POST-PRINT VERSION

Catalytic Functionalization of C-H Bonds of Azulene by Carbene/Nitrene Incorporation

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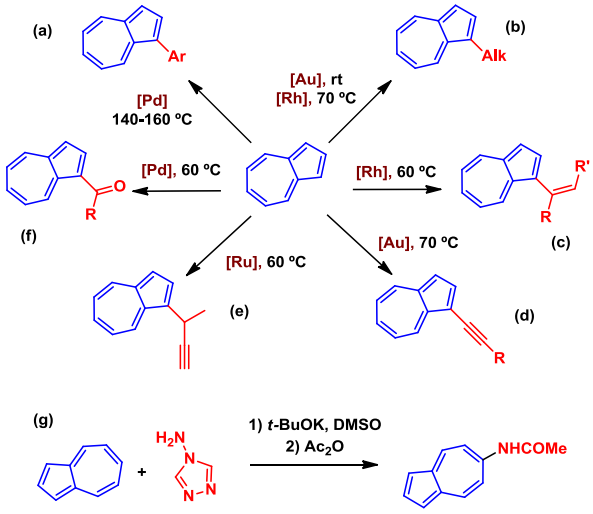
ABSTRACT: The selective catalytic functionalization of the C-H bond of azulene upon incorporation of carbene or nitrene units with metal-based catalysts is described. Ethyl diazoacetate or ArI=NTs are employed as carbene or nitrene precursors, respectively. The azulene derivatives are subsequently employed as building blocks toward more complex structures with potential use as biodegradable materials.

INTRODUCTION

Since its chemical synthesis nearly eighty years ago,[1] azulene $C_{10}H_8$, has been in the center of extensive research.[2] Isomeric with naphthalene (a white crystalline solid), azulene displays a characteristic deep blue color and a large dipole moment of 1.08 D, due to an asymmetric π-polarization between the 5- and 7-membered rings. These characteristics make azulene an attractive building block for the construction of advanced functional materials for optoelectronic devices, light-emitting diodes (OLEDs) or organic field-effect transistors (OFETs), among others. [3,4] Azulene is also gaining interest due to its reversible stimuli-responsive nature,[5] antibacterial[6] properties or some potential medicinal and bioimaging applications[7] as well.

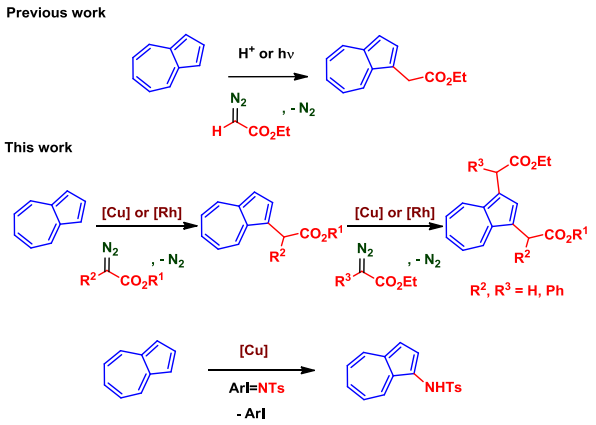
Despite the interest in the availability of azulene-modified skeletons toward their use in the above-mentioned systems, there are only a few examples of the direct incorporation of substituents onto this bicyclic molecule.[8] The functionalization of C-H bonds at the 5-member ring and, particularly, the formation of carbon-carbon bonds are relevant for subsequent uses of the modified azulene. Scheme 1 contains the representative examples of such metal-catalyzed processes, showing arylation (a),[9] alkylation (b),[10] alkenylation (c),[11] alkynylation (d),[12] propargylation (e)[13] and carbonylation (f)[14]

Scheme 1. Reported metal-catalyzed methods for azulene C-H bond functionalization and C-C bond formation (a-f) and stoichiometric C-N bond generation (g)



reactions. On the other hand, the direct amination of azulene C-H bonds has been scarcely reported, mainly following the stoichiometric Vicarious nucleophilic substitution of hydrogen[15] (Scheme 1g), photoinduced amina-

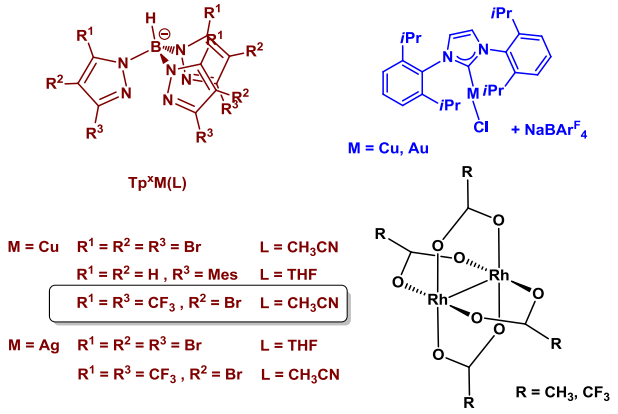
Scheme 2. Azulene C-H bond functionalization and C-C and C-N bond formation by carbene or nitrene insertion



tions involving *N*-centered radicals[16] or preparation of azo derivatives.[17]

For some applications such as biocompatible oligomers and polymers, the availability of sites that can undergo readily substitution patterns, such as esters or amines, is highly desirable. In this sense, a potential strategy toward that end could consist of the incorporation of $CHCO_2Et$ or NTs units from N_2=$CHCO_2Et$ (ethyl diazoacetate, EDA) or PhI=NTs, serving as carbene or nitrene sources, respectively. At variance with the large number of examples on metal-catalyzed carbene transfer from EDA to a plethora of organic substrates,[18] we have found no precedent with azulene. Only a single metal free protocol was described half a century ago, leading to monosubstitution at C1 (Scheme 2).[19] Additionally, the functionalization via metal-catalyzed nitrene transfer remains unreported. In this this work, we describe the metal-catalyzed (Cu or Rh) reaction of azulene and diazoacetates yielding mono- (at C1) or disubstituted (C1 and C3) derivatives, the latter being symmetric- or asymmetrically substituted (Scheme 2). These derivatives have been employed as starting materials toward the construction of novel azulene-dimeric structures with ester or amide linkages between the azulene units. The direct amination at C1 upon copper-catalyzed nitrene transfer from ArI=NTs is also reported, in the first example of this reaction with azulene as the substrate.

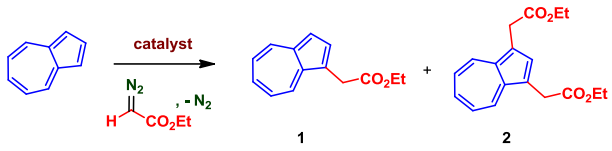
Scheme 3. Catalysts screened for the reaction of azulene with ethyl diazoacetate



RESULTS AND DISCUSSION

On the basis of our experience in the design of late transition metal-based catalysts for carbene transfer reactions from diazocompounds and concomitant functionalization of unsaturated substrates,[20,21] we studied the reaction of azulene and EDA with a series of previously described catalysts for such transformations. Coinage metals complexes with either trispyrazolylborate or *N*-heterocyclic carbene ligands or well-known dirhodium carboxylate complexes were tested (Scheme 3). Most of the experiments led to negative results, either by no EDA consumption or by formation of an untreatable mixture of compounds (see Figure S1 in the SI). However, the copper complex $Tp^{(CF_3)_2,Br}Cu(NCCH_3)$[22] afforded a mixture of two compounds **1** and **2** derived from the incorporation of one or two $CHCO_2Et$ units at the azulene skeleton at positions C1 or C1, C3, respectively (Table 1). Optimization of reaction conditions showed that the use of 1-2 mol% of the catalyst with respect to azulene and adjusting the EDA:azulene ratio allows the preferential formation of **1** or **2**. The reactions included in Table 1 provide a substantial amounts of the functionalized products: 0,73 mmol of **1** (entry 1) or 1.5 mmol of **2** (entry 3, along with 0.43 of **1**). Both products and the unreacted azulene are readily separated upon column chromatography.

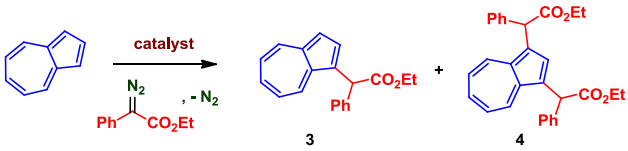
Table 1. Catalytic functionalization of azulene by carbene transfer from ethyl diazoacetate catalyzed by $Tp^{(CF_3)_2,Br}Cu(NCCH_3)$.[a]



entry	cat:EDA:azulene[b]	mmol EDA	1%	2%
1	1:50:100	1.98	37	0
2	1:75:50	0.62	28	6
3	1:120:50	9.4	11	39

[a]Conditions: azulene was dissolved in CH_2Cl_2 along with $Tp^{(CF_3)_2,Br}Cu(NCCH_3)$ and a solution of EDA in the same solvent was added for 14 h with a syringe pump under inert atmosphere. See the Table S1 in the SI for experimental details. [b]Mmol ratio.

Table 2. Catalytic functionalization of azulene with ethyl 2-phenyldiazoacetate.[a]

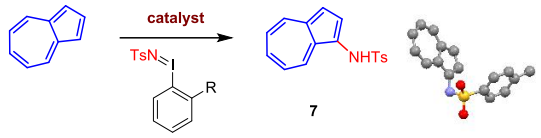


entry	catalyst	cat:PhEDA:azulene[b]	3%	4%
1	$Tp^{(CF_3)_2,Br}Cu(L)$	1:50:100	21	0
2	$Rh_2(OOCCF_3)_4$	1:50:100	40	0
3	$Tp^{(CF_3)_2,Br}Cu(L)$	1:100:50	32	6
4	$Rh_2(OOCCF_3)_4$	1:100:50	0	46

[a]Conditions employed as described Table 1. L = CH_3CN. See Table S2 in the SI for full experimental details. [b]Mmol ratio.

We next planned the use of a different diazo derivative such as ethyl diazo(phenyl)acetate (PhEDA). We examined the previously optimized conditions with $Tp^{(CF_3)2,Br}Cu(NCCH_3)$, as well as $Rh_2(OOCCF_3)_4$ and $Rh_2(OAc)_4$. The rhodium complex bearing trifluoroacetate ligands improved the reactivity of the copper complex with PhEDA as the reactant (Table 2). Using the optimal set of reaction conditions described above, and $Rh_2(OOCCF_3)_4$ as the catalyst, the appropriate tuning of the diazo-azulene ratio led to 40% of ethyl 2-(azulen-1-yl)-2-phenylacetate (**3**) (entry 2) or 46% of the disubstituted derivative **4**, as a mixture of diastereomers (entry 4), both reactions performed at a 2 mmol scale of azulene.

Table 3. Catalytic functionalization of azulene by nitrene insertion from ArINTs derivatives catalyzed by $Tp^{Br3}Cu(NCCH_3)$.[a]

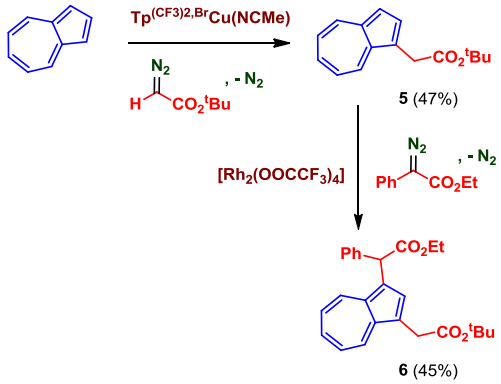


entry	R	cat:ArINTs:azulene[b]	mmol ArINTs	7%
1	H	1:50:100	0.20	15
2	O*i*Pr	1:50:100	0.80	26
3	SO_2tBu	1:50:100	0.80	43
4	SO_2tBu	1:50:100	1.40	40

[a]Conditions: Azulene was dissolved in CH_2Cl_2 along with $Tp^{Br3}Cu(NCCH_3)$ and a solution of ArINTs in the same solvent was added for 14 h with a syringe pump under inert atmosphere (PhINTs was added in one portion). See Table S3 in the SI for full experimental details. [b]Mmol ratio.

We also studied the consecutive addition of two different diazo reagents. First, *tert*-butyl diazoacetate was reacted with azulene in the presence of $Tp^{(CF_3)2,Br}Cu(NCCH_3)$ to obtain the monosubstituted derivative (**5**) in good yield (Scheme 4). After isolation, this compound was subjected to a second C-H functionalization process using PhEDA and $Rh_2(OOCCF_3)_4$ as catalyst, affording the unsymmetrical bis-substituted azulene **6** as the only product (Scheme 4).

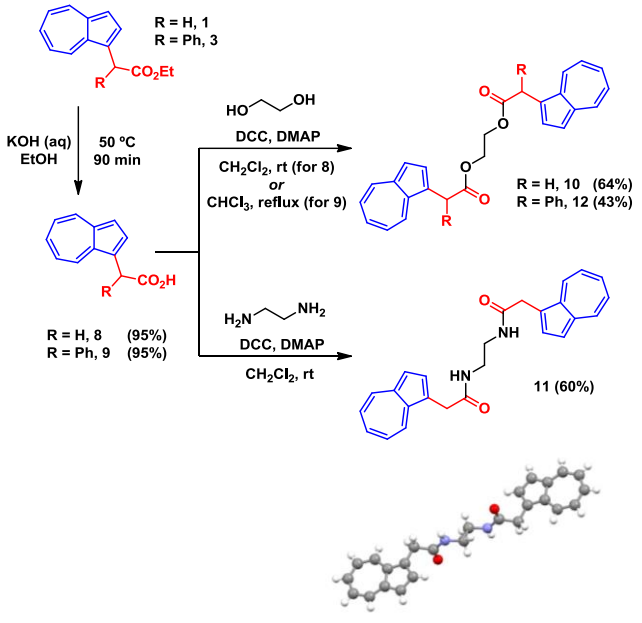
Scheme 4. Synthesis of asymmetrically disubstituted azulenes.



Our study was extended to copper-catalyzed nitrene transfer reactions from *N*-tosyliminoiodanes derivatives (ArINTs) to azulene. Initial screening of the catalysts shown in Scheme 3 identified $Tp^{Br3}Cu(NCCH_3)$ as the complex with higher activity on this transformation. Besides the reaction conditions (reaction time, reactants ratio, catalyst loading) we also tested different nitrene sources, moving from the parent PhI=NTs[23] to more soluble derivatives with substituents in the *ortho* position of the aromatic ring (Table 3).[24] In all cases, the *N*-tosyl-1-amino azulene (**7**) was obtained as the only product in the reaction. This compound has been characterized by NMR as well as by X-ray crystallography (see Figures S8 and S20 in the SI for complete description). Better yields in the reaction were achieved using *ortho*-sulfonyl- or *ortho-iso*propoxy substituted *N*-tosyliminoiodane derivatives compared with PhI=NTs. The solubility of these reagents in dichloromethane allowed us the slow addition of the reagent, reducing decomposition pathways. On the optimized conditions *ortho*-sulfonyl-*N*-tosyliminoiodane led to 40% of *N*-tosyl-1-amino azulene in 1.4 mmol scale, in the first example, to the best of our knowledge, of azulene C-H bond catalytic functionalization by nitrene transfer.

The potential of the functionalized azulene derivatives as building blocks for the preparation of degradable azulene-based materials was demonstrated by constructing azulene-dimeric structures. First, the mono-substituted azulenes **1** and **3** were readily hydrolyzed under basic

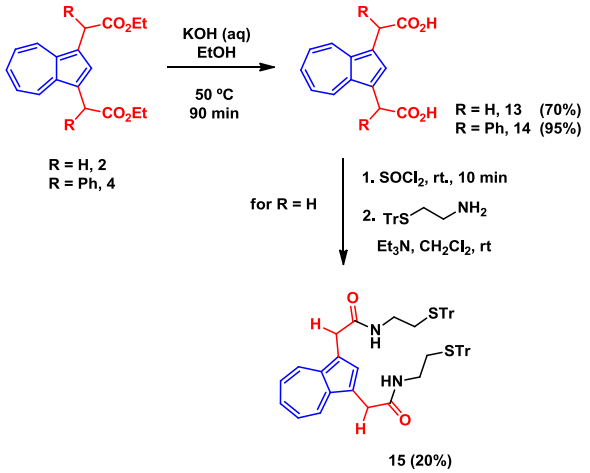
Scheme 5. Synthesis of azulene-dimeric structures.



conditions (Scheme 5) to obtain the corresponding 2-(azulen-1-yl)acetic acid (**8**) and 2-(azulen-1-yl)-2-phenylacetic acid (**9**), respectively, in high yields. Next, the azulene-dimeric compounds **10-12** were prepared in good yields through Steglich coupling reactions[25] treating **8-9** with either ethylene glycol or ethylenediamine in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC) as coupling agent and with catalytic amounts of 4-dimethylaminopyridine (DMAP) (Scheme 5). These previously unknown compounds were fully characterized by NMR and HRMS, and the solid structure of the blue amide **11** was also determined upon growing single crystals from cold dichloromethane solution.

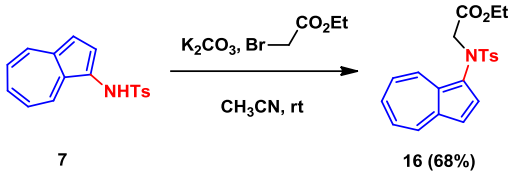
We studied the reactivity of the disubstituted azulene derivatives **2** and **4** as well. In a similar fashion to the mono-substituted azulene acids, hydrolyses of the di-functionalized azulene esters **2** and **4** were carried out under basic conditions, affording the corresponding azulene diacids **13** and **14** in high yields (Scheme 6). Diacid **13** exhibited poor solubility in dichloromethane and other common organic solvents precluding esterification or amidation reactions. Nevertheless, it could be successfully converted into the corresponding bis(acyl chloride) by treatment with thionyl chloride for 10 min. at room temperature. The intermediate, which was found to decompose upon standing, was subsequently reacted with 2-(tritylthio)ethan-1-amine to obtain the disubstituted amide derivative **15** in moderate yield (Scheme 6).

Scheme 6. Derivatization of di-functionalized azulenes 2,4.



Finally, we also examined further functionalization of amino azulene **7**. Alkylation of the amine was performed with ethyl 2-bromoacetate leading to a protected glycine-azulene derivative **16** in good yield (Scheme 7), as an example of the synthesis of an azulene-containing α-aminoacid derivative.

Scheme 7. Derivatization of 1-amino azulene 7.



CONCLUSIONS

In summary, we have developed the first metal-catalyzed systems for azulene C-H bond functionalization by carbene/nitrene transfer using diazocompounds or ArI=NTs, respectively. The process is regioselective toward the C1 position. By adjusting the diazo-azulene ratio, both mono or disubstituted azulene (C1 and C3 positions) derivatives can be targeted with high selectivity and good yields. Furthermore, asymmetric disubstituted products are also accessible *via* sequential addition of two different diazo reagents. These novel azulene derivatives can be further converted into azulene-dimeric compounds bearing *O*- or *N*- based bridges. Further use of such compounds toward the preparation of (bio)degradable azulene-based materials is currently under development.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, reactions were carried out under nitrogen atmosphere with standard Schlenck techniques. Solvents were purchased from commercial sources or dried in a solvent purification system (MB SPS-800, MBRAUN). Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merck 60 F254) and UV light as visualizing agent. Chromatography purifications were carried out using silica gel (0.035-0.070 mm, 60 Å). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. NMR spectra were recorded at 298 K on an Agilent 400 MR spectrometer. Chemical shift values for ^{1}H and ^{13}C are reported as δ values (ppm) relative to the deuterated solvent and coupling constants (*J*) in Hz. X-ray diffraction measurements were performed on an ApexDuo (Bruker-AXS) diffractometer system, using MoKα (λ = 0.7107 Å) radiation. The analyzed crystals were grown by slow evaporation of acetone solutions and freeze-cooled to ca. 110 K. Mass spectra were obtained on a SYNAPT - High Definition Mass Spectrometry or Orbitrap Elite mass spectrometer. Ionization methods: ESI (positive or negative) and APPI (atmospheric pressure photo ionization). All commercially available compounds were used as received. Catalyst have been prepared by described methodologies: $Tp^{Br3}Cu(NCCH_3)$,[26] $Tp^{Mes}Cu(THF)$,[20a,27] $Tp^{(CF3)2Br}Cu(NCCH_3)$,[22] $Tp^{Br3}Ag(THF)$,[28] $Tp^{(CF3)2Br}Ag(THF)$,[22] Rh_2OAc_4,[29] Rh_2TFA_4,[30] IPrAuCl,[31] IPrCuCl.[32] *N*-Tosyliminoiodanes derivatives (ArINTs, Ar = C_6H_5,[23] 2-SO_2tBu-C_6H_4,[24] 2-*i*PrO-C_6H_4[24]) were synthetized by described methods.

Ethyl 2-(azulen-1-yl)acetate (**1**). Azulene (507 mg, 3.95 mmol, 2 eq.) and $Tp^{(CF_3)_2Br}Cu(NCCH_3)$ (38.1 mg, 0.04 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (10 mL) under inert atmosphere. To this solution, EDA (0.23 mL, 1.98 mmol, 1 eq.) in dry CH_2Cl_2 (5 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 100:0 to 95:5) to obtain the azulene derivative **1** as a blue oil (158 mg, 37%) and to recover 267 mg (53%) of azulene. Average of two runs. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.7 Hz, 1H, CH_{arom}), 8.31 (d, *J* = 9.4 Hz, 1H, CH_{arom}), 7.89 (d, *J* = 3.8 Hz, 1H, CH_{arom}), 7.60 (t, *J* = 9.9 Hz, 1H, CH_{arom}), 7.36 (d, *J* = 3.8 Hz, 1H, CH_{arom}), 7.18 (t, *J* = 9.8 Hz, 1H, CH_{arom}), 7.14 (t, *J* = 9.7 Hz, 1H, CH_{arom}), 4.15 (q, *J* = 7.1 Hz, 2H, $CO_2C\underline{H_2}CH_3$), 4.10 (s, 2H, $C\underline{H_2}CO_2Et$), 1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2C\underline{H_3}$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.0 ($\underline{C}O_2Et$), 141.1 (C_{arom}), 138.1 (CH_{arom}), 137.8 (CH_{arom}), 136.9 (CH_{arom}), 136.5 (C_{arom}), 133.9 (CH_{arom}), 123.0 (CH_{arom}), 122.5 (CH_{arom}), 121.8 (C_{arom}), 117.0 (CH_{arom}), 61.0 ($CO_2\underline{C}H_2CH_3$), 34.0 ($\underline{C}H_2CO_2Et$), 14.4 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{14}H_{14}O_2$ 214.0994; Found 214.0988.

Diethyl 2,2'-(azulene-1,3-diyl)diacetate (**2**). Azulene (500 mg, 3.90 mmol, 1 eq.) and $Tp^{(CF_3)_2Br}Cu(NCCH_3)$ (75.1 mg, 0.08 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (15 mL) under inert atmosphere. To this solution, EDA (1.09 mL, 9.36 mmol, 2.4 eq.) in dry CH_2Cl_2 (7 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 95:5 to 90:10) to obtain the azulene derivative **2** as a blue oil (456 mg, 39%) and 92 mg (11%) of azulene derivative **1**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 9.5 Hz, 2H, CH_{arom}), 7.85 (s, 1H, CH_{arom}), 7.58 (t, *J* = 9.8 Hz, 1H, CH_{arom}), 7.13 (t, *J* = 9.9 Hz, 2H, CH_{arom}), 4.14 (q, *J* = 7.2 Hz, 4H, $CO_2C\underline{H_2}CH_3$), 4.06 (s, 4H, $C\underline{H_2}CO_2Et$), 1.24 (t, *J* = 7.1 Hz, 6H, $CO_2CH_2C\underline{H_3}$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.9 ($\underline{C}O_2Et$), 139.2 (CH_{arom}), 138.1 (CH_{arom}), 137.3 (C_{arom}), 133.9 (CH_{arom}), 122.6 (CH_{arom}), 120.6 (C_{arom}), 61.0 ($CO_2\underline{C}H_2CH_3$), 33.8 ($\underline{C}H_2CO_2Et$), 14.4 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{18}H_{20}O_4$ 300,1362; Found 300.1365.

Ethyl 2-(azulen-1-yl)-2-phenylacetate (**3**). Azulene (250 mg, 1.95 mmol, 2 eq.) and $Rh_2(OOCCF_3)_4$ (12.8 mg, 0.02 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (5 mL) under inert atmosphere. To this solution, PhEDA (185 mg, 0.97 mmol, 1 eq.) in dry CH_2Cl_2 (5 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 100:0 to 95:5) to obtain the azulene derivative **3** as a blue oil (115 mg, 41%) and to recover 132 mg (53%) of azulene. Average of two runs. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 3.9 Hz, 1H, CH_{arom}), 8.34 (d, *J* = 3.4 Hz, 1H, CH_{arom}), 8.06 (d, *J* = 4.0 Hz, 1H, CH_{arom}), 7.60 (t, *J* = 9.9 Hz, 1H, CH_{arom}), 7.42 (d, *J* = 4.0 Hz, 1H, CH_{arom}), 7.41 – 7.38 (m, 2H, CH_{arom}), 7.36 – 7.32 (m, 2H, CH_{arom}), 7.29 – 7.25 (m, 1H, CH_{arom}), 7.17 (t, *J* = 9.7 Hz, 2H, CH_{arom}), 5.73 (s, 1H, $AzC\underline{H}CO_2Et$), 4.26 (AB of ABX_3; J_{AB} = 10.8 Hz, J_X = 7.1 Hz, 2H, $CO_2C\underline{H_2}CH_3$), 1.29 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2C\underline{H_3}$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.0 ($\underline{C}O_2Et$), 141.2 (C_{arom}), 139.7 (C_{arom}), 137.8 (CH_{arom}), 137.3 (CH_{arom}), 137.1 (CH_{arom}), 135.9 (C_{arom}), 133.3 (CH_{arom}), 128.6 (CH_{arom}), 128.4 (CH_{arom}), 127.1 (CH_{arom}), 126.0 (C_{arom}), 123.2 (CH_{arom}), 122.7 (CH_{arom}), 117.2 (CH_{arom}), 61.3 ($CO_2\underline{C}H_2CH_3$), 50.3 ($Az\underline{C}HCO_2Et$), 14.3 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{20}H_{18}O_2$ 290.1307; Found 290.1309.

Diethyl 2,2'-(azulene-1,3-diyl)bis(2-phenylacetate) (**4**). Azulene (250 mg, 1.95 mmol, 1 eq.) and $Rh_2(OOCCF_3)_4$ (26.7 mg, 0.04 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (5 mL) under inert atmosphere. To this solution, PhEDA (779 mg, 4.10 mmol, 2.1 eq.) in dry CH_2Cl_2 (5 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 95:5 to 90:10) to obtain the azulene derivative **4** (1:1 mixture of diastereomers) as a blue solid (404 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.3 Hz, 2H, CH_{arom}), 8.27 (d, *J* = 8.4 Hz, 2H, CH_{arom}), 8.17 (s, 1H, CH_{arom}), 8.14 (s, 1H, CH_{arom}), 7.55 (t, *J* = 9.8 Hz, 1H, CH_{arom}), 7.55 (t, *J* = 9.7 Hz, 1H, CH_{arom}), 7.37 – 7.28 (m, 16H, CH_{arom}), 7.27 – 7.21 (m, 4H, CH_{arom}), 7.11 (t, *J* = 10.0 Hz, 2H, CH_{arom}), 7.10 (t, *J* = 10.0 Hz, 2H, CH_{arom}), 5.68 (s, 4H, $AzC\underline{H}CO_2Et$), 4.23 (q, *J* = 7.1 Hz, 4H, $CO_2C\underline{H_2}CH_3$), 4.21 (q, J = 7.1 Hz, 4H, $CO_2C\underline{H_2}CH_3$), 1.27 (t, *J* = 7.1 Hz, 6H, $CO_2CH_2C\underline{H_3}$), 1.22 (t, *J* = 7.1 Hz, 6H, $CO_2CH_2C\underline{H_3}$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.8 ($\underline{C}O_2Et$), 172.8 ($\underline{C}O_2Et$), 139.5 (C_{arom}), 138.2 (CH_{arom}), 138.2 (CH_{arom}), 137.8 (CH_{arom}), 137.7 (CH_{arom}), 136.9 (C_{arom}), 136.8 (C_{arom}), 133.7 (CH_{arom}), 133.6 (CH_{arom}), 128.6 (CH_{arom}), 128.6 (CH_{arom}), 128.5 (CH_{arom}), 128.5 (CH_{arom}), 127.1 (CH_{arom}), 127.1 (CH_{arom}), 125.0 (C_{arom}), 124.9 (C_{arom}), 123.0 (CH_{arom}), 61.3 ($CO_2\underline{C}H_2CH_3$), 61.3 ($CO_2\underline{C}H_2CH_3$), 50.5 ($Az\underline{C}HCO_2Et$), 50.4 ($Az\underline{C}HCO_2Et$), 14.3 ($CO_2CH_2\underline{C}H_3$), 14.3 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and

HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{30}H_{28}O_4$ 452.1988; Found 452.1983.

Tert-butyl 2-(azulen-1-yl)acetate (**5**). Azulene (500 mg, 3.87 mmol, 2 eq.) and $Tp^{(CF_3)_2Br}Cu(NCCH_3)$ (37 mg, 0.04 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (10 mL) under inert atmosphere. To this solution, tBuEDA (268 µL, 1.93 mmol, 1 eq.) in dry CH_2Cl_2 (5 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 100:0 to 95:5) to obtain the azulene derivative **5** as a blue oil (219 mg, 47%) and to recover 253 mg (51%) of azulene. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 9.7 Hz, 1H, CH_{arom}), 8.32 (d, *J* = 9.4 Hz, 1H, CH_{arom}), 7.95 (d, *J* = 3.9 Hz, 1H, CH_{arom}), 7.60 (t, *J* = 9.9 Hz, 1H, CH_{arom}), 7.41 (d, *J* = 3.8 Hz, 1H, CH_{arom}), 7.19 (t, *J* = 9.5 Hz, 1H, CH_{arom}), 7.14 (t, *J* = 9.5 Hz, 1H, CH_{arom}), 4.06 (s, 2H, $C\underline{H}_2CO_2tBu$), 1.49 (s, 9H, $CO_2C(C\underline{H}_3)_3$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.2 ($\underline{C}O_2tBu$), 140.9 (C_{arom}), 138.0 (CH_{arom}), 137.6 (CH_{arom}), 136.7 (CH_{arom}), 136.4 (C_{arom}), 133.8 (CH_{arom}), 122.7 (CH_{arom}), 122.4 (C_{arom}), 122.2 (CH_{arom}), 116.9 (CH_{arom}), 80.7 ($CO_2\underline{C}(CH_3)_3$), 35.2 ($\underline{C}H_2CO_2tBu$), 28.1 ($CO_2C(\underline{C}H_3)_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{16}H_{18}O_2$ 242.1307; Found 242.1322.

Ethyl 2-(3-(2-(tert-butoxy)-2-oxoethyl)azulen-1-yl)-2-phenylacetate (**6**). Azulene derivative **5** (219 mg, 0.90 mmol, 1 eq.) and $Rh_2(OOCCF_3)_4$ (11.9 mg, 0.02 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (3 mL) under inert atmosphere. To this solution, PhEDA (215 mg, 1.13 mmol, 1.25 eq.) in dry CH_2Cl_2 (3 mL) was added during 14 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 95:5 to 90:10) to obtain the azulene derivative **6** as a blue oil (163 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 9.7 Hz, 1H, CH_{arom}), 8.15 (d, *J* = 9.7 Hz, 1H, CH_{arom}), 7.88 (s, 1H, CH_{arom}), 7.44 (t, *J* = 9.8 Hz, 1H, CH_{arom}), 7.29 – 7.23 (m, 2H, CH_{arom}), 7.23 – 7.16 (m, 2H, CH_{arom}), 7.16 – 7.10 (m, 1H, CH_{arom}), 7.02 (t, *J* = 9.5 Hz, 1H, CH_{arom}), 6.97 (t, *J* = 9.6 Hz, 1H, CH_{arom}), 5.56 (s, 1H, $AzC\underline{H}CO_2Et$), 4.12 (q, *J* = 7.1 Hz, 2H, $CO_2C\underline{H}_2CH_3$), 3.88 (s, 2H, $C\underline{H}_2CO_2tBu$), 1.31 (s, 9H, $CO_2C(C\underline{H}_3)_3$), 1.15 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2C\underline{H}_3$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.0, 171.0 ($\underline{C}O_2Et$, $\underline{C}O_2tBu$), 139.6 (C_{arom}), 138.4 (CH_{arom}), 138.0 (CH_{arom}), 137.4 (C_{arom}), 136.6 (C_{arom}), 134.1 (CH_{arom}), 133.2 (CH_{arom}), 128.3 (CH_{arom}), 128.5 (CH_{arom}), 127.1 (CH_{arom}), 124.7 (C_{arom}), 122.6 (CH_{arom}), 122.6 (CH_{arom}), 121.5 (C_{arom}), 80.8 ($CO_2\underline{C}(CH_3)_3$), 61.3 ($CO_2\underline{C}H_2CH_3$), 50.1 ($AzCHCO_2Et$), 35.3 ($\underline{C}H_2CO_2tBu$), 28.1 ($CO_2C(\underline{C}H_3)_3$), 14.3 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{26}H_{28}O_4$ 404.1988; Found 404.1999.

N-(Azulen-1-yl)-4-methylbenzenesulfonamide (**7**). Azulene (358 mg, 2.80 mmol, 2 eq.) and $Tp^{Br3}Cu(NCCH_3)$ (29 mg, 0.03 mmol, 0.02 eq.) were mixed in dry CH_2Cl_2 (3 mL) under inert atmosphere. To this solution, *ortho*-sulfonyl-*N*-tosyliminoiodane (690 mg, 1.40 mmol, 1 eq.) in dry CH_2Cl_2 (12 mL) was added during 7 hours *via* syringe pump. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/AcOEt 8:2) to obtain the azulene derivative **7** as a blue solid (166 mg, 40%) and to recover 207 mg (58%) of azulene. Mp: 145–146 °C. ^{1}H NMR (500 MHz, CD_3OD) δ 8.21 (dd, *J* = 9.4, 0.5 Hz, 1H, CH_{arom}), 8.08 (d, *J* = 9.4 Hz, 1H, CH_{arom}), 7.56 – 7.50 (m, 2H, CH_{arom}), 7.49 – 7.45 (m, 2H, CH_{arom}), 7.19 – 7.14 (m, 3H, CH_{arom}), 7.09 (t, *J* = 9.7 Hz, 1H, CH_{arom}), 6.98 (t, *J* = 9.8 Hz, 1H, CH_{arom}), 2.31 (s, 3H, $SO_2C_6H_4C\underline{H}_3$) ppm. $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ 144.7 (C_{arom}), 140.0 (C_{arom}), 139.5 (CH_{arom}), 138.8 (CH_{arom}), 138.2 (C_{arom}), 134.7 (CH_{arom}), 134.5 (CH_{arom}), 133.7 (C_{arom}), 130.4 (CH_{arom}), 128.2 (CH_{arom}), 124.2 (CH_{arom}), 124.2 (C_{arom}), 123.5 (CH_{arom}), 116.2 (CH_{arom}), 21.4 ($SO_2C_6H_4\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-ion trap) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{15}NO_2SNa$ 320,0716; Found 320,0711. CCDC 1848245.

2-(Azulen-1-yl)acetic acid (**8**). Azulene derivative **1** (165 mg, 0.77 mmol) was dissolved in EtOH (15 mL), followed by the addition of KOH 1M (10 mL). The reaction was refluxed for 1.5 h, cooled to rt. and acidified with HCl 1M. Then, the crude product was extracted with EtOAc (2 x 20 mL), the combined extracts were washed repeatedly with H_2O, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The blue oil obtained was used without further purification (136 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 3.5 Hz, 1H), 8.29 (d, *J* = 3.7 Hz, 1H), 7.86 (d, *J* = 4.0 Hz, 1H), 7.60 (t, *J* = 9.6 Hz, 1H), 7.35 (d, *J* = 4.0 Hz, 1H), 7.18 (t, *J* = 10.0 Hz, 1H), 7.15 (t, *J* = 9.6 Hz, 1H), 4.12 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.3, 141.1, 138.2, 137.9, 137.1, 136.6, 133.8, 123.2, 122.7, 120.6, 117.1, 33.6 ppm. HRMS (APPI-Q-TOF) m/z: $[M-H]^-$ Calcd for $C_{12}H_9O_2$ 185.0603; Found 185.0611.

2-(Azulen-1-yl)-2-phenylacetic acid (**9**). Azulene derivative **9** was prepared correspondingly to **8** *via* the hydrolysis of **3** (138 mg, 0.47 mmol), yielding a blue oil (117 mg, 95%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 9.6 Hz, 1H), 8.29 (d, *J* = 9.6 Hz, 1H), 8.00 (d, *J* = 4.0 Hz, 1H), 7.58 (t, *J* = 10 Hz, 1H), 7.39 – 7.27 (m, 6H), 7.26 – 7.21 (m, 1H), 7.15 (t, *J* = 9.6 Hz, 1H), 7.14 (t, *J* = 9.8 Hz, 1H), 5.70 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100

MHz, $CDCl_3$) δ 178.5, 141.3, 138.9, 138.0, 137.7, 137.4, 136.0, 133.3, 128.7, 128.6, 127.4, 125.0, 123.5, 123.0, 117.3, 50.1 ppm. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{18}H_{14}O_2$ 262.0994; Found 262.0990.

Ethane-1,2-diyl bis(2-(azulen-1-yl)acetate) (**10**). Ethylene glycol (6.8 mg, 0.11 mmol), DCC (54.5 mg, 0.26 mmol) and DMAP (1.3 mg, 0.011 mmol) were added to a solution of **8** (41 mg, 0.22 mmol) in dry DCM (10 mL) and the reaction was stirred at rt. for 16 h under nitrogen atmosphere. Then, the reaction was filtered and the solvent was removed under reduced pressure. The crude was dissolved in DCM (2 mL) and filtered through a 0.22 μm syringe filter. The product was isolated as a dark blue oil by silica chromatography using 15% EtOAc in hexane (56 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 9.4 Hz, 2H), 8.28 (d, *J* = 9.4 Hz, 2H), 7.84 (d, *J* = 3.6 Hz, 2H), 7.59 (t, *J* = 9.6 Hz, 2H), 7.35 (d, *J* = 3.6 Hz, 2H), 7.15 (t, *J* = 9.7 Hz, 2H), 7.14 (t, *J* = 9.7 Hz, 2H), 4.26 (s, 4H), 4.03 (s, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.6, 141.1, 138.1, 137.8, 137.0, 136.5, 133.8, 123.1, 122.6, 121.3, 117.1, 62.5, 33.7 ppm. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{26}H_{22}O_4$ 398.1518; Found: 398.1544.

N,N′-(ethane-1,2-diyl)bis(2-(azulen-1-yl)acetamide) (**11**). Ethylenediamine (6.6 mg, 0.11 mmol), DCC (54.5 mg, 0.26 mmol) and DMAP (1.3 mg, 0.011 mmol) were added to a solution of **8** (41 mg, 0.22 mmol) in dry DCM (10 mL) and the reaction was stirred at rt. for 16 h under nitrogen atmosphere. Then, the reaction was filtered and the solvent was removed under reduced pressure. The crude was dissolved in DCM (2 mL) and filtered through a 0.22 μm syringe filter. The product was isolated as a dark blue solid on deactivated (5% H_2O) basic alumina using 1% MeOH in EtOAc (52 mg, 60%). Mp: 183–184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 9.6 Hz, 2H), 8.11 (d, *J* = 9.6 Hz, 2H), 7.71 (d, *J* = 4.0 Hz, 2H), 7.61 (t, *J* = 9.6 Hz, 2H), 7.37 (d, *J* = 4.0 Hz, 2H), 7.18 (t, J = 9.7 Hz, 2H), 7.13 (t, J = 9.8 Hz, 2H), 5.71 (brs, 2H), 3.88 (s, 4H), 3.11 (d, *J* = 2.4 Hz, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.6, 141.3, 138.5, 138.3, 137.3, 136.9, 133.9, 123.5, 123.0, 122.0, 117.4, 39.6, 35.9 ppm. HRMS (EI-magnetic sector) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}O_2N_2$ 397.1911; Found: 397.1922. CCDC 1829375.

Ethane-1,2-diyl bis(2-(azulen-1-yl)-2-phenylacetate) (**12**). Azulene derivative **12** was prepared correspondingly to **10** using **9** (25 mg, 0.096 mmol), ethylene glycol (3 mg, 0.048 mmol), DCC (30 mg, 0.14 mmol) and DMAP (1.2 mg, 0.01 mmol) in $CHCl_3$ at reflux, yielding a blue solid (11 mg, 43%). Mp: 159–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 9.4 Hz, 1H) 8.28 (d, J = 9.4 Hz, 1H), 8.24 (d, *J* = 6.2 Hz, 1H), 8.21 (d, *J* = 6.2 Hz, 1H), 7.94 (t, *J* = 4.0 Hz, 2H), 7.56 (t, *J* = 9.8 Hz, 1H), 7.55 (t, *J* = 9.8 Hz, 1H), 7.32-7.20 (m, 12H), 7.16-7.04 (m, 4H), 5.63 (s, 1H), 5.62 (s, 1H), 4.35 (s, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.8, 141.2, 139.3, 137.9, 137.3, 137.2, 135.9, 133.3, 128.6, 128.5, 127.2, 125.6, 123.3, 122.8, 117.3, 62.8, 50.1 ppm. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{38}H_{30}O_4$ 550.2144; Found: 550.2143.

2,2′-(Azulene-1,3-diyl)diacetic acid (**13**). Diacid **13** was prepared correspondingly to **8** *via* the hydrolysis of **2** (150 mg, 0.5 mmol), yielding a blue solid (85 mg, 70%) which was used without further purification. Mp: 220–221 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.33 (brs, 2H), 8.30 (d, *J* = 9.8 Hz, 2H), 7.77 (s, 1H), 7.63 (t, *J* = 9.8 Hz, 1H), 7.15 (t, *J* = 9.8 Hz, 2H), 4.00 (s, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 172.9, 139.1, 138.1, 136.5, 134.0, 122.0, 121.3, 33.0 ppm. HRMS (EI-magnetic sector) m/z: $[M-H]^-$ Calcd for $C_{14}H_{11}O_4$ 243.0633; Found 243.0662.

2,2′-(Azulene-1,3-diyl)bis(2-phenylacetic acid) (**14**). Diacid **14** was prepared correspondingly to **8** *via* the hydrolysis of **4** (167 mg, 0.37 mmol), yielding a dark blue solid (139 mg, 95%, mixture of diastereomers) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.21 (d, *J* = 9.8 Hz, 2H), 8.19 (s, 1H), 8.12 (d, *J* = 9.8 Hz, 2H), 7.56 (t, *J* = 9.6 Hz, 1H), 7.51 (t, *J* = 9.6 Hz, 1H), 7.32 – 7.20 (m, 16H), 7.10 (t, *J* = 9.8 Hz, 2H), 7.03 (t, *J* = 9.8 Hz, 2H), 5.72 (s, 1H), 5.70 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.1, 179.1, 138.9, 138.8, 138.7, 137.1, 136.2, 134.4, 133.8, 128.8, 128.7, 128.6, 127.5, 123.6, 123.5, 123.3, 50.9, 50.2 ppm. HRMS (EI-Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{20}O_4Na$ 419,1254; Found: 419,1255.

2,2′-(Azulene-1,3-diyl)bis(N-(2-(tritylthio)ethyl)acetamide) (**15**). A flame-dried flask containing **13** (40 mg, 0.16 mmol) was cooled in an ice bath and $SOCl_2$ (230 μL, 3.2 mmol) was added dropwise under nitrogen atmosphere. Upon completion, the bath was removed and the reaction was stirred at rt. for 10 min., followed by removal of the $SOCl_2$ excess under reduced pressure. Then, the red-brown residue was dissolved in dry DCM (10 mL), 2-(tritylthio)ethan-1-amine (102 mg, 0.32 mmol) and Et_3N (180 μL, 1.28 mmol) were added and the reaction was stirred at rt. for 16 h under nitrogen atmosphere. After removal of the solvent under reduced pressure the product was isolated as a blue solid by silica chromatography using 80% EtOAc in hexane (9.7 mg, 20%). Mp: 202–203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 9.6 Hz, 2H), 7.69 (s, 1H), 7.51 (t, *J* = 9.6 Hz, 1H), 7.24-7.16 (m, 30H), 7.07 (t, *J* = 9.6 Hz, 2H), 5.46 (t, *J* = 5.6 Hz, 2H), 3.91 (s, 4H), 2.90 (q, *J* = 6.2 Hz, 4H), 2.27 (t, *J* = 6.4 Hz, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.2, 144.7, 139.6, 138.9, 137.8, 134.6, 129.5, 128.0, 126.9, 123.4, 121.3, 66.6, 38.1, 35.8, 31.9 ppm. HRMS (EI-magnetic sector) m/z: $[M+Na]^+$ Calcd for $C_{56}H_{50}O_2N_2S_2Na$ 869.3206; Found: 869.3217.

Ethyl N-(azulen-1-yl)-N-tosylglycinate (**16**). Amino azulene derivative **7** (44 mg, 0.15 mmol) and K_2CO_3 (41 mg, 0.30 mmol, 2 eq.) were dissolved in acetonitrile (2 mL), fol-

lowed by the addition of ethyl 2-bromoacetate (25 µL, 0.22 mmol, 1.5 eq.), and the reaction was stirred at rt. for 5 hours. Then, the solvent was evaporated and the crude was purified by flash column chromatography (petroleum ether/Et_2O 1:1) to obtain the azulene derivative **16** as a blue oil (39 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 9.7 Hz, 1H, CH_{arom}), 8.29 (d, *J* = 9.5 Hz, 1H, CH_{arom}), 7.67 (t, *J* = 9.7 Hz, 1H, CH_{arom}), 7.55 – 7.51 (m, 2H, CH_{arom}), 7.35 (d, *J* = 4.2 Hz, 1H, CH_{arom}), 7.31 – 7.20 (m, 4H, CH_{arom}), 7.16 (d, *J* = 4.2 Hz, 1H, CH_{arom}), 4.49 (s, 2H, $NC\underline{H}_2CO_2Et$), 4.10 (q, *J* = 7.2 Hz, 2H, $CO_2C\underline{H}_2CH_3$), 2.42 (s, 3H, $SO_2C_6H_4C\underline{H}_3$), 1.17 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2C\underline{H}_3$) ppm. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.2 ($\underline{C}O_2Et$), 143.7 (C_{arom}), 139.1 (C_{arom}), 139.0 (CH_{arom}), 138.3 (CH_{arom}), 136.3 (C_{arom}), 135.8 (C_{arom}), 135.3 (CH_{arom}), 134.8 (CH_{arom}), 129.4 (CH_{arom}), 128.1 (CH_{arom}), 125.7 (C_{arom}), 124.4 (CH_{arom}), 115.1 (CH_{arom}), 61.5 ($CO_2\underline{C}H_2CH_3$), 54.5 ($N\underline{C}H_2CO_2Et$), 21.7 ($SO_2C_6H_4\underline{C}H_3$), 14.2 ($CO_2CH_2\underline{C}H_3$) ppm. Resonance assignment was carried out using COSY and HSQC experiments. HRMS (EI-ion trap) m/z: $[M+H]^+$ Calcd for $C_{21}H_{22}NO_4S$ 384,1264; Found 384,1259.

Additional compounds: *Benzyl 2-(azulen-1-yl)-2-phenylacetate* (**S1**). Benzyl alcohol (11 mg, 0.1 mmol), DCC (31 mg, 0.26 mmol) and DMAP (1.2 mg, 0.01 mmol) were added to a solution of **9** (26 mg, 0.1 mmol) in $CHCl_3$ (5 mL) and the reaction was refluxed for 16 h under nitrogen atmosphere. Then, the reaction was filtered and the solvent was removed under reduced pressure. The crude was dissolved in DCM (2 mL) and filtered through a 0.22 µm syringe filter. The product was isolated as a dark blue oil by silica chromatography using 5% EtOAc in hexane (20 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.8 Hz, 1H), 8.28 (d, J = 10.1 Hz, 1H), 7.99 (d, *J* = 3.6 Hz, 1H), 7.56 (t, *J* = 9.6 Hz, 1H), 7.37 (m, 3H), 7.31-7.23 (m, 8H), 7.14 (t, *J* = 9.7 Hz, 1H), 7.10 (t, *J* = 9.7 Hz, 1H), 5.76 (s, 1H), 5.21 (s, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.9, 141.2, 139.4, 137.8, 137.4, 137.1, 135.9, 133.3, 128.6, 128.6, 128.5, 128.3, 127.2, 125.8, 123.3, 122.7, 117.2, 67.0, 50.3 ppm. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{25}H_{20}O_2$ 352.1463; Found: 352.1468.

Dibenzyl 2,2'-(azulene-1,3-diyl)bis(2-phenylacetate) (**S2**). Benzyl alcohol (14 mg, 0.13 mmol), DCC (34 mg, 0.16 mmol) and DMAP (1.6 mg, 0.013 mmol) were added to a solution of **14** (26 mg, 0.065 mmol) in $CHCl_3$ (5 mL) and the reaction was refluxed for 16 h under nitrogen atmosphere. Then, the reaction was filtered and the solvent was removed under reduced pressure. The crude was dissolved in DCM (2 mL) and filtered through a 0.22 µm syringe filter. The product was isolated as a blue viscous oil (mixture of diastereomers) by silica chromatography using 5% EtOAc in hexane (23 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 9.6 Hz, 1H), 8.20 (d, *J* = 9.6 Hz, 1H), 8.11 (s, 1H), 7.51 (t, *J* = 10.0 Hz, 1H), 7.29 – 7.21 (m, 20H), 7.03 (t, *J* = 9.6 Hz, 2H), 5.70 (s, 2H), 5.16 (s, 4H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.7, 139.3, 139.2, 138.2, 137.9, 137.6, 136.9, 136.9, 135.9, 135.8, 133.8, 133.7, 128.6, 128.5, 128.2, 127.2, 124.6, 123.1, 67.1, 67.0, 50.4 ppm. HRMS (EI-magnetic sector) m/z: $[M]^+$ Calcd for $C_{40}H_{32}O_4$ 576.2301; Found: 576.2294.

Supporting Information

NMR spectra (PDF) and cif files for compounds **7** and **11**.

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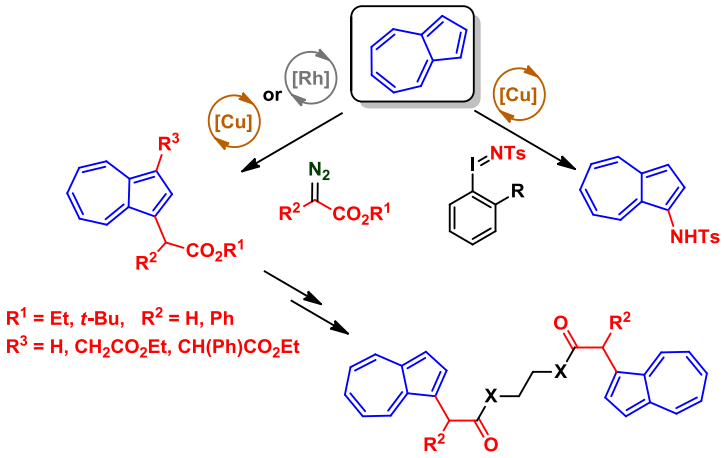
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NHTs
R1 = Et, t-Bu, R2 = H, Ph
R3 = H, CH2CO2Et, CH(Ph)CO2Et
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