Synthesis of Novel 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic Acid Derivatives through the Application of Rongalite: A Synergistic Combination of [2+2+2]- and [4+2]-Cycloaddition Reactions

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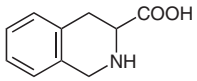
Abstract: An efficient route for the synthesis of several novel 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic) derivatives has been reported. A synergistic combination of [2+2+2]- and [4+2]-cycloaddition reactions has been used for the synthesis of the desired targets.

Key words: 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, Rongalite, cycloaddition, amino acids, quinones

1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid (**1**, Tic; Figure 1) is a constrained analogue of phenylalanine (Phe).[1] The main advantage of constrained amino acids and their derivatives is their stability towards enzymatic degradation.[2] Incorporation of constrained amino acid moieties in a peptide chain can modify the physiological as well as the binding properties of the resulting peptide.[3] In 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, the six-membered heterocyclic ring is formed by incorporation of a methylene unit between the amino group and the aromatic ring of phenylalanine. Since the nitrogen atom in 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid is protected, this type of amino acid can play an important role in the design of peptidomimetics.[4] It was found that the insertion of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid in the second position of an opioid receptor exerts conformational restrictions and results in drastic changes in its intrinsic activity.[5] The tetrahydroisoquinoline unit has been extensively used in peptide-based drugs and, in several instances, it appears to play a crucial role in the design of various lead molecules.[6]



1

Figure 1

Recently, Lipkowski and co-workers have reported that 6-hydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (6HTc) can simulate tyrosine conformation in an opioid ligand receptor complex.[7] The tetrahydroisoquinoline unit is also a critical component of inhibitors of phenylethanolamine *N*-methyltransferase.[8] Similarly, the 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid unit has also been incorporated in farnesyl transferase inhibitor **3** and its analogues (Figure 2) as a replacement for phenylalanine.[9] Moexipril (**2**), an ACE inhibitor, contains 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid as a core structural unit (Figure 2).[10] In view of the various applications of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives, a need remains for new synthetic strategies. Some of the common methods for the preparation of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid and its derivatives are: Pictet–Spengler reaction, Bischler–Napieralski reaction, or by alkylation strategies.[11] These methods, however, employ a preformed benzene ring derivative as a starting material and they provide limited opportunities for the introduction of diverse functional groups in the benzene ring.

In view of our interest in developing new methodologies for 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid–quinone hybrids[12] via a 'building block approach',[13] we sought a general and useful approach based on [2+2+2] cycloaddition[14] and Diels–Alder reactions as key steps.[15] The strategy based on cycloaddition reactions has a unique advantage over existing methods as diverse substituents can be introduced in the aromatic ring by judicious selection of the reacting partners. Although there are several methods available for the construction of tetrahydroisoquinoline units, these strategies cannot easily be extended to 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives.

Given the synthetic challenge of developing new strategies to 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives, cycloaddition approaches provide a unique advantage in terms of diversification.[16] Unlike other routes, this approach is well suited to the generation of annulated benzene derivatives and it can also be used to generate a library of compounds by varying the reacting partners. The retrosynthetic analysis for 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid based on cycloaddition reactions is shown in Scheme 1.

In view of our earlier experience in generating *o*-xylylene intermediates under mild reaction conditions, we envisaged that a novel sultine building block **7** would be useful for the synthesis of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid based amino acid derivatives.[17] We preferred sultine **7** as a latent diene intermediate over the other pos-

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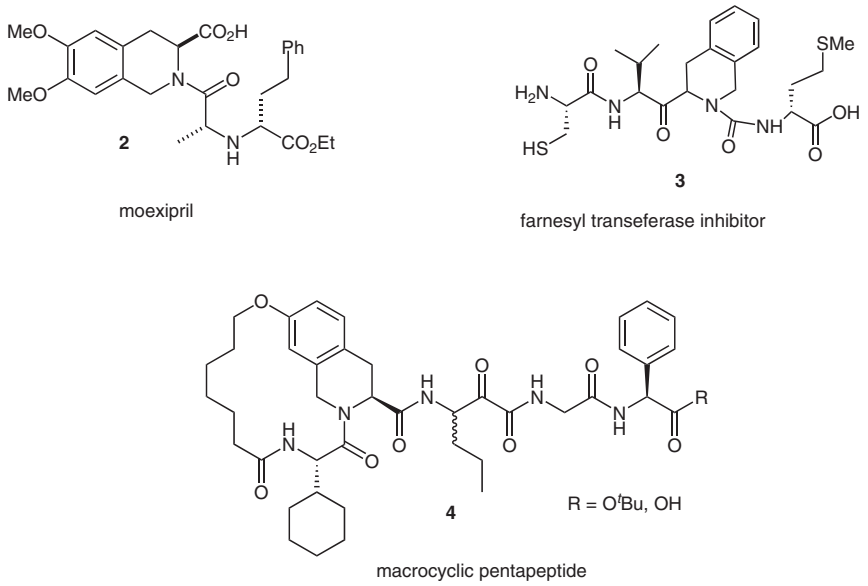
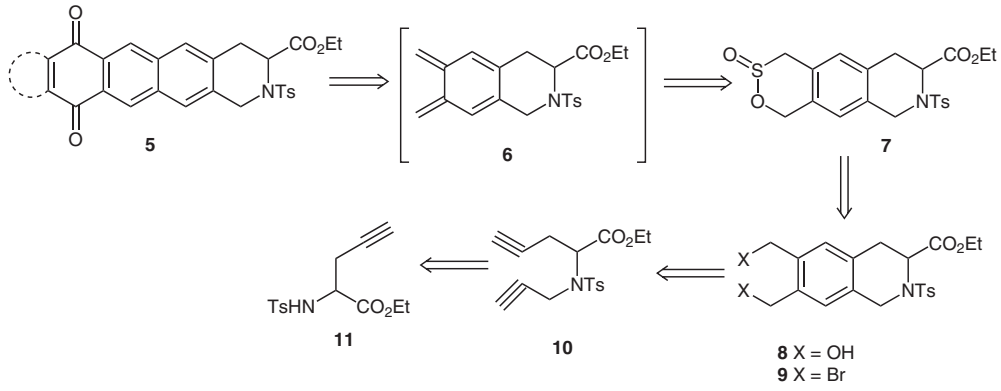


Figure 2 Biologically relevant compounds containing the 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid moiety

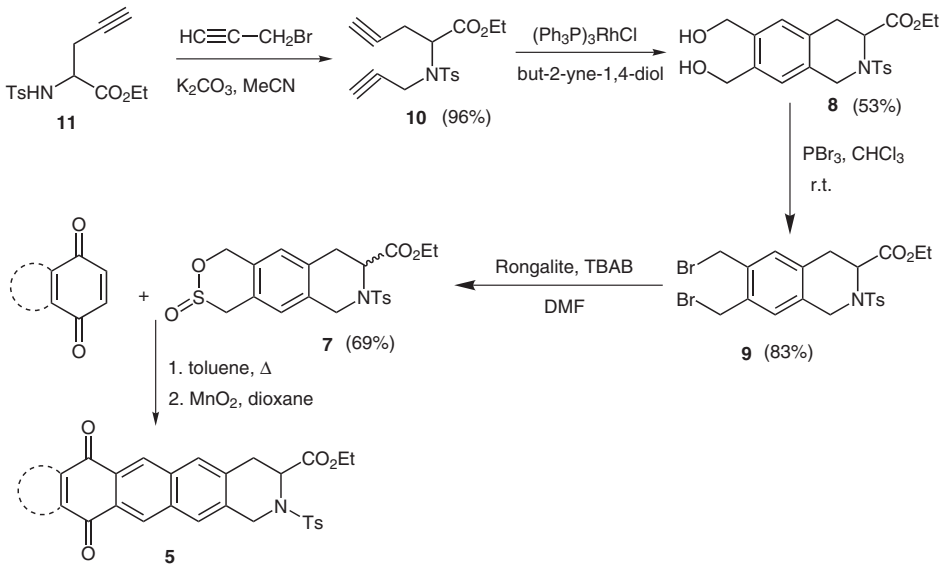
sible precursors such as benzocyclobutene derivatives because sultine derivatives can be transformed into a highly reactive *o*-xylylene intermediate **6** under milder conditions by chelotropic elimination of sulfur dioxide.[18] The transient diene **6** thus generated under thermal conditions is well suited to the Diels–Alder strategy. Herein, we report the realization of the proposed strategy (Scheme 1) for the preparation of various 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid based amino acid derivatives.

The required diol building block **8** was prepared by following literature procedure starting from the alkyne building block **11**, which in turn can be obtained from benzophenone imine.[19] The diol **8** was treated with phosphorus tribromide in anhydrous chloroform to generate the corresponding dibromo derivative **9** in 83% yield. The formation of **9** was confirmed by the disappearance of protons attached to the hydroxy group at $\delta = 3.76$ and the appearance of the CH_2Br protons at $\delta = 4.58$ in the high-field ^1H NMR spectrum. Next, the dibromo derivative was treated with Rongalite (sodium hydroxymethanesulfinate, $CH_3NaO_3S{\cdot}2\ H_2O$) in the presence of tetrabutylammonium bromide in anhydrous *N*,*N*-dimethylformamide to give the sultine derivative **7** as a mixture of diastereomers. Since the stereochemistry of the sultine is of no consequence in the generation of the *o*-xylylene intermediate **6**, it was not necessary to separate the isomers. Moreover, TLC behavior indicated that the mixtures of isomers would be inseparable by column chromatography. Having the sultine derivative in hand, its Diels–Alder chemistry with various quinone-based dienophiles was undertaken. The sultine derivative was heated at 85–90 °C in the presence of excess dienophiles **12**–**16** to give the Diels–Alder adducts. The Diels–Alder adducts were slightly contaminated with the aromatized product and therefore no attempts were made to isolate the Diels–Alder adducts. Aromatization of the Diels–Alder adducts was achieved using activated manganese dioxide to furnish the 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives **17**–**21** (Table 1).

The aromatized products **17**–**21** were characterized based on their spectral data, such as ^1H and ^{13}C NMR and HRMS. The mild reaction conditions employed and the



Scheme 1 Retrosynthetic analysis of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives

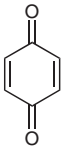
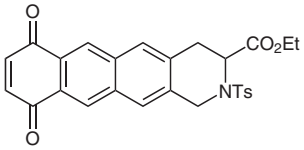
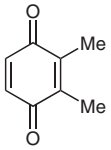
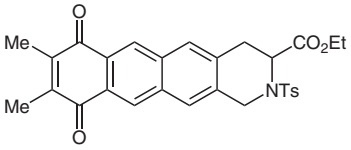
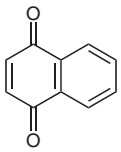
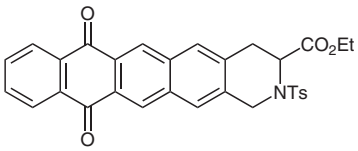
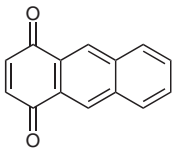
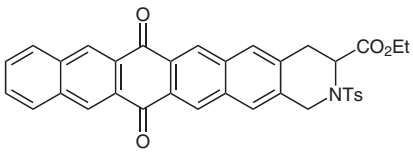
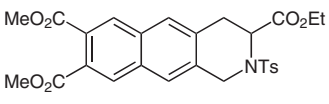


Scheme 2 Synthetic approach to highly functionalized 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives

atom economy process involved make this route attractive for the preparation of several previously inaccessible unusual amino acid derivatives embodying the 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid moiety.

We have developed a short and an efficient route for the synthesis of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid–quinone hybrids. We found that a combination of [2+2+2]- and [4+2]-cycloaddition reactions is extremely

Table 1 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic Acid Derivatives Prepared by Diels–Alder Reaction/Aromatization[a]

Entry	Dienophile		Aromatized product		Yield[b] (%)
1		**12**		**17**	71
2		**13**		**18**	72
3		**14**		**19**	77
4		**15**		**20**	82
5		**16**		**21**	70

[a] Diels–Alder reaction was carried out in toluene at reflux.
[b] Isolated overall yield after Diels–Alder and aromatization step.

useful for the generation of polycyclic molecules in an efficient and atom-economic manner. Since enantiomerically pure building blocks related to **11** are commercially available, the methodology can easily be adopted for the preparation of optically active 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives. We anticipate that the introduction of a variety of quinone moieties in 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid will have impact in medicinal chemistry and also for the design of new peptidomimetics.

All reactions were monitored by TLC carried out on glass plates coated with silica gel GF 254 (containing 13% calcium sulfate as a binder, Acme). Visualization of the spots on TLC plates was achieved either by exposure to I_2 vapor or UV light. Flash chromatography was performed using silica gel (100–200 mesh, Acme). Petroleum ether (PE) has bp 60–80 °C. All the commercial grade reagents were used without further purification. IR spectra were recorded on a Nicolet Impact 400 FT-IR spectrometer in KBr, $CHCl_3$, or CCl_4. ^{1}H NMR (300 and 400 MHz) and ^{13}C NMR (75 and 100.6 MHz) spectra were determined at r.t. on a Varian VXR 300 or AX 400 mercury plus in $CDCl_3$ soln with TMS as internal reference (^{1}H). HRMS were determined on Micromass Q-Tof spectrometer.

Ethyl 6,7-Bis(bromomethyl)-2-tosyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (9)

To a stirred soln of the diol **8** (0.30 g, 0.7 mmol) in anhyd $CHCl_3$ (30 mL) was added PBr_3 (0.33 mL, 3.5 mmol) at 0 °C and the mixture was stirred at r.t. for 6 h. The mixture was then poured into ice-cold H_2O (40 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined organic extracts were washed with H_2O and brine and dried ($MgSO_4$). The solvent was concentrated under reduced pressure and the crude product was purified by column chromatography (silica gel, EtOAc–PE, 25:75) to afford the dibromide **9** as a colorless solid; yield: 0.32 g (83%); mp 156 °C; R_f = 0.40 (silica gel, EtOAc–PE, 2:8).

IR (neat): 1163, 1738 cm^{-1} (ester C=O).

^{1}H NMR (300 MHz; $CDCl_3$): δ = 1.01 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 2.41 (s, 3 H, $ArCH_3$), 3.16 (d, J = 5.6 Hz, 2 H, $CHCH_2$), 3.91–3.98 (m, 2 H, OCH_2CH_3), 4.45 ($^1/_2$ ABq, J = 15.6 Hz, 1 H), 4.58 (s, 4 H, CH_2Br), 4.69 ($^1/_2$ ABq, J = 16.2 Hz, 1 H), 4.99 (t, J = 4.2 Hz, 1 H, $CHCH_2$), 7.05 (s, 1 H, ArH), 7.09 (s, 1 H, ArH), 7.28 (d, J = 8.1 Hz, 2 H, ArH), 7.71 (d, J = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.9, 21.7, 29.71, 29.74, 31.7, 44.1, 53.6, 61.6, 127.5, 128.9, 129.7, 131.6, 132.4, 133.1, 135.2, 135.9, 143.8, 170.1.

HRMS (Q-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{24}Br_2NO_4S$: 543.9793; found 543.9780.

Sultine 7

To a suspension of Rongalite (0.30 g, 1.94 mmol) in DMF (15 mL) was added dibromo **9** (0.08 g, 0.15 mmol) and TBAB (0.03 g, 0.09 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 3 h and then at r.t. for 4 h. The mixture was quenched with H_2O (10 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography (silica gel, EtOAc–PE, 3:7) to afford compound **7** as a colorless liquid; yield: 46 mg (69%); R_f = 0.30 (silica gel, EtOAc–PE, 3:7).

IR (neat): 1738 (ester C=O), 1454, 1347, 1162 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, J = 6.9 Hz, 3 H, OCH_2CH_3), 2.41 (s, 3 H, Ar–CH_3), 3.18 (d, J = 4.2 Hz, 2 H, $CHCH_2$), 3.51 ($^1/_2$ ABq, J = 15.3 Hz, 1 H), 3.93–3.99 (m, 2 H, OCH_2CH_3), 4.28 ($^1/_2$ ABq, J = 15.3 Hz, 1 H), 4.50 ($^1/_2$ ABq, J = 15.9 Hz, 1 H), 4.70 ($^1/_2$ ABq, J = 15.6 Hz, 1 H), 4.89 ($^1/_2$ ABq, J = 13.8 Hz, 1 H), 5.01 (t, J = 3.2 Hz, 1 H, $CHCH_2$), 5.21 ($^1/_2$ ABq, J = 13.8 Hz, 1 H), 6.93 (d, J = 8.1 Hz, 2 H, ArH), 7.29 (d, J = 8.1 Hz, 2 H, ArH), 7.71 (s, 1 H, ArH), 7.73 (s, 1 H, ArH).

HRMS (Q-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{24}NO_6S_2$: 450.1045; found: 450.1054.

Ethyl 7,10-Dioxo-2-tosyl-1,2,3,4,7,10-hexahydronaphtho[2,3-*g*]isoquinoline-3-carboxylate (17); Typical Procedure

1,4-Benzoquinone (**12**, 6 mg, 0.06 mmol) was added to a soln of the sultine **7** (14 mg, 0.03 mmol) in anhyd toluene (5 mL) and the mixture was heated at 90 °C for 12 h). The soln was concentrated under reduced pressure. The crude mixture was dissolved in anhyd dioxane (7 mL) and then treated with activated MnO_2 (180 mg, 2.07 mmol). The mixture was then allowed to stir at reflux for 30 h and then filtered through a Celite pad. The residue was washed with dioxane (3 × 5 mL) and the solvent was removed from the washings under reduced pressure to give a crude product that was purified by column chromatography (silica gel, EtOAc–PE, 3:7) to afford **17** as a yellow crystalline solid; yield: 11 mg (71%); mp 170–172 °C (dec.); R_f = 0.35 (silica gel, EtOAc–PE, 3:7).

IR (neat): 1731 (ester C=O), 1644 cm^{-1} (ArC=O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 2.38 (s, 3 H, $ArCH_3$), 3.41 (d, J = 4 Hz, 2 H, $CHCH_2$), 3.86–3.98 (m, 2 H, OCH_2CH_3), 4.72 ($^1/_2$ ABq, J = 16 Hz, 1 H), 4.91 ($^1/_2$ ABq, J = 16.2 Hz, 1 H), 5.05 (t, J = 4.8 Hz, 1 H, CH_2CH), 7.06 (s, 2 H, $COCH{=}CH$), 7.29 (d, J = 8 Hz, 2 H, ArH), 7.74–7.77 (m, 4 H, ArH), 8.50 (s, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.0, 21.7, 32.8, 45.0, 54.2, 61.7, 127.3, 127.6, 128.5, 128.6, 129.6, 129.8, 133.7, 133.8, 134.1, 134.7, 135.8, 140.3, 144.0, 170.2, 184.7.

HRMS (Q-TOF): m/z [M + H$^+$] calcd for $C_{27}H_{24}NO_6S$: 490.1324; found: 490.1325.

UV ($CHCl_3$): λ_{max} (ε) = 240 nm (11428).

Ethyl 8,9-Dimethyl-7,10-dioxo-2-tosyl-1,2,3,4,7,10-hexahydronaphtho[2,3-*g*]isoquinoline-3-carboxylate (18)

According to the typical procedure using 2,3-dimethyl-1,4-benzoquinone (**13**, 6 mg, 0.04 mmol) and sultine **7** (13 mg, 0.03 mmol) at 90 °C for 12 h, followed by aromatization with activated MnO_2 (200 mg, 2.29 mmol) at reflux for 30 h; purification by flash column chromatography (silica gel, EtOAc–PE, 3:7) afforded **18** as a yellow crystalline solid; yield: 11 mg (72%); mp 178–180 °C (dec.); R_f = 0.30 (silica gel, EtOAc–PE, 3:7).

IR (neat): 1731 (ester C=O), 1654 cm^{-1} (ArC=O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, J = 7.02 Hz, 3 H, OCH_2CH_3), 2.23 (s, 6 H, 2 CH_3), 2.38 (s, 3 H, Ar-CH_3), 3.39 (d, J = 5.04 Hz, 2 H, $CHCH_2$), 3.86–3.97 (m, 2 H, OCH_2CH_3), 4.69 ($^1/_2$ ABq, J = 16.2 Hz, 1 H), 4.91 ($^1/_2$ ABq, J = 15.9 Hz, 1 H), 5.04 (t, J = 4 Hz, 1 H, $CHCH_2$), 7.24–7.26 (m, 2 H, ArH), 7.73–7.77 (m, 4 H, ArH), 8.50 (s, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.4, 14.1, 21.7, 32.8, 45.1, 54.3, 61.7, 127.1, 127.6, 128.0, 128.1, 128.9, 129.4, 129.8, 133.6, 133.7, 133.8, 134.2, 135.9, 144.0, 145.33, 145.34, 170.3, 184.54, 184.55.

HRMS (Q-TOF): m/z [M + H]$^+$ calcd for $C_{29}H_{28}NO_6S$: 518.1637; found: 518.1629.

UV ($CHCl_3$): λ_{max} (ε) = 240 nm (11270).

Ethyl 7,12-Dioxo-2-tosyl-1,2,3,4,7,12-hexahydroanthra[2,3-*g*]isoquinoline-3-carboxylate (19)

According to the typical procedure using 1,4-naphthoquinone (**14**, 7 mg, 0.04 mmol) and sultine **7** (14 mg, 0.03 mmol) at 90 °C for 24 h, followed by aromatization with activated MnO_2 (250 mg, 2.87 mmol) at reflux for 30 h; purification by flash column chromatography (silica gel, EtOAc–PE, 3:7) afforded **19** as a yellow crystalline solid; yield: 13 mg (77%); mp 205–207 °C (dec.); R_f = 0.35 (silica gel, EtOAc–PE, 4:6).

IR (neat): 1730 (ester C=O), 1648 cm^{-1} (ArC=O).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 6.8 Hz, 3 H, OCH_2CH_3), 2.38 (s, 3 H, Ar-CH_3), 3.42 (d, *J* = 3.6 Hz, 2 H, CH_2CH), 3.88–3.99 (m, 2 H, OCH_2CH_3), 4.72 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 4.94 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 5.05 (t, *J* = 5 Hz, 1 H, CH_2CH), 7.26–7.29 (m, 2 H, ArH), 7.75–7.84 (m, 6 H, ArH), 8.37–8.40 (m, 2 H, ArH), 8.74 (s, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.1, 21.7, 32.9, 45.1, 54.2, 61.7, 127.1, 127.63, 127.68, 129.1, 129.2, 129.5, 129.8, 129.9, 134.02, 134.07, 134.1, 134.4, 134.60, 134.64, 135.8, 144.0, 170.3, 183.0.

HRMS (Q-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{26}NO_6S$: 540.1481; found: 540.1461.

UV ($CHCl_3$): λ_{max} (ε) = 240 nm (11419)

Ethyl 7,14-Dioxo-2-tosyl-1,2,3,4,7,14-hexahydrotetraceno[2,3-*g*]isoquinoline-3-carboxylate (20)

According to the typical procedure using 1,4-anthraquinone **15** (11 mg, 0.05 mmol) and sultine **7** (11 mg, 0.02 mmol) at 90 °C for 20 h, followed by aromatization with activated MnO_2 (200 mg, 2.29 mmol) at reflux for 28 h; purification by flash column chromatography (silica gel, EtOAc–PE, 3:7) afforded **20** as a yellow crystalline solid; yield: 12 mg (82%); mp 262 °C (dec.); R_f = 0.30 (silica gel, EtOAc–PE, 4:6).

IR (neat): 1731 (ester C=O), 1658 cm^{-1} (Ar C=O).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 6.8 Hz, 3 H, OCH_2CH_3), 2.38 (s, 3 H, $ArCH_3$), 3.43 (d, *J* = 6.4 Hz, 2 H, $CHCH_2$), 3.87–3.99 (m, 2 H, OCH_2CH_3), 4.73 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 4.95 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 5.05 (dd, *J* = 5.4, 4.2 Hz, 1 H), 7.26–7.28 (m, 2 H, ArH), 7.71–7.86 (m, 6 H, ArH), 8.12–8.14 (m, 2 H, ArH), 8.83 (s, 2 H, ArH), 8.93 (s, 1 H, ArH), 8.94 (s, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.0, 21.7, 32.9, 45.1, 54.3, 61.7, 127.1, 127.6, 129.3, 129.4, 129.7, 129.8, 129.9, 130.3, 130.7, 130.8, 134.0, 134.1, 134.2, 134.7, 135.4, 135.9, 143.9, 170.3, 182.9.

MS (MALDI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{35}H_{27}NO_6S$: 590.16; found: 590.32.

UV ($CHCl_3$): λ_{max} (ε) = 308 nm (22410).

3-Ethyl 7,8-Dimethyl 2-Tosyl-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline-3,7,8-tricarboxylate (21)

According to the typical procedure using dimethyl acetylenedicarboxylate (**16**, 7 mg, 0.05 mmol) and sultine **7** (12 mg, 0.03 mmol) at 90 °C for 24 h, followed by aromatization with activated MnO_2 (200 mg, 2.29 mmol) at reflux for 30 h; purification by flash column chromatography (silica gel, EtOAc–PE, 3:7) afforded **21** as a semisolid; yield: 10 mg (70%); R_f = 0.30 (silica gel, PE–EtOAc, 3:7).

IR (neat): 1729 cm^{-1} (ester C=O).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 2.37 (s, 3 H, Ar-CH_3), 3.72 (d, *J* = 4.4 Hz, 2 H, $CHCH_2$), 3.89–3.96 (m, 8 H, 2 $COOCH_3$, OCH_2CH_3), 4.69 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 4.95 ($^1/_2$ ABq, *J* = 16 Hz, 1 H), 5.00 (t, *J* = 4.4 Hz, 1 H, CH_2CH), 7.26 (d, *J* = 6.4 Hz, 2 H, ArH), 7.47 (d, *J* = 6.8 Hz, 2 H, ArH), 7.60 (s, 1 H, ArH), 7.65 (s, 1 H, ArH), 8.13 (s, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.0, 21.6, 32.8, 45.1, 52.9, 54.4, 61.6, 125.7, 127.6, 128.0, 128.6, 129.7, 129.8, 132.3, 132.9, 133.6, 143.9, 168.2, 170.4.

HRMS (Q-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{28}NO_8S$: 526.1536; found: 526.1536.

UV ($CHCl_3$): λ_{max} (ε) = 240 nm (11043).

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