, 143.4, 138.7, 134.5, 132.0, 129.8, 129.7, 128.3, 127.7, 118.7, 114.8 (C-17), 110.4, 109.2, 84.4 (C-13), 83.0 (C-15), 69.8 (C-16), 67.0 (C-14), 62.3, 61.9, 61.7, 60.2 (4 −$CH_2$, C-9, C-10, C-11, C-12), 56.0, 55.9 (2 −$OCH_3$, C-7, C-8), 44.5 (−$CH_2$, C-6), 21.5 (−$CH_3$, C-5), 15.4, 14.3, 14.1, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2959, 2923, 2853, 1760, 1749, 1734, 1595, 1519, 1337, 1238, 1161, 1026, 922, 869 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + H]$^+$ calcd for $C_{38}H_{46}NO_{12}S$ 740.2741, found 740.2735

*Triethyl 6a-Ethoxy-2-(4-methoxyphenyl)-4-phenyl-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3b**).* Reaction time: 3 h, **1b** (0.2 g, 0.68 mmol), **2a** (0.28 g, 0.68 mmol), white solid, mp 118 °C, 0.3 g, yield 62%, $R_f$ value 0.39 (EtOAc/hexane) = 2:10 (v/v).

***3b***. $^1$H NMR (400 MHz): $\delta$ 7.42 (d, $J$ = 8.3 Hz, 2H), 7.21 (d, $J$ = 8.5 Hz, 4H), 7.08−6.98 (m, $J$ = 8.2, 7.1, 6.8 Hz, 4H), 6.86 (d, $J$ = 8.6 Hz, 3H), 6.55 (s, 1H), 5.20 (dd, $J$ = 10.9, 4.5 Hz, 1H), 4.43−4.33 (m, $J$ = 7.0, 6.8, 3.9 Hz, 4H), 4.29−4.19 (m, $J$ = 6.3, 3.7, 3.4 Hz, 2H), 4.02−3.94 (m, $J$ = 6.7, 2.4 Hz, 1H), 3.81−3.71 (m, $J$ = 6.1, 2.7 Hz, 1H), 3.79 (s, 3H), 2.36 (s, 3H), 2.02 (dd, $J$ = 11.3, 1.5 Hz, 1H), 1.89 (dd, $J$ = 13.3, 4.7 Hz, 1H), 1.49 (t, $J$ = 7.2 Hz, 3H), 1.34 (t, $J$ = 7.0 Hz, 3H), 1.30 (t, $J$ = 7.0 Hz, 3H), 1.08 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.6, 166.0, 166.0 (3 −C═O, C-17, C-18, C-19), 159.6, 143.3, 138.4, 134.9, 131.0, 129.8, 129.7, 128.4, 127.7, 127.7, 114.6 (C-16), 113.9, 84.0 (C-12), 82.8 (C-14), 69.8 (C-15), 67.1(C-13), 62.4, 61.9, 61.7, 60.1 (4 −$CH_2$, C-8, C-9, C-10, C-11), 55.3 (−$OCH_3$, C-7), 44.1 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.5, 14.3, 14.1, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2983, 1758, 1730, 1609, 1512, 1456, 1345, 1261, 1159, 1034, 746 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{37}H_{43}NO_{11}SNa$ 732.2455, found 732.2373

*Triethyl 6a-Ethoxy-4-phenyl-5-tosyl-2-(3,4,5-trimethoxyphenyl)-tetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3c**).* Reaction time: 1.5 h, **1c** (0.2 g, 0.56 mmol), **2a** (0.23 g, 0.56 mmol), viscous liquid, 0.28 g, yield 65%, $R_f$ value 0.20 (EtOAc/hexane) = 2:10 (v/v).

***3c***. $^1$H NMR (400 MHz): $\delta$ 7.54 (d, $J$ = 8.1 Hz, 2H), 7.12−7.04 (t, $J$ = 7.8 Hz, 2H), 7.00 (d, $J$ = 8.3 Hz, 3H), 6.93−6.72 (m, 2H), 6.60 (s, 2H), 6.56 (s, 1H), 5.18 (dd, $J$ = 10.8, 4.3 Hz, 1H), 4.48−4.34 (m, $J$ = 6.9, 6.6, 4.3 Hz, 4H), 4.29−4.24 (m, $J$ = 4.3, 3.7, 3.4 Hz, 2H), 4.03−3.99 (m, $J$ = 6.9, 2.6 Hz, 1H), 3.89 (s, 6H), 3.83 (s, 3H), 3.78−3.81 (m, $J$ = 6.9, 2.6 Hz, 1H), 2.37 (s, 3H), 2.07 (dd, $J$ = 11.0, 2.3 Hz, 1H), 1.95 (dd, $J$ = 8.7, 4.3 Hz, 1H), 1.50 (t, $J$ = 7.1 Hz, 3H), 1.36 (t, $J$ = 7.2 Hz, 3H), 1.32 (t, $J$ = 7.4 Hz, 3H), 1.10 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.6, 166.2, 165.9 (3 −C═O, C-19, C-20, C-21), 153.3, 143.5, 138.8, 137.5, 135.4, 134.4, 129.9, 129.8, 128.3, 127.8, 114.9 (C-18), 103.1, 84.6 (C-14), 83.10 (C-16), 69.8 (C-17), 67.1 (C-15), 62.3, 62.0, 61.8, 60.9 (4 −$CH_2$, C-10, C-11, C-11, C-12), 60.3 (−$OCH_3$, C-8), 56.3 (−$OCH_3$, C-7, C-9), 44.7 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.5, 14.4, 14.2, 13.9 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2983, 2928, 2849, 1759, 1735, 1594, 1509, 1462, 1423, 1335, 1256, 1157, 1122, 923, 867, 816, 755 cm$^{-1}$. HRMS (ESI, Q-TOF) $m/z$: [M + Na]$^+$ calcd for $C_{39}H_{47}NO_{13}SNa$ 792.2666, found 792.2686.

*Triethyl 6a-Ethoxy-2-(furan-2-yl)-4-phenyl-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3d**).* Reaction time: 1 h, **1e** (0.2 g, 0.79 mmol), **2a** (0.33 g, 0.79 mmol), viscous liquid, 0.32 g, yield 60%, $R_f$ value 0.39 (EtOAc/hexane) = 2:10 (v/v).

***3d***. $^1$H NMR (400 MHz): $\delta$ 7.36 (d, $J$ = 8.2 Hz, 3H), 7.12 (t, $J$ = 7.3 Hz, 3H), 7.00 (d, $J$ = 8.1 Hz, 4H), 6.52 (s, 1H), 6.31−6.26 (m, $J$ = 9.7, 3.0 Hz, 2H), 5.26 (dd, $J$ = 10.9, 4.3 Hz, 1H), 4.39−4.28 (m, $J$ = 3.9, 3.4, 2.9 Hz, 4H), 4.21−4.25 (m, $J$ = 7.6, 3.8 Hz, 2H), 4.01−3.97 (m, $J$ = 7.1, 2.8 Hz, 1H), 3.84−3.80 (m, $J$ = 7.1, 2.6 Hz, 1H), 2.35 (s, 3H), 2.21−2.31 (dd, $J$ = 11.9 Hz, 1H), 1.89 (dd, $J$ = 12.8, 4.3 Hz, 1H), 1.47 (t, $J$ = 6.9 Hz, 3H), 1.31 (t, $J$ = 7.3 Hz, 3H), 1.23 (t, $J$ = 7.0 Hz, 3H), 1.10 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.4, 165.9, 165.5 (3 −C═O, C-16, C-17, C-18), 151.0, 143.3, 142.8, 141.7, 138.2, 135.0, 130.0, 129.7, 128.4, 127.9, 114.7 (C-15), 110.4, 110.1, 108.7, 106.8, 82.4 (C-11), 76.9 (C-13), 69.2 (C-14), 67.1 (C-12), 62.2, 61.9, 61.8, 60.3 (4 −$CH_2$, C-7, C-8, C-9, C-10), 39.5 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.5, 14.3, 14.1, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2920, 2851, 1733, 1598, 1496, 1458, 1366, 1343, 1254, 1154, 1043, 813, 743, 676 cm$^{-1}$. HRMS (ESI, Q-TOF) $m/z$: [M + Na]$^+$ calcd for $C_{34}H_{39}NO_{11}SNa$ 692.2142, found 692.2162.

*Triethyl 2-(Benzo[d][1,3]dioxol-5-yl)-6a-ethoxy-4-phenyl-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3e**).* Reaction time: 2 h, **1g** (0.2 g, 0.65 mmol), **2a** (0.27 g, 0.65 mmol), white solid, mp 115 °C, 0.28 g, yield 60%, $R_f$ value 0.33 (EtOAc/hexane) = 2:10 (v/v).

***3e***. $^1$H NMR (400 MHz): $\delta$ 7.34 (d, $J$ = 8.3 Hz, 2H), 7.19 (s, 1H). 7.08−6.98 (m, $J$ = 7.9, 6.9, 6.6 Hz, 2H), 6.95 (d, $J$ = 8.2 Hz, 3H), 6.75 (s, 2H), 6.66 (s, 2 H), 6.48 (s, 1 H), 5.88 (s, 2H), 5.10 (dd, $J$ = 10.4, 4.0 Hz, 1H), 4.39−4.28 (m, $J$ = 7.4, 7.0, 3.5 Hz, 4H), 4.23−4.14 (m, $J$ = 6.9, 3.6, 3.2 Hz, 2H), 3.95−3.90 (m, $J$ = 6.9, 2.5 Hz, 1H), 3.74−3.70 (m, $J$ = 6.9, 2.6 Hz, 1H), 2.29 (s, 3H), 1.94 (dd, $J$ = 12.7, 7.8 Hz, 1H), 1.81 (dd, $J$ = 8.3, 4.1 Hz, 1H), 1.42 (t, $J$ = 7.1 Hz, 3H), 1.27 (dt, $J$ = 7.0, 2.84 Hz, 6H), 1.02 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.5, 166.0, 165.9 (3 −C═O, C-17, C-18, C-19), 147.8, 147.6, 143.9, 138.3, 134.8, 132.8, 129.7, 128.5, 127.8, 120.0, 114.6 (C-16), 108.1, 106.7, 101.1 (C-7), 84.0 (C-12), 82.7 (C-14), 69.7 (C-15), 67.0 (C-13), 62.4, 62.0, 61.7, 60.2 (4 −$CH_2$, C-7, C-8, C-9, C-10), 44.1 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.4, 14.3, 14.1, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2978, 2929, 1775, 1737, 1597, 1502, 1454, 1343, 1244, 1203, 1186, 1033, 930, 86 cm$^{-1}$. HRMS (ESI, Q-TOF) $m/z$: [M + Na]$^+$ calcd for $C_{38}H_{41}NO_{12}SNa$ 746.2247, found 746.2269.

*Triethyl 6a-Ethoxy-2,4-diphenyl-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3f**).* Reaction time: 5 h, **1h** (0.2 g, 0.76 mmol), **2a** (0.32 g, 0.76 mmol), white solid, mp 158 °C, 0.26 g, yield 50%, $R_f$ value 0.32 (EtOAc/hexane) = 2:10 (v/v).

***3f***. $^1$H NMR (400 MHz) $\delta$ 7.42 (d, $J$ = 8.2 Hz, 2H), 7.35−7.26 (m, $J$ = 8.8, 6.2, 5.9 Hz, 5H), 7.15−6.76 (m, $J$ = 8.2, 7.1 Hz, 7H), 6.56 (s, 1 H), 5.25 (dd, $J$ = 6.5, 4.09 Hz, 1H), 4.46−4.36 (m, $J$ = 7.0, 6.8, 3.4 Hz, 4H), 4.30−4.22 (m, $J$ = 6.6, 3.3 Hz, 2H), 4.05−3.97 (m, $J$ = 6.7, 2.3 Hz, 1H), 3.84−3.77 (m, $J$ = 7.0, 2.4 Hz, 1H), 2.37 (s, 3H), 2.03 (dd, $J$ = 10.8, 1.8 Hz, 1H), 1.94 (dd, $J$ = 8.5, 4.1 Hz, 1H), 1.49 (t, $J$ = 7.0 Hz, 3H), 1.35 (dt, $J$ = 5.5 Hz, 3H), 1.32 (t, $J$ = 5.4 Hz, 3H), 1.09 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (100 MHz): 169.6, 166.0, 165.9 (3 −C═O, C-16, C-17, C-18), 143.3, 139.1, 138.3, 134.9, 129.8, 128.6, 128.4, 128.3, 127.7, 126.2, 114.8 (C-15), 84.1 (C-11), 82.7 (C-13), 69.8 (C-14), 67.1 (C-12), 62.4, 62.0, 61.8, 60.2 (4 −$CH_2$, C-7, C-8, C-9, C-10), 44.2 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.5, 14.3, 14.2, 13.9 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2982, 2925, 1761, 1734, 1596, 1494, 1456, 1367, 1344, 1294, 1221, 1033, 931, 877, 682 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{36}H_{41}NO_{10}SNa$ 702.2349, found 702.2293.

*Triethyl 6a-Ethoxy-4-phenyl-2-(p-tolyl)-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3g**).* Reaction time: 4 h, **1i** (0.2 g, 0.72 mmol), **2a** (0.3 g, 0.72 mmol), viscous liquid, 0.27 g, yield 55%, $R_f$ value: 0.27 (EtOAc/hexane) = 2:10 (v/v).

***3g***. $^1$H NMR (400 MHz): $\delta$ 7.42 (d, $J$ = 8.1 Hz, 2H), 7.19−7.12 (m, $J$ = 9.7, 7.8 Hz, 5H), 7.07−6.90 (m, $J$ = 8.1, 6.2 Hz, 6H), 6.55 (s, 1 H), 5.22 (dd, $J$ = 6.6, 4.2 Hz, 1H), 4.45−4.34 (m, $J$ = 7.5, 6.2, 3.3 Hz, 4H), 4.29−4.20 (m, $J$ = 6.7, 3.9 Hz, 2H), 4.03−3.96 (m, $J$ = 6.6, 2.8 Hz, 1H), 3.83−3.76 (m, $J$ = 7.0, 2.5 Hz, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.01 (dd, $J$ = 11.0, 2.6 Hz, 1H), 1.91 (dd, $J$ = 8.3, 4.3 Hz, 1H), 1.49 (t, $J$ = 6.9 Hz, 3H), 1.34 (dt, $J$ = 7.1 Hz, 3H), 1.32 (t, $J$ = 7.3 Hz, 3H), 1.09 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.6, 166.0, 165.9 (3 −C═O, C-17, C-18, C-19), 143.3, 138.3, 138.1, 136.1, 134.9, 129.8, 129.7, 129.2, 128.4, 127.7, 126.2, 114.7 (C-16), 84.1 (C-12), 82.7 (C-14), 69.8 (C-15), 67.1 (C-13), 62.4, 62.0, 61.7, 60.1 (4 −$CH_2$, C-8, C-9, C-10, C-11), 44.2 (−$CH_2$, C-7), 21.6, 21.3 (2 −$CH_3$, C-5, C-6), 15.5, 14.3, 14.2, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2981, 2960, 1759, 1739, 1672, 1597, 1485, 1441, 1366, 1249, 1156, 1158, 933, 703, 682 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{37}H_{43}NO_{10}SNa$ 716.2505, found 716.2404.

*Triethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-(p-tolyl)-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3h**).* Reaction time: 3 h, **1a** (0.25 g, 0.77 mmol), **2b** (0.33 g, 0.77 mmol), pale yellow solid, mp 117 °C 0.38 g, yield 65%, $R_f$ value 0.28 (EtOAc/hexane) = 2:10 (v/v).



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***3h***. $^1$H NMR (400 MHz): $\delta$ 7.44 (d, $J$ = 8.2 Hz, 2H), 7.19 (s, 1H), 6.93 (t, $J$ = 8.3 Hz, 3H), 6.83−6.53 (m, 5 H), 6.44 (s, 1H), 5.13 (dd, $J$ = 10.8, 4.1 Hz, 1H), 4.36−4.26 (m, $J$ = 4.9, 3.9, 3.7 Hz, 4H), 4.21−4.14 (m, $J$ = 7.9, 3.7 Hz, 2H), 3.95−3.88 (m, 1H), 3.91 (s, 3H), 3.79 (s, 3H), 3.75−3.71 (m, $J$ = 4.3, 2.3 Hz, 1H), 2.30 (s, 3H), 2.12 (s, 3H), 2.01 (dd, $J$ = 12.0, 8.7 Hz, 1H), 1.87 (dd, $J$ = 13.0, 4.3 Hz, 1H), 1.42 (t, $J$ = 7.3 Hz, 3H), 1.27 (dt, $J$ = 7.0 Hz, 3H), 1.22 (t, $J$ = 7.3 Hz, 3H), 1.02 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.6, 166.2, 166.0 (3 −C═O, C-19, C-20, C-21), 149.3, 148.9, 143.3, 138.7, 137.5, 132.1, 131.5, 129.8, 128.2, 118.7, 114.8 (C-18), 110.4, 109.2, 84.4 (C-14), 82.9 (C-16), 69.8 (C-17), 66.9 (C-15), 62.3, 62.0, 61.7, 60.2 (4 −$CH_2$, C-10, C-11, C-12, C-13), 56.1, 56.0 (2 −$OCH_3$, C-8, C-9), 44.6 (−$CH_2$, C-7), 21.6, 21.1 (2 −$CH_3$, C-5, C-6), 15.5, 14.4, 14.2, 13.9 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2984, 2923, 2853, 1760, 1735, 1595, 1520, 1466, 1380, 1258, 1159, 1113, 1028, 922, 818 cm$^{-1}$. HRMS (ESI, Q-TOF) $m/z$: [M + Na]$^+$ calcd for $C_{39}H_{47}NO_{12}SNa$ 776.2717, found 776.2730.

*Triethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-(4-isopropylphenyl)-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3i**).* Reaction time: 1.5 h, **1a** (0.2 g, 0.62 mmol), **2c** (0.28 g, 0.62 mmol), viscous liquid, 0.31 g, yield 65%, $R_f$ value 0.45 (EtOAc/hexane) = 2:10 (v/v).

***3i***. $^1$H NMR (400 MHz): $\delta$ 7.44 (d, $J$ = 8.3 Hz, 2H), 7.19 (s, 1H), 7.05−6.81 (m, 4 H), 6.71 (s, 4H), 6.44 (s, 1H), 5.15 (dd, $J$ = 10.8, 4.0 Hz, 1H), 4.37−4.27 (m, $J$ = 6.9, 3.4, 3.1 Hz, 4H), 4.22−4.14 (m, $J$ = 7.1, 3.6 Hz, 2H), 3.95−3.89 (m, 1H), 3.93 (s, 3H), 3.80 (s, 3H), 3.77−3.71 (m, $J$ = 7.1, 2.7 Hz, 1H), 2.66 (m, $J$ = 6.5 Hz, 1H), 2.29 (s, 3H), 2.08 (dd, $J$ = 12.2, 2.7 Hz, 1H), 1.89 (dd, $J$ = 13.0, 4.5 Hz, 1H), 1.43 (t, $J$ = 7.1 Hz, 3H), 1.28 (dt, $J$ = 7.1 Hz, 3H), 1.22 (t, $J$ = 6.8 Hz, 3H), 1.08−1.01 (m, $J$ = 7.0 Hz, 9H). $^{13}$C NMR (100 MHz): $\delta$ 169.7, 166.3, 165.9 (3 −C═O, C-21, C-22, C-23), 149.3, 149.0, 148.3, 143.1, 138.8, 132.2, 131.6, 130.0, 129.7, 128.3, 118.8, 114.9 (C-20), 110.4, 109.2, 84.5 (C-16), 82.9 (C-18), 69.7 (C-19), 66.8 (C-17), 62.3, 61.9, 61.7, 60.2 (4 −$CH_2$, C-12, C-13, C-14, C-15), 56.1, 56.0 (2 −$OCH_3$, C-10, C-11), 44.6 (−$CH_2$, C-9), 33.7 (−CH, C-8), 24.2, 23.8 (2 −$CH_3$, C-6, C-7), 21.6 (−$CH_3$, C-5), 15.5, 14.3, 14.2, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2961, 2919, 1757, 1596, 1518, 1464, 1379, 1257, 1158, 1026, 921, 799, 675 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{41}H_{51}NO_{12}SNa$ 804.3030, found 804.2954.

*Triethyl 4-(4-Chlorophenyl)-2-(3,4-dimethoxyphenyl)-6a-ethoxy-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3j**).* Reaction time: 1.5 h, **1a** (0.2 g, 0.62 mmol), **2e** (0.28 g, 0.62 mmol), viscous liquid, 0.29 g, yield 60%, $R_f$ value 0.28 (EtOAc/hexane) = 2:10 (v/v).

***3j***. $^1$H NMR (400 MHz): $\delta$ 7.49 (d, $J$ = 8.2 Hz, 2H), 7.19 (s, 1H), 7.00−6.88 (m, $J$ = 8.1 Hz, 5H), 6.79−6.65 (s, 3H), 6.46 (s, 1H), 5.15 (dd, $J$ = 9.8, 4.7 Hz, 1H), 4.38−4.28 (m, $J$ = 6.7, 3.8 Hz, 4H), 4.22−4.15 (m, $J$ = 7.2, 4.2 Hz, 2H), 3.96−3.88 (m, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.81−3.70 (m, $J$ = 6.7, 2.3 Hz, 1H), 2.32 (s, 3H), 1.88 (dd, $J$ = 9.7, 4.6 Hz, 2H), 1.41 (t, $J$ = 7.2 Hz, 3H), 1.28 (dt, $J$ = 7.5 Hz, 3H), 1.23 (t, $J$ = 7.1 Hz, 3H), 1.03 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.4, 166.2, 165.8 (3 −C═O, C-21, C-22, C-23), 149.4, 149.2, 143.8, 138.7, 133.8, 133.4, 131.9, 131.2, 129.7, 128.5, 118.7, 114.9 (C-17), 110.7, 109.2, 84.4 (C-13), 83.06 (C-15), 69.7 (C-16), 66.5 (C-14), 62.4, 62.0, 61.8, 60.3 (4 −$CH_2$, C-9, C-10, C-11, C-12), 56.1, 56.0 (2 −$OCH_3$, C-7, C-8), 44.6 (−$CH_2$, C-6), 21.6 (−$CH_3$, C-5), 15.4, 14.3, 14.2, 13.8 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2981, 2932, 1759, 1734, 1596, 1517, 1492, 1462, 1367, 1255, 1156, 1028, 912, 764 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{38}H_{44}ClNO_{12}SNa$ 796.2170, found 796.2201.

*Triethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-(naphthalen-1-yl)-5-tosyltetrahydro-2H-furo[2,3-c]pyrrole-3a,6,6(6aH)-tricarboxylate (**3k**).* Reaction time: 2 h, **1a** (0.2 g, 0.62 mmol), **2e** (0.29 g, 0.62 mmol), viscous liquid, 0.32 g, yield 65%, $R_f$ value 0.27 (EtOAc/hexane) = 2:10 (v/v).

***3k***. $^1$H NMR (400 MHz): $\delta$ 8.29 (d, $J$ = 8.6 Hz, 1H), 7.77 (d, $J$ = 8.3 Hz, 1H), 7.57−7.40 (m, $J$ = 10.0, 7.5 Hz, 4H), 7.23−7.16 (m, $J$ = 8.5, 6.8 Hz, 3H), 6.90−6.86 (m, $J$ = 8.5, 4.9 Hz, 3H), 6.74−6.61 (m, $J$ = 8.5, 5.2 Hz, 3H), 5.08 (dd, $J$ = 10.8, 4.9 Hz, 1H), 4.50−4.39 (m, $J$ = 7.2, 6.2, 3.6 Hz, 4H), 4.33−4.24 (m, $J$ = 7.7, 4.1 Hz, 2H), 4.11−4.05 (m, $J$ = 6.4, 2.9 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 3.86−3.77 (m, $J$ = 7.0, 2.9 Hz, 1H), 2.32 (s, 3H), 2.01 (dd, $J$ = 13.0, 4.7 Hz, 1H), 1.91 (dd, $J$ = 13.3, 2.7 Hz, 1H), 1.56 (t, $J$ = 7.2 Hz, 3H), 1.37 (dt, $J$ = 7.3 Hz, 3H), 1.33 (t, $J$ = 7.5 Hz, 3H), 1.13 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 169.6, 166.4, 166.1 (3 −C═O, C-18, C-19, C-20), 149.1, 148.8, 143.1, 138.2, 133.6, 131.8, 131.5, 131.2, 130.3, 129.6, 128.6, 128.2, 126.6, 125.6, 123.9, 123.8, 118.4, 115.6 (C-17), 110.6, 109.1, 84.0 (C-13), 82.3 (C-15), 69.7 (C-16), 62.8, 62.4, 62.1, 62.0 (4 −$CH_2$, C-9, C-10, C-11, C-12), 59.9 (C-14), 56.0 (2 −$OCH_3$, C-7, C-8), 43.9 (−$CH_2$, C-6), 21.5 (−$CH_3$, C-5), 15.4, 14.3, 14.2, 13.9 (4 −$CH_3$, C-1, C-2, C-3, C-4). IR (neat): 2979, 1758, 1739, 1595, 1516, 1461, 1345, 1257, 1029 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{42}H_{47}NO_{12}SNa$ 812.2717, found 812.2592.

**Decarboxylation of Triethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-phenyl-5-tosyltetrahydro-2*H*-furo[2,3-*c*]pyrrole-3a,6,6(6a*H*)-tricarboxylate (3a) to 4a.** To the solution of adduct **3a** (0.15 g, 0.2 mmol, 1 equiv) in DMSO (3 mL) were added LiCl (0.05 g, 1.2 mmol, 6 equiv) and $H_2O$ (1 drop), and the reaction mixture was heated at 160 °C for 2 h. Three milliliters of water was added to the mixture, and the mixture was extracted with diethyl ether, dried over $Na_2SO_4$, and purified by flash column chromatography in a 10−20% acetone/hexane solvent system.

*Diethyl 2-(3,4-Dimethoxyphenyl)-6a-ethoxy-4-phenyl-3,3a,4,6a-tetrahydro-2H-furo[2,3-c]pyrrole-3a,6-dicarboxylate (**4a**).* Reaction time: 2 h, **3a** (0.15 g, 0.20 mmol), yellow viscous oil, 0.06 g, yield 60%, $R_f$ value 0.45 (acetone/hexane) = 2:10 (v/v).

***4a***. $^1$H NMR (400 MHz): $\delta$ 7.69 (d, $J$ = 8.0 Hz, 2H), 7.37−7.33 (m, $J$ = 6.3 Hz, 1H), 7.32−7.27 (m, $J$ = 7.8, 7.1 Hz, 2H), 6.83 (s, 1H), 6.79−6.67 (m, $J$ = 8.2 2H), 5.30 (dd, $J$ = 5.6, 4.7 Hz, 1H), 5.04 (s, 1H), 4.22−4.15 (m, $J$ = 7.3, 6.4 Hz, 3H), 4.03−3.99 (m, $J$ = 5.7, 3.3 Hz, 1H), 3.87−3.81 (m, $J$ = 6.2, 3.5 Hz, 2H), 3.79 (s, 3H), 3.79 (s, 3H), 3.27 (dd, $J$ = 6.8, 5.4 Hz, 1H), 1.93 (dd, $J$ = 10.3, 2.6 Hz, 1H), 1.19 (t, $J$ = 7.7 Hz, 3H), 1.15 (t, $J$ = 7.4 Hz, 3H), 1.07 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (100 MHz): $\delta$ 172.6, 169.0, 168.8 (2 −C═O, 1 −C═N, C-12, C-15, C-16), 149.3, 149.0, 132.3, 131.9, 131.3, 128.7, 128.6, 118.8, 118.6, 111.2 (C-14), 110.9, 109.3, 84.2 (C-10), 77.9 (C-11), 75.5 (C-13), 61.9, 61.2, 59.9 (3 −$CH_2$, C-7, C-8, C-9), 56.0 (2 −$OCH_3$, C-5, C-6), 44.1 (−$CH_2$, C-4), 15.5, 14.3, 14.0 (3 −$CH_3$, C-1, C-2, C-3). IR (neat): 2979, 1735, 1619, 1516, 1461, 1261, 1187, 1029, 751 cm$^{-1}$. HRMS (ESI, quadrupole) $m/z$: [M + Na]$^+$ calcd for $C_{29}H_{33}NO_8Na$ 512.2284, found 512.2221.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Copies of $^1$H and $^{13}$C NMR spectra, mass data of all new compounds, and single-crystal X-ray data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00705.

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### Notes

The authors declare no competing financial interest.

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