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CO_2 on a Tightrope: Stabilization, Room-Temperature Decarboxylation, and Sodium-Induced Carboxylate Migration

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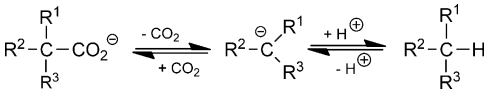
Abstract: A sterically shielded 3-substituted zwitterionic *N,N*-dimethylisotryptammonium carboxylate has been synthesized by consecutive chemoselective double alkylation of indole. The carboxylate undergoes a quantitative and unusually facile decarboxylation in dimethyl sulfoxide (DMSO) or dimethyl formamide (DMF) at room temperature. The breaking of a nearly equidistant hydrogen bond by solvent molecules initiates heterolytic C–C cleavage. The decarboxylation rate decreases with increasing CO_2 partial pressure, proving the competitiveness of protonation and re-carboxylation of the carbanionic intermediate. Corresponding spiro compounds containing silylene and stannylene moieties show high thermal stability. Addition of an excess of methyllithium to the sodium salt triggers a reaction sequence comprising a deprotonation, carboxylate transfer, and nucleophilic trapping of the rearranged carboxylate by another equivalent of methyllithium. Hydrolytic work-up of the geminal diolate leads to an acetyl product. The role of the sodium counterion and the mechanism of the rearrangement have been unraveled by deuteration experiments.

Keywords: carbon dioxide · decarboxylation · rearrangement · spiro compounds · zwitterions

Introduction

Scientific and industrial interest in reactions of CO_2 with inexpensive organic substrates to produce useful bulk chemicals has greatly increased recently.[1] In such reactions, carboxylates are a mandatory intermediate or the final product. Controlling the stability of carboxylates is crucial for carbon dioxide fixation with a low thermodynamic driving force, which is tantamount to energy efficiency. In natural CO_2 fixation, the alternatives of hydrogen bonding versus magnesium coordination to the carboxylate in the ribulose-1,5-bisphosphate carboxylase oxygenase (RuBisCo) active site are a matter of recent discussions.[2] Besides CO_2 fixation, carboxylic acids and the corresponding carboxylates are ubiquitous both in organic chemistry as well as in biochemistry.[3] Various classes of pharmacologically or industrially important compounds, such as stilbenes,[4] hydroxystyrenes,[5] or indoles,[6] as well as chiral auxiliaries for asymmetric synthesis,[7] are prepared from their parent acids by decarboxylation (Scheme 1). Ketonization by decarboxylation,[8] decarboxylative palladation reactions in Heck-type olefination,[9] the synthesis of biaryls by catalytic decarboxylative coupling,[10] and the Kolbe reaction,[11] a decarboxylative electrochemical dimerization, are valuable tools for the synthesis of various substances starting from carboxylic acids.



Scheme 1. General scheme of anionic aliphatic decarboxylation and of CO_2 fixation.

Besides ambient enzymatic decarboxylative systems in nature, the decarboxylation reaction in organic synthesis has remained one of the more difficult transformations. There are numerous procedures in the literature for the elimination of CO_2 from organic substrates. The simplest transformations merely require heating, for example the preparation of tryptamine from tryptophan.[12] Generally, however, decarboxylation reactions require the use of a base[6d,13] or prior activation by a metal catalyst.[14] Microwave heating provides a useful tool for acceleration of reactions and broadening the scope of usable substrates.[5a,6a,13,15] Conversion into Barton esters followed by treatment with tributyltin hydride,[16] photochemical decarboxylation,[17] or ketone catalysis[18] are further decarboxylation methods.

The decarboxylation reactions mentioned above either involve a catalyst or some kind of activation by ultraviolet radiation, microwave radiation, or thermal energy. There are only a few carboxylic acids that undergo decarboxylation at room temperature. A well-known reaction is the decarboxylation of 3-keto acids (Scheme 2, top), first reported by Pollak et al. in 1907.[19] Numerous studies concerning the decarboxylation of 3-keto acid derivatives and the acceleration thereof by amine catalysts have been carried out.[20] Some acetic acid derivatives bearing strong electron-withdrawing

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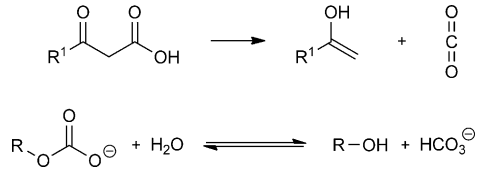
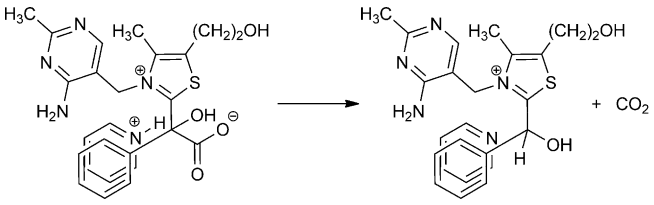


Scheme 2. Decarboxylation of 3-keto acid derivatives (top row); decomposition of monoalkyl carbonates (bottom row).

substituents undergo C–C bond cleavage at ambient temperature. 2,4,6-Trinitrobenzoic acid in ethanol[21] and nitroacetic acid in aqueous solution[22] easily eliminate carbon dioxide. Tribromoacetic acid is unstable at ambient temperature[23] and triiodoacetic acid decomposes rapidly in solution.[24] The decarboxylation of monoalkyl carbonates is rapid in aqueous alkali and depends on the basicity of the residual alkoxide.[25] Sauers and co-workers showed that the rate of decarboxylation of a series of monoalkyl carbonates has a linear dependence on the pK_a value of the residual alkoxides.[26] This correlation can provide an estimation of the pK_a values of weakly acidic alcohols (Scheme 2, bottom).

Enzyme-catalyzed decarboxylations in biochemistry are a fundamental field of research. Hilvert and co-workers investigated the decarboxylation of 5-nitro-3-carboxybenzisoxazoles,[27] which is particularly sensitive to solvation in organic solvents and towards antibody catalysis. Decomposition increases rapidly on changing from a protic to an aprotic solvent. 4-Pyridylacetic acid is also an excellent model substrate for enzyme-catalyzed decarboxylations. A common feature of these reactions is charge neutralization of the zwitterionic intermediate.[28] Furthermore, the enzymatic decarboxylation of benzoylformic acid to benzaldehyde, catalyzed by the thiamine diphosphate (ThDP)-dependent enzyme benzoyl formate decarboxylase (BFD), was thoroughly investigated by Kluger and co-workers (Scheme 3).[3a,b,29] They used mandelylthiamine (MTh), a



Scheme 3. Pre-association in pyridinium-catalyzed decarboxylation of mandelylthiamine.[3c,30d]

conjugate of thiamine and benzoyl formate, as a model of the intermediate in BFD in their studies. They found that the decarboxylation of MTh is subject to catalysis by pyridine-based buffers.[30] An explanation of their findings is given by the assumption that if a catalyst can block the reverse reaction, the net decarboxylation rate will be enhanced. Pyridinium accelerates the elimination of carbon dioxide from MTh by efficiently transferring a proton to the nascent carbanion, thereby facilitating the separation process between the carbanion and carbon dioxide. The fact that other Brønsted acids show no effect led Kluger to propose that pyridinium pre-associates with the substrate by π-stacking effects between the positively charged pyridinium and the phenyl ring of benzoyl formate (Scheme 3).

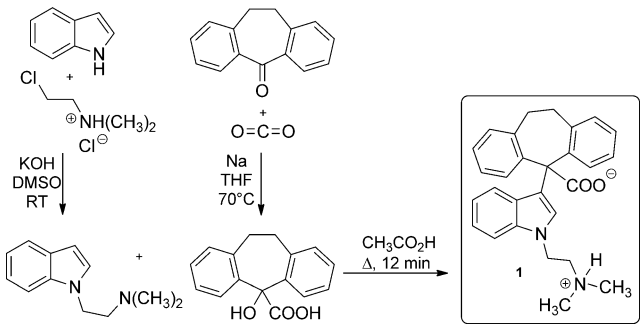
In this particular arrangement, the proton is in special proximity to enter an effective proton-transfer process. It promotes the departure of carbon dioxide by preventing internal return of this molecule. The acceleration of the decarboxylation of MTh by pyridinium ions results from pre-association forming a weak complex and effective protonation of the nascent carbanion formed upon decarboxylation. Building on the concept of pre-association catalysis, Kluger et al. revealed another important factor that can control the rate of a reaction.[3c] The fact that many ThDP-dependent decarboxylases contain a nucleophile at their active site that could facilitate the expulsion of carbon dioxide highlights the importance of reversibility in decarboxylation processes.[3b,29,31]

Apart from enzymatic decarboxylation, there are only a limited number of decarboxylation reactions that proceed at room temperature. While working on tridentate ligands for transition metal catalysis, we observed that a 3-substituted *N*,*N*-dimethylisotryptamine (isoDMT)-based amino acid shows unprecedented mobility of its CO_2 fragment. We investigated the decarboxylation of compound **1** to understand the origin of this facile process, and to identify factors that stabilize or destabilize carboxylates.

Results and Discussion

Amino acid **1** was prepared on a multigram scale by a three-step procedure starting from commercially available indole and dibenzosuberone. First, we optimized the N-alkylation of indole to afford 1-[2-(*N*,*N*-dimethylamino)ethyl]indole (*N*,*N*-dimethylisotryptamine, isoDMT), a reaction that has been described previously by several groups (Scheme 4, left column).[32]

The second fragment of amino acid **1**, 5-hydroxydibenzo[*a*,*d*]cycloheptene-5-carboxylic acid, was synthesized by reductive carboxylation of commercially available dibenzosuberone (Scheme 4, middle column).[33] The insoluble crude



Scheme 4. Synthesis of 5-{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (**1**).

product, presumably a polyester, was recrystallized from boiling 1,4-dioxane. Soluble, colorless crystals composed of 5-hydroxydibenzo[*a*,*d*]cycloheptene-5-carboxylic acid and 1,4-dioxane in a 2:1 ratio were obtained. Single-crystal X-ray analysis revealed the presence of dimers bridged by two hydrogen bonds between the hydroxy and carbonyl moieties. These dimers form a chain structure with 1,4-dioxane through hydrogen bonding (Figure 1).

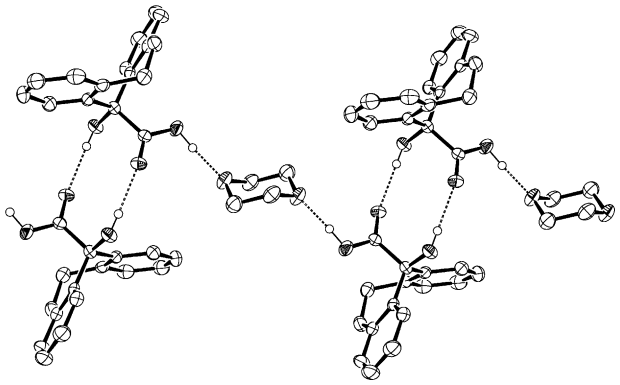


Figure 1. ORTEP plot of the chain structure of 5-hydroxydibenzo-[*a*,*d*]cycloheptene-5-carboxylic acid based on intermolecular hydrogen bonding. Dimers are connected through hydrogen bonding with 1,4-dioxane molecules. Ellipsoids are drawn at the 50% probability level; some hydrogen atoms have been omitted for clarity.

To complete the synthesis of amino acid **1**, isoDMT and the suberone-derived hydroxy acid **2** were combined in an electrophilic aromatic substitution reaction with an intermediary carbocation carboxylate zwitterion acting as an electrophilic reagent (Scheme 4). The use of acetic acid as solvent was necessary for two reasons. Firstly, a Brønsted acid is mandatory for the elimination of water, thereby generating the benzhydryl cation that is the actual reactive alkylating reagent. Secondly, acetic acid as solvent inhibits decarboxylation of product **1**. In the solid state, two amino acid molecules **1** are connected by nearly linear hydrogen bonds between the carboxylic acids and the amino units (Figure 2). The electron density distribution shows that the acidic proton is located almost in the middle between the carboxylate oxygen atom and the amino nitrogen atom. In other A-H···B systems, the A-H distance is typically about 100–110 pm, whereas the H···B distance is about 160–200 pm. The dimer has similar O-H (127 pm) and N-H (130 pm) distances. The observed N-O distance of 255 pm is much shorter than the typical N-O distance of 275–285 ppm.[34]

Decarboxylation: In general, decarboxylations are thermodynamically favorable but kinetically unfavorable. The high intrinsic barrier for decarboxylation originates from the high distortion energy in the transition state. The angle change at the carboxylate carbon amounts to roughly 60° due to sp^2-sp rehybridization.[20a] Amino acid **1**, whilst being stable in the solid state, quantitatively eliminates carbon dioxide in DMSO or DMF solution with half-lives of 5 h and 7 h, respectively (Scheme 5). Heating solid compound **1** to 200 °C for 30 s also results in the formation of the decarboxylated product **2**.

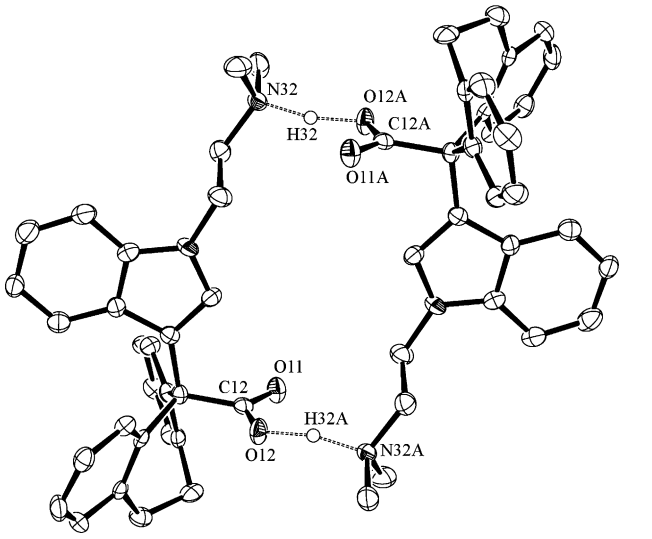
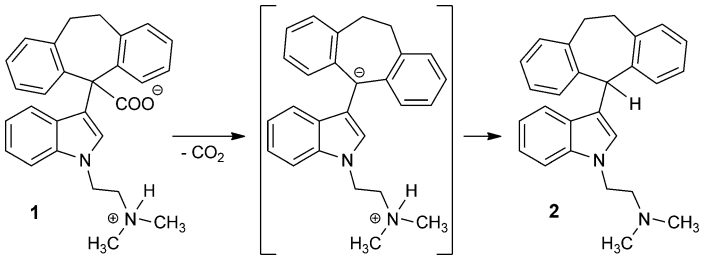


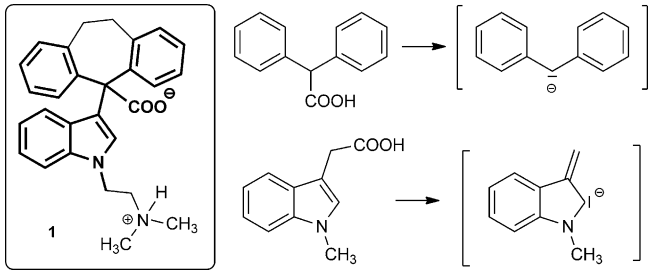
Figure 2. ORTEP plot of **1**; ellipsoids are drawn at the 50% probability level, some hydrogen atoms have been omitted for clarity. Selected lengths [Å]: N32−H32 1.302, H32−O12A 1.272, N32−O12A 2.555; angles [°]: O12A-H32-N32 166.0.



Scheme 5. Synthesis of 5-{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene (**2**).

An important factor influencing the rate of decarboxylation is the thermodynamic stability of the carbanion being formed. In his work on the decomposition of monoalkyl carbonates, Sauers quantified the influence of the basicity of the residual ion on the decarboxylation rate.[26] He found that electron-donating substituents stabilize the monoalkyl carbonates relative to the free alkoxides. These findings extrapolate logically to carbanions, implying that electron-withdrawing substituents should stabilize the nascent carbanion and favor decarboxylation. In the present case, there are two phenyl rings and an indole residue attached, making the carbanion a strong base. The pK_a value should be comparable to that of triphenylmethane (33) or diphenylmethane (35).[35] Sharma et al. investigated the decarboxylation of a variety of *N*-heteroaryl carboxylic acids and aromatic acid derivatives incorporating the two fragments of structure **1**.[15c] Precisely the two characteristic fragments that consti-

tute compound **1** showed the best results in their respective classes due to good stabilization of the arising intermediates (Scheme 6). Moreover, carboxylate solvation is hindered by steric crowding increasing the energy of the carboxylate. These findings support the assumption that decarboxylation of **1** is accelerated by mesomeric, inductive, and steric effects of the substituents.



Scheme 6. Compound **1** as a combination of two substrates investigated by A. Sharma et al.[15c]

Kinetic data for the decarboxylation of compound **1** in DMSO and in DMF were determined by ^{1}H NMR spectroscopy. Multiple consecutive ^{1}H NMR spectra were recorded at 25 °C, displaying the formation of product signals and the disappearance of starting material signals. To ensure that integrals were reliable, relaxation times were determined (see the Supporting Information). The decarboxylation kinetics differ for DMSO and DMF as solvents (Figure 3). In the

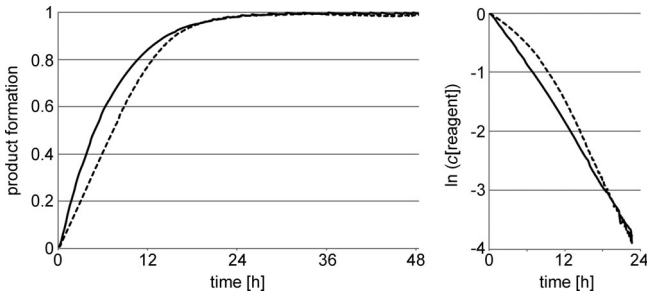
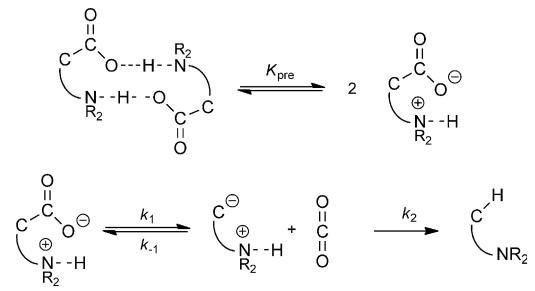


Figure 3. Kinetic ^{1}H NMR measurements of the decarboxylation of **1** in DMSO (continuous curve) and DMF (dotted curve); left side: formation rate of decarboxylated product; right side: ln(*c*[reagent]) versus time.

case of DMSO, the kinetic data for decarboxylation conform to a first-order rate dependence (Figure 3, continuous curve). The linear dependence of ln(*c*[reagent]) on time (Figure 3, right side) is in accordance with an S_E1 mechanism. This mechanism has been found for substrates with electron-withdrawing groups at the α-carbon atom,[36] for which carbon-carbon bond cleavage is rate-determining. In the case of DMF as solvent, however, the decarboxylation rate is constant over the first 10 h (Figure 3, dotted curve).

Since decarboxylation almost always starts from a free carboxylate ion, and since compound **1** favors a dimeric form, the initial step should be breaking of the hydrogen bonds in a pre-equilibrium to generate free carboxylate ions (Scheme 7). DMSO separates ion pairs better than DMF due to its ability to replace the hydrogen bonds in the dimer. In DMSO, compound **1** predominantly exists as the monomeric zwitterion that can directly release carbon dioxide according to a first-order rate law. In DMF, ion pair separation is not as good as in DMSO, and the reactive species first has to evolve in a pre-equilibrium. Assuming that the substrate undergoes reversible dissociation prior to the carbon-carbon bond-breaking step, leading to product formation and release of carbon dioxide, the graph of decarboxylation in DMF (Figure 3, dotted curve) is plausible. An autocatalytic effect of the evolving free amine might influence the decarboxylation rate in DMF.



Scheme 7. Pre-equilibrium forming the free carboxylate prior to C–C cleavage.

In a modified experimental set-up, the decarboxylation rate was quantified under an atmospheric pressure of carbon dioxide. The ^{1}H NMR kinetics showed that the rate of decarboxylation was strongly retarded under a carbon dioxide atmosphere. Changing the atmosphere resulted in an enhancement in the half-life of amino acid **1** in DMSO from 5 h (argon, 1 bar) to 17 h (carbon dioxide, 1 bar) (Figure 4, left side). The linear dependence of ln(*c*[reagent]) on time (Figure 4, right side) indicates that decarboxylation follows a first-order rate law both under argon and carbon dioxide atmosphere and that there is no change in mechanism. Major and Gao calculated that for the decarboxylation of picolinic acid there is only a very small inherent barrier for recombination of carbanion and carbon dioxide.[37] This provides an explanation for the observed decrease in decarboxylation rate of **1** under carbon dioxide atmosphere. Increas-

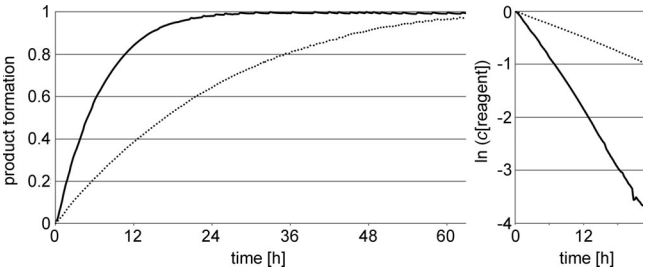


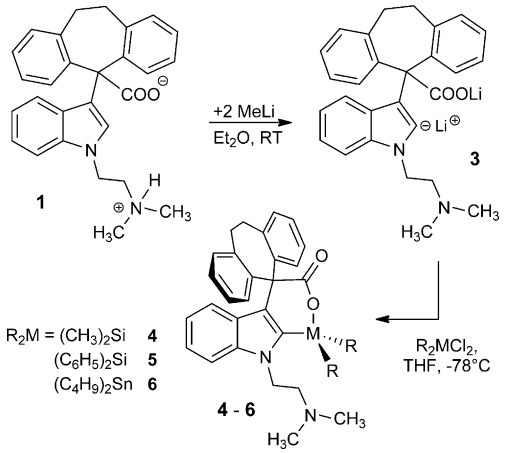
Figure 4. Kinetic ^{1}H NMR measurements of the decarboxylation of **1** in DMSO under argon atmosphere (continuous curve) and carbon dioxide atmosphere (dotted curve); left side: formation rate of decarboxylated product; right side: ln(*c*[reagent]) versus time.

ing partial pressure of carbon dioxide increases the rate of recombination, thereby resulting in a decreased overall decarboxylation rate.

The influence of carbon dioxide on the enzymatic decarboxylation rate has been explained by Kluger.[3c,30d] His key assumption was that re-carboxylation of the intermediate carbanion strongly influences the reaction rate. The decarboxylation produces a molecule of carbon dioxide and a reactive carbanion in the immediate vicinity of one another. The barrier for recombination of the carbanion and carbon dioxide can be considered to be near to or lower than that for diffusion.[37] This is supported by the fact that decarboxylation is retarded under carbon dioxide atmosphere. The internal return of carbon dioxide is probable and a significant component in the overall reaction rate.[3c,30d,38] To retard the reverse reaction, the products have to separate rapidly or react with another species, for example, an adjacent protic fragment in the active site of the enzyme. For the decarboxylation of compound **1**, the carbanion has to be protonated by an ammonium moiety of a second amino acid **1**. The linker between the carbanion and ammonium fragment is too rigid to allow for an intramolecular process. Thus, external CO_2 has ample time to compete with the slow intermolecular, irreversible protonation of the highly reactive carbanion.

We were interested in stabilizing the carboxylic fragment. Substitution of the indole core at the C2 position seemed to be promising. The use of *n*-butyllithium led to unselective deprotonation of the indole core, whereas the use of *tert*-butyllithium resulted in decomposition of the starting material. However, reaction of compound **1** with two equivalents of methyllithium in diethyl ether resulted in precipitation of the corresponding dilithium salt **3** as a yellow solid. The coordination of lithium apparently stabilizes the carboxylate fragment. The deprotonation yield was determined by treating the reaction mixtures with deuterium oxide and integrating the respective signals in the ^{1}H NMR spectra. Lithium salt **3** yielded the C2-deuterated compound $\mathbf{d_1}$**-1**. The steric demand of methyllithium might be decisive for the deprotonation, since the adjacent carboxylate and *N,N*-dimethylaminoethyl groups only leave a small gap for the attacking base. This limits the size of an introduced functional group that may be introduced to stabilize the carboxylic moiety. We introduced silicon- and tin-containing fragments to utilize the strength of the arising silicon-oxygen and tin-oxygen bonds. Transmetallations of dilithium salt **3** with dichlorodimethylsilane, dichlorodiphenylsilane, and dibutyltin dichloride yielded the corresponding spiro compounds **4**, **5**, and **6** (Scheme 8).

These spiro compounds are stable with regard to decarboxylation. The silicon derivatives **4** and **5** show no sign of decomposition even at 300 °C. Tin derivative **6** starts to lose carbon dioxide at 188 °C. The three spiro compounds are stable in DMSO or DMF solution and under basic conditions at room temperature. Besides their enhanced stability towards decarboxylation, the spiro compounds **4**–**6** have different coordination numbers of the silicon and tin atoms.



Scheme 8. Syntheses of silicon- and tin-containing spiro compounds **4**–**6**.

Single-crystal X-ray analysis revealed that both silicon derivatives **4** and **5** are monomeric species having a pseudo-tetrahedral coordination environment at silicon (Figure 5).

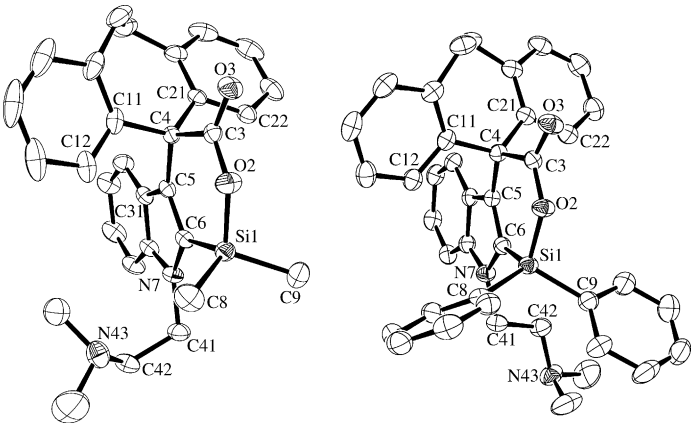


Figure 5. ORTEP plots of the molecular structures of silanes **4** and **5**. Ellipsoids are drawn at the 50% probability level; hydrogen atoms have been omitted for clarity; left: compound **4**: selected bond lengths [Å]: Si1−C6 1.838, Si1−O2 1.672, angles [°]: C6-Si1-O2 99.6, Si1-O2-C3 134.4, O2-Si1-C8 107.4, dihedral angles [°]: C5-C4-C3-O2 −19.9, C5-C6-Si1-O2 −0.4, C6-N7-C41-C42 101.1; right: compound **5**: selected bond lengths [Å]: Si1−C6 1.835, Si1−O2 1.672, angles [°]: C6-Si1-O2 99.9, Si1-O2-C3 134.1, O2-Si1-C8 108.3, dihedral angles [°] C5-C4-C3-O2 −17.7, C5-C6-Si1-O2 −11.2, C6-N7-C41-C42 −89.3.

The spiro compound **6** forms a hypervalent pentacoordinated tin species. Single-crystal X-ray analysis revealed a trigonal-bipyramidal coordination environment at the tin atom (Figure 6).

The indolyl ligand and the two *n*-butyl ligands are situated in equatorial positions. According to Bent's rule, the less electron-donating ligands are situated in the apical positions.[39]

Carboxylate rearrangement—methylation reaction: In initial attempts to synthesize compound **1**, we were unable to isolate it after work-up with aqueous sodium chloride solution.

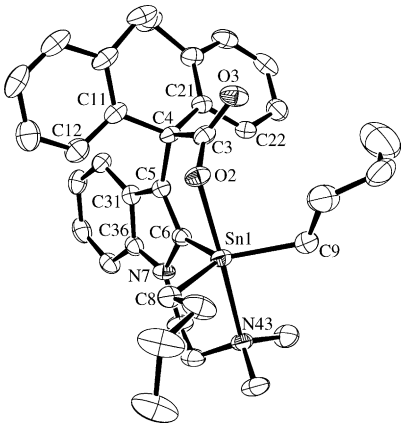


Figure 6. ORTEP plot of the molecular structure of stannane **6**. Ellipsoids are drawn at the 50% probability level; hydrogen atoms have been omitted for clarity; selected bond lengths [Å]: Sn1−C6 2.125, Sn1−O2 2.156, Sn1−N43 2.400, angles [°]: C6-Sn1-O2 84.1, Sn1-O2-C3 122.6, O2-Sn-C8 91.5, O2-Sn1-N43 171.3, dihedral angles [°] C5-C4-C3-O2 −36.1, C5-C6-Sn1-O2 5.3.

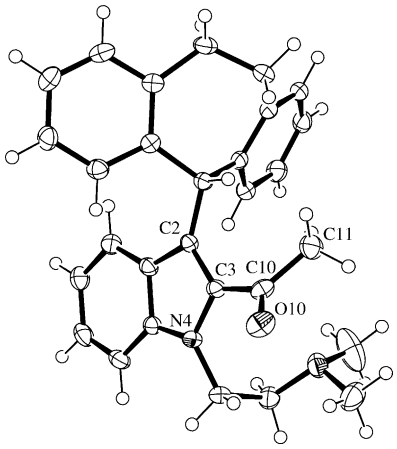
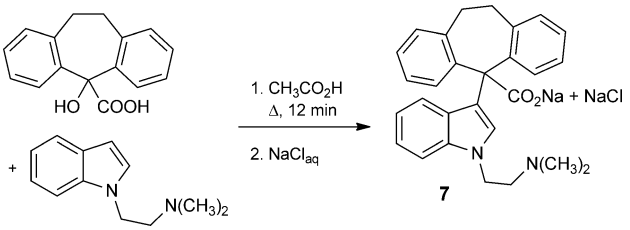


Figure 7. ORTEP plot of the molecular structure of the rearrangement product **8**; ellipsoids are drawn at the 50% probability level; selected bond lengths [Å]: C3−C10 1.486, C10−O10 1.220; angles [°]: C3-C10-C11 118.7, C3-C10-O10 120.5; dihedral angles [°]: C2-C3-C10-C11 −42.7, N4-C3-C10-O10 −38.42.

Instead, we obtained a colorless solid that turned yellow in air within minutes. The ^{1}H NMR spectrum nearly matched that of compound **1**, except for the slightly shifted proton signals of the *N*,*N*-dimethylaminoethyl group. This yellow compound gave decreased yields in the syntheses of spiro compounds, but one additional side-product. The elemental analysis matched that of a mixture of a sodium carboxylate and sodium chloride in a 1:1 ratio (Scheme 9).

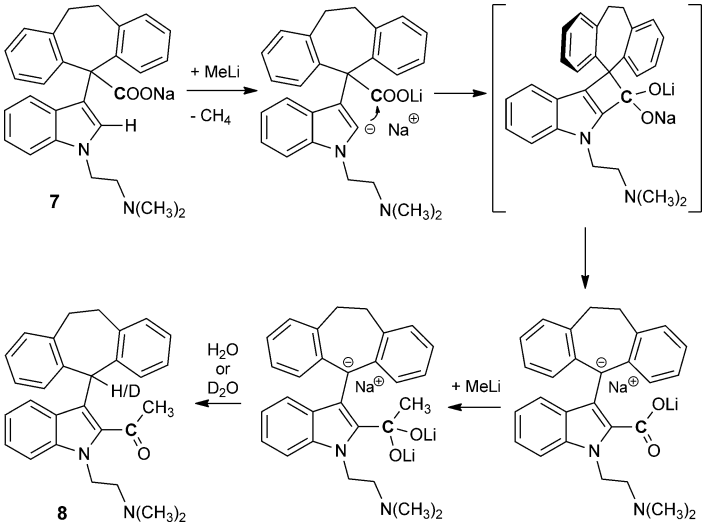


Scheme 9. Synthesis of sodium carboxylate **7**.

Knowing the nature of the double salt **7**, we investigated the identity of the by-product in the syntheses of spiro compounds **4**–**6**. To avoid separation problems, the reaction mixture was quenched with water instead of with alkyl silicon and alkyl tin chlorides after deprotonation. An acetyl derivative **8** was easily separated from the starting material by column chromatography. Its structure was confirmed by single-crystal X-ray analysis (Figure 7). The former carboxylic group had been shifted and transformed into an acetyl group situated at the C2 indole carbon atom. Normally, a coplanar arrangement of the indole core and the acetyl group would be expected, maximizing the π-interaction between the indole π-system and the carbonyl group. Due to steric crowding at the C2 position, the acetyl group is distorted by roughly 40° towards the indole plane.

There are well investigated compounds in which combinations of lithium and potassium/sodium ions play a crucial role, for example Schlosser's reagent LICKOR.[40] In the Lochmann–Schlosser, a combination of *tert*-butyllithium and potassium *tert*-butoxide, the high oxophilicity of lithium leads to a superbase. In the present case, a similar effect can explain the formation of the rearrangement product **8**. A possible rearrangement mechanism based on a method for preparing ketones from organolithium reagents and carboxylic acids,[41] explaining the formation of **8**, is shown in Scheme 10.

Compound **8** was synthesized directly by treating sodium carboxylate **7** with an excess of methyllithium in diethyl ether. The first mechanistic step is a selective deprotonation at the C2 position. Driven by the higher oxophilicity of lithi-



Scheme 10. Mechanism of the rearrangement–methylation sequence leading to 2-acetylindole **8**.

um, a lithium carboxylate is formed, leaving a sodium 2-indolate ion. The negative charge at the indole core is much less shielded by the sodium ion than it was before by the lithium ion. This provides a more distinct ionic character, resulting in nucleophilic attack on the carboxylate carbon atom, thereby yielding a cyclobutanediolate intermediate. Ring opening forms an indole-2-carboxylate. In the following step, the lithium carboxylate is attacked by another molecule of methyllithium, thereby forming a dilithium diolate. The dilithium intermediate, which is more stable than other metal dialkoxides,[41a] precipitates as a bright-yellow solid. To release the final product **8**, water was added to the reaction mixture. Similarly, deuterium oxide was used as a mechanistic probe. The obtained monodeuterium species **d_1-8** contained a non-deuterated $COCH_3$ group and a tertiary C-D moiety. Thus, the mechanistic alternative of intramolecular protonation of the triaryl carbanion by the acetyl group to give an enolate can be ruled out.

A positive effect of NaCl and water on the rearrangement reaction was ruled out (Table 1). The stoichiometric presence of the sodium carboxylate appears to be essential.

Table 1. Effect of water and sodium chloride addition on the rearrangement of amino acid **1** to acetyl derivative **8**.

Starting materials[a]	Detection of **8**[b]
compound **1**	–
compound **1**, 1 equiv H_2O	–
compound **1**, 1 equiv NaCl	–
compound **7**	++
compound **7**, compound **1** (1:5 ratio)	+

[a] Conditions: suspension in diethyl ether, r.t., 4.2 equiv methyllithium, 16 h. [b] Work-up: addition of water, extraction with dichloromethane, compound **8** was detected using TLC (– not detected, + detected (small amount), ++ detected (large amount)).

The compositions of the product mixtures derived from the comparative experiments were determined by thin-layer chromatography. Neither the addition of sodium chloride nor of water to compound **1** before adding methyllithium led to the formation of the rearranged product **8**. A possible influence of water or sodium chloride on the rearrangement can thus be ruled out. The fact that a mixture of sodium carboxylate **7** and the protonated acid **1** gives low yields of the rearrangement product **8** supports our proposed mechanism. A stoichiometric amount of sodium carboxylate is necessary for full conversion. The rearrangement is apparently not catalyzed by sodium salts.

Conclusion

We have synthesized a carboxylic acid derived from *N,N*-dimethylisotryptamine that features a unique set of reactivity patterns. The carboxylate zwitterion is stable in the solid state but quantitatively decarboxylates in polar aprotic solvents even at room temperature. A single-crystal X-ray analysis revealed dimerization of the amino acid through two nearly equidistant hydrogen bonds. Breaking of these strong hydrogen bonds in DMSO and DMF is responsible for destabilizing the sterically shielded carboxylate fragment. Thus, a highly basic carbanion was released that was competitively trapped by external CO_2.

Stable derivatives have been obtained by bridging the carboxylate and the 2-position of the indole moiety with silylene or stannylene moieties. These spiro compounds show high thermal stability even in basic media.

The sodium salt undergoes a carboxylate walk upon deprotonation of the adjacent 2-indolyl fragment with an excess of methyllithium. The stoichiometric presence of both counterions lithium and sodium is mandatory for carboxylate transfer to the 2-indolide fragment. The rearrangement is followed by a nucleophilic attack of methyllithium.

In summary, we have presented a carboxylic acid that undergoes facile deprotonation, features a re-carboxylation mechanism of the resulting carbanionic intermediate, and is prone to intramolecular transfer of the carboxylate to give a 2-indolide fragment.

Experimental Section

Materials and methods: All starting materials and deuterated solvents were obtained from commercial suppliers (Acros Organics, Sigma–Aldrich, Scientific-Fisher, Deutero, euriso-top) and were used without further purification unless otherwise noted. Dry tetrahydrofuran was taken from an MBRAUN MB SCS-800 solvent purification system and kept under nitrogen. Dry diethyl ether was obtained by distillation from sodium and benzophenone and kept under nitrogen. Air- and moisture-sensitive reactions were conducted in oven-dried glassware by using standard Schlenk or dry-box techniques under an inert atmosphere of dry nitrogen or dry argon.

Physical and spectroscopic measurements: ^{1}H NMR spectra were recorded on Bruker ARX-250 (250 MHz), Bruker Avance 300 (300 MHz), and Bruker Avance 500 (500 MHz) spectrometers. ^{13}C NMR spectra were recorded on Bruker Avance 300 (75 MHz) and Bruker Avance 500 (125 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm) and were calibrated to the residual signals of the deuterated solvents [$\delta_H(CDCl_3) = 7.26$ ppm, $\delta_H([D_6]DMSO) = 2.50$ ppm, $\delta_H([D_8]THF) = 1.72$ and 3.58 ppm]. Selected NMR spectra are available in the Supporting Information. ESI mass spectra were obtained on a JEOL JMS-700 instrument. IR spectra were recorded on a Bruker Vector 22 FTIR instrument. Melting points were determined using a Gallenkamp hot-stage microscope and are uncorrected.

X-ray structure analyses: Single-crystal X-ray diffraction data sets were collected at 200(2) K on a Bruker Smart CCD diffractometer for 5-hydroxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid, **1**, and **8**, or on a Bruker APEX diffractometer for **4**, **5**, and **6**, both equipped with a CCD area detector and a standard sealed tube $Mo_{K\alpha}$ ($\lambda = 0.71073$ Å) radiation source. 0.3° omega scans covering a whole sphere in reciprocal space were taken in each case, and an empirical absorption correction was applied using SADABS based on the Laue symmetry of the reciprocal space.[42] Structures were solved by direct methods and refined against F^2 with a full-matrix least-squares algorithm using the SHELXTL-PLUS (6.10) software package.[43] The Supporting Information or CCDC-792003 (for 5-hydroxy-10,11-dihydro-5*H*-dibenzo-[*a*,*d*]cycloheptene-5-carboxylic acid), CCDC-792002 (for **1**), CCDC-792004 (for **4**), CCDC-792006 (for **5**), CCDC-792005 (for **6**), and CCDC-792007 (for **8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-[2-(*N*,*N*-Dimethylamino)ethyl]indole: Under an atmosphere of nitrogen, 2-(dimethylamino)ethyl chloride hydrochloride (85 g, 0.59 mol) was slowly added to a mixture of potassium hydroxide (129 g, 2.30 mol), indole (60 g, 0.51 mol), and dimethyl sulfoxide (300 mL) at 0 °C. After stirring at room temperature for 48 h, water was added and the product was extracted three times with diethyl ether. The combined extracts were washed with water, dried over magnesium sulfate and concentrated in vacuo to afford a brown oil. Distillation gave the title compound as a colorless liquid (80.8 g, 429 mmol). Yield: 84 %; b.p. 100 °C (1 mbar); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.86–7.82 (m, 1H; 4-H_{indole}), 7.53–7.49 (m, 1H; 7-H_{indole}), 7.44–7.38 (m, 1H; 6-H_{indole}), 7.34–7.28 (m, 1H; 5-H_{indole}), 7.25 (d, ^3J(H,H) = 3.0 Hz, 1H; 2-H_{indole}), 6.69 (d, ^3J(H,H) = 3.0 Hz, 1H; 3-H_{indole}), 4.28 (t, ^3J(H,H) = 7.5 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 2.77 (t, ^3J(H,H) = 7.5 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.41 ppm (s, 6H; N(CH$_3$)$_2$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C): δ = 135.7 (7a-C_{indole}), 128.3 (3a-C_{indole}), 127.7 (2-C_{indole}), 121.1 (6-C_{indole}), 120.7 (4-C_{indole}), 119.0 (5-C_{indole}), 108.9 (7-C_{indole}), 100.9 (3-C_{indole}), 58.6 (*C*H$_2$N(CH$_3$)$_2$), 45.4 (N(CH$_3$)$_2$), 44.3 ppm (*C*H$_2$CH$_2$N(CH$_3$)$_2$); IR (KBr): $\tilde{\nu}$ = 3055 (w), 2972 (m), 2943 (s), 2860 (w), 2821 (m), 2770 (s), 1617 (w), 1512 (s), 1481 (m), 1463 (s), 1361 (w), 1334 (m), 1316 (s), 1257 (w), 1223 (w), 1171 (w), 1154 (w), 1055 (w), 1042 (w), 763 (m), 740 (s), 716 cm^{-1} (m); MS (EI+): *m*/*z* (%): 188.1 (35) [M^+], 130.1 (5) [M^+−CH$_2$N(CH$_3$)$_2$], 58.1 (100) [CH$_2$N(CH$_3$)$_2^+$]; elemental analysis calcd (%) for $C_{12}H_{16}N_2$: C 76.55, H 8.57, N 14.88; found: C 76.40, H 8.60, N 14.94; alternative procedures for the synthesis have been published previously.[32]

5-Hydroxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid·0.5 (1,4-dioxane): Under an atmosphere of nitrogen, dibenzosuberone (100 g, 466 mmol) was dissolved in dry tetrahydrofuran (800 mL) and sodium lumps (29.3 g, 1.27 mol, 2.7 equiv) were slowly added. The yellow solution turned dark blue within minutes. Carbon dioxide was continuously passed into the solution, changing the color to red. The reaction mixture was heated under reflux conditions for 8 h at 70 °C, stirred overnight at room temperature, and heated again for 8 h at 70 °C. Excess sodium metal was quenched by carefully (!) adding water. Tetrahydrofuran was removed from the aqueous reaction mixture by rotary evaporation. The remaining alkaline aqueous layer was extracted with diethyl ether to remove any remaining dibenzosuberone, and then glacial acetic acid (1 L) was added. The acidic aqueous solution was extracted with diethyl ether. The organic extracts were washed with water, dried over magnesium sulfate, and concentrated in vacuo to give the yellow crude product. Recrystallization from 1,4-dioxane containing a small amount of water gave the title compound as white crystals (containing 0.5 equivalents of 1,4-dioxane in the crystal) (98.4 g, 330 mmol). Yield: 71 %; m.p. 232 °C (decomposition); ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 12.85 (s, 1H; CO_2H), 7.78–7.73 (m, 2H; H_{aryl}), 7.20–7.12 (m, 4H; H_{aryl}), 7.12–7.07 (m, 2H; H_{aryl}), 6.89 (s, 1H; OH), 3.55 (s, 4H; dioxane), 3.34–3.20 (m, 2H; CH_2), 2.94–2.80 ppm (m, 2H; CH_2); ^{13}C{^{1}H} NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 174.2 (CO_2H), 142.0 (C_{aryl}), 137.4 (C_{aryl}), 129.7 (CH_{aryl}), 127.1 (CH_{aryl}), 125.1 (CH_{aryl}), 124.7 (CH_{aryl}), 78.0 (C(OH)), 31.6 ppm (CH_2); IR (KBr): $\tilde{\nu}$ = 3441 (br), 3018 (br), 2935 (br), 2888 (br), 2610 (m), 1706 (s), 1484 (m), 1257 (s), 1243 (s), 1217 (s), 1166 (m), 1114 (s), 1078 (s), 1041 (s), 863 (s), 758 (s), 748 (s), 718 (s), 709 (s), 656 (s), 613 cm^{-1} (s); MS (ESI+): *m*/*z* (%): 747.2 (100) [3*M*−2H$_2$O+Na$^+$], 495.2 (61) [2*M*−2H$_2$O+Na$^+$], 299.1 (8) [*M*−H+2Na$^+$], 259.1 (26) [*M*−H$_2$O+Na$^+$]; elemental analysis calcd (%) for $C_{16}H_{14}O_3$·0.5 $C_4H_8O_2$: C 72.47, H 6.08; found: C 72.40, H 6.14. For X-ray structure determination, a single crystal was obtained by recrystallization from 1,4-dioxane; alternative procedures for analogous syntheses have been reported in the literature.[33]

5-{1-[2-(*N*,*N*-Dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo-[*a*,*d*]cycloheptene-5-carboxylic acid (1): A mixture of 1-[2-(*N*,*N*-dimethylamino)ethyl]indole (18.1 g, 96.0 mmol) and 5-hydroxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid·0.5 (1,4-dioxane) (28.6 g, 96.0 mmol) in glacial acetic acid (200 mL) was heated under reflux conditions for 12 min at 118 °C, and then rapidly cooled to room temperature. Water (500 mL) was added to the red solution, and the product was extracted with dichloromethane. The combined organic layers were washed with water and dried over magnesium sulfate. The organic solvent was removed by rotary evaporation. The crude product was recrystallized from chloroform/diethyl ether to give the title compound as a colorless powder. Residual chloroform in the solid could be removed by stirring in diethyl ether, filtering, and drying in vacuo (34.2 g, 80.8 mmol). Yield: 84 %; m.p. 154 °C (decomposition, gas evolution); ^{1}H NMR (500 MHz, [D$_6$]DMSO/1 % CF_3COOD, 25 °C): δ = 7.55–7.53 (m, 1H; H_{indole}), 7.34 (s, 1H; 2-H_{indole}), 7.16–7.13 (m, 2H; H_{aryl}), 7.11–7.05 (m, 5H; 1 × H_{indole}, 4 × H_{aryl}), 6.95–6.92 (m, 2H; H_{aryl}), 6.74–6.70 (m, 1H; H_{indole}), 6.52–6.49 (m, 1H; H_{indole}), 4.62 (t, ^3J(H,H) = 7.5 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.53 (t, ^3J(H,H) = 7.5 Hz, 2H; CH_2N(CH$_3$)$_2$), 3.18–3.06 (m, 4H; CH_2), 2.87 ppm (s, 6H; N(CH$_3$)$_2$); ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 7.43–7.41 (m, 1H; H_{indole}), 7.25 (s, 1H; H_{indole}), 7.14–6.97 (m, 7H; 1 × H_{indole}, 6 × H_{aryl}), 6.91–6.89 (m, 2H; H_{aryl}), 6.66–6.64 (m, 1H; H_{indole}), 6.46–6.44 (m, 1H; H_{indole}), 4.30 (t, ^3J(H,H) = 6.9 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.23–2.99 (m, 4H; CH_2), 2.70 (t, ^3J(H,H) = 6.9 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.24 ppm (s, 6H; N(CH$_3$)$_2$); ^{13}C{^{1}H} NMR (125 MHz, [D$_6$]DMSO/1 % CF_3COOD, 25 °C): δ = 175.5 (CO_2H), 141.7 (C_{aryl}), 139.9 (C_{aryl}), 136.4 (C_{indole}), 132.2 (CH_{aryl}), 130.0 (CH_{aryl}), 128.4 (CH_{indole}), 126.9 (C_{indole}), 126.8 (CH_{aryl}), 125.2 (CH_{aryl}), 121.8 (CH_{indole}), 121.5 (CH_{indole}), 120.2 (C_{indole}), 119.1 (CH_{indole}), 110.0 (CH_{indole}), 65.0 (*C*(CO_2H), weak signal), 55.2 (*C*H$_2$N(CH$_3$)$_2$), 42.8 (N(CH$_3$)$_2$), 40.7 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 34.8 ppm (CH_2); IR (KBr): $\tilde{\nu}$ = 3440 (br), 3016 (m), 2939 (m), 2894 (m), 2836 (m), 2771 (w), 2710 (w), 1705 (m), 1161 (br), 1481 (s), 1466 (s), 1367 (m), 1340 (m), 1326 (m), 1256 (m), 1233 (m), 1212 (m), 1161 (m), 1017 (w), 779 (s), 751 (s), 739 (s), 719 (s), 647 (w), 640 (w), 531 cm^{-1} (w); MS (ESI+): *m*/*z* (%): 425.4 (100) [*M*+H$^+$], 353.3 (7) [*M*−CH$_2$CH$_2$N(CH$_3$)$_2$+H$^+$], 214.9 (21) [$C_{15}H_{12}$+Na$^+$], 211.8 [$C_{12}H_{16}N_2$+Na$^+$]; HRMS (ESI+): calcd (*m*/*z*) for $C_{28}H_{29}N_2O_2^+$: 425.22235; found: 425.22274; elemental analysis calcd (%) for $C_{28}H_{28}N_2O_2$: C 79.22, H 6.65, N 6.60, O 7.54; found: C 79.07, H 6.64, N 6.66. For X-ray structure determination, a single crystal was obtained by recrystallization from chloroform.

5-{1-[2-(*N*,*N*-Dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo-[*a*,*d*]cycloheptene (2): Method (a): 5-{1-[2-(*N*,*N*-Dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (549 mg, 1.29 mmol) was heated in a small crucible to 200 °C for 30 s until the evolution of gas was complete. The hot melt was poured into a mold made of aluminum foil. The mold was then cooled, whereupon a dark glassy mass solidified. The product was pounded in a cooled mortar. Without further purification, the title compound was obtained as a brown powder (490 mg, 1.29 mmol); yield: 99 %. Method (b): 5-{1-[2-(*N*,*N*-Dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo-[*a*,*d*]cycloheptene-5-carboxylic acid (466 mg, 1.10 mmol) was stirred in DMSO (20 mL) overnight. Water (300 mL) was then added to the yellow reaction mixture. The aqueous solution was extracted three times with diethyl ether. The combined organic extracts were washed with water, dried over magnesium sulfate, and concentrated in vacuo to give a brown glassy solid, pounding of which in a cooled mortar gave the title compound as a brown powder (410 mg, 1.08 mmol). Yield: 98 %; m.p. 47.5 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 7.51–7.46 (m, 2H; H_{aryl}), 7.37–7.35 (m, 1H; H_{indole}), 7.22–7.16 (m, 4H; H_{aryl}), 7.14–7.09 (m, 2H; H_{aryl}), 7.03–7.00 (m, 1H; H_{indole}), 6.93–6.91 (m, 1H; H_{indole}), 6.77–6.75 (m, 1H; H_{indole}), 6.45 (s, 1H; H_{indole}), 5.44 (s, 1H; CH), 4.12 (t, ^3J(H,H) = 6.6 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.31–3.20 (m, 2H; CH_2), 2.73–2.60 (m, 2H; CH_2), 2.45 (t, ^3J(H,H) = 6.6 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.09 ppm (s, 6H; N(CH$_3$)$_2$); ^{13}C{^{1}H} NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 140.7 (C_{aryl}), 139.6 (C_{aryl}), 136.4 (C_{indole}), 130.4 (CH_{aryl}), 130.4 (CH_{aryl}), 127.5 (CH_{indole}), 126.9 (CH_{aryl}), 126.0 (C_{indole}), 125.9 (CH_{aryl}), 120.8 (CH_{indole}), 119.6 (CH_{indole}), 118.5 (CH_{indole}), 117.8 (C_{indole}), 109.6 (CH_{indole}), 58.6 (*C*H$_2$N(CH$_3$)$_2$), 51.0 (CH), 45.2 (N(CH$_3$)$_2$), 43.5 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 31.2 ppm (CH_2); IR (KBr): $\tilde{\nu}$ = 3450 (br), 3058 (w), 3015 (w), 2932 (w), 2864 (w), 2819 (w), 2767 (w), 1635 (w), 1611 (w), 1491 (w), 1480 (w), 1465 (m), 1455 (m), 1360 (w), 1329 (w), 1158 (w), 773 (s), 753 (s), 739 (s), 587 (w), 425 cm^{-1} (w); MS (ESI+): *m*/*z* (%): 381.2 (100) [*M*+H$^+$], 395.2 (15), 775.4 (8); HRMS (ESI+): calcd (*m*/*z*) for $C_{27}H_{29}N_2^+$: 381.23253; found: 381.23263; elemental analysis calcd (%) for $C_{27}H_{28}N_2$: C 85.22, H 7.42, N 7.36; found: C 84.77, H 7.24, N 7.19.

Lithium 5-(2-lithio{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl})-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylate (3): 5-{1-[2-(*N*,*N*-Dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (631 mg, 1.45 mmol) and diethyl ether (5 mL)

were placed in a 20 mL flask under an argon atmosphere. A solution of methyllithium in diethyl ether (2.71 mL, 1.6 M, 4.34 mmol) was slowly added. After stirring for 16 h, the yellow precipitate was collected by filtration, washed three times with diethyl ether, and dried in vacuo. The title compound was obtained as a yellow, highly moisture-sensitive powder (574 mg, 1.32 mmol). Yield: 95%.

5-(2-Deutero{1-[2-(*N,N*-dimethylamino)ethyl]indol-3-yl})-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid ([D_1]1): Lithium 5-(2-lithio{1-[2-(*N,N*-dimethylamino)ethyl]indol-3-yl})-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylate (100 mg, 229 mmol) and diethyl ether (2 mL) were placed in a 10 mL flask under an argon atmosphere. Addition of D_2O (1 mL) to the yellow suspension led to the precipitation of a colorless solid, which was collected by filtration, washed with water and diethyl ether, and dried in vacuo. The product was obtained as a colorless powder (92.7 mg, 217 mmol). Yield: 95%; ^{1}H NMR (250 MHz, [D_6]DMSO/1% F_3CCOOD, 25°C): δ = 7.53–7.51 (m, 1H; H_{indole}), 7.20–6.89 (m, 9H; 1 × H_{indole}, 8 × H_{aryl}), 6.73–6.69 (m, 1H; H_{indole}), 6.49–6.45 (m, 1H; H_{indole}), 4.61 (t, ^3J(H,H) = 8.3 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.51 (t, ^3J(H,H) = 8.3 Hz, 2H; CH_2N(CH$_3$)$_2$), 3.22–2.96 (m, 4H; CH$_2$), 2.86 ppm (s, 6H; N(CH$_3$)$_2$).

Spiro[10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5,1′-(4′,4′-dimethyl{3′-oxa-4′-silacyclohexan-2′-one[4′*a*,9′*b*-*b*′]-5′-[2″-(*N,N*-dimethylamino)ethyl]indole})] (4): A 100 mL Schlenk flask was charged with a suspension of 5-{1-[2-(*N,N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (2.0 g, 4.7 mmol) in diethyl ether (20 mL) under an argon atmosphere. A solution of methyllithium in diethyl ether (6.5 mL, 1.6 M, 10 mmol, 2.2 equiv) was slowly added by means of a syringe. The reaction mixture was stirred for 16 h at room temperature. The resulting yellow suspension was cooled to −78°C, whereupon a pre-cooled solution of dichlorodimethylsilane (1.8 g, 1.7 mL, 14 mmol) in THF (30 mL) was injected into the flask. The reaction mixture was stirred at room temperature overnight. The solvent was then removed in vacuo. Diethyl ether was added to the initially orange crude product, stirred for a few hours, and filtered. This process was repeated twice more. The nearly colorless powder was recrystallized from methanol to afford the title compound as colorless crystals (1.71 g, 3.55 mmol). Yield: 76%; m.p. 204°C; ^{1}H NMR (300 MHz, [D_6]DMSO, 25°C): δ = 7.51–7.48 (m, 1H; 7-H_{indole}), 7.23–7.19 (m, 2H; H_{aryl}), 7.08–7.04 (m, 3H; 5-H_{indole}, H_{aryl}), 7.00–6.85 (m, 4H; H_{aryl}), 6.70–6.64 (m, 1H; 6-H_{indole}), 6.55–6.51 (m, 1H; 4-H_{indole}), 4.44 (t, ^3J(H,H) = 6.3 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.62–3.54 (m, 2H; CH$_2$), 3.19–3.11 (m, 2H; CH$_2$), 2.81 (t, ^3J(H,H) = 6.3 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.36 (s, 6H; N(CH$_3$)$_2$), 0.77 ppm (s, 6H; Si(CH$_3$)$_2$); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 7.34–7.32 (m, 1H; H_{indole}), 7.18–7.03 (m, 5H; 1 × H_{indole}, 4 × H_{aryl}), 6.91–6.83 (m, 4H; H_{aryl}), 6.73–6.71 (m, 1H; H_{indole}), 6.63–6.61 (m, 1H; H_{indole}), 4.47 (t, ^3J-(H,H) = 7.3 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.76–3.66 (m, 2H; CH$_2$), 3.23–3.13 (m, 2H; CH$_2$), 2.89 (t, ^3J(H,H) = 7.3 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.49 (s, 6H; N(CH$_3$)$_2$), 0.75 ppm (s, 6H; Si(CH$_3$)$_2$); ^{1}H NMR (250 MHz, [D_8]THF, 25°C): δ = 7.40–7.36 (m, 1H; H_{indole}), 7.16–7.11 (m, 2H; $H_{indole/aryl}$), 7.06–6.93 (m, 5H; $H_{indole/aryl}$), 6.84–6.78 (m, 2H; $H_{indole/aryl}$), 6.65–6.58 (m, 2H; $H_{indole/aryl}$), 4.39 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.77–3.68 (m, 2H; CH$_2$), 3.19–3.10 (m, 2H; CH$_2$), 2.75 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.29 (s, 6H; N(CH$_3$)$_2$), 0.73 ppm (s, 6H; Si-(CH$_3$)$_2$); ^{13}C{^{1}H} NMR (75 MHz, [D_6]DMSO, 25°C): δ = 170.4 (CO_2H), 142.9 (C_{aryl}), 140.2 (C_{aryl}), 139.5 (7a-C_{indole}), 131.7 (CH_{aryl}), 131.7 (3a-C_{indole}), 130.4 (2-C_{indole}), 130.2 (CH_{aryl}), 126.7 (CH_{aryl}), 125.9 (CH_{aryl}), 125.3 (3-C_{indole}), 123.0 (4-CH_{indole}), 120.3 (5-CH_{indole}), 119.2 (6-CH_{indole}), 110.2 (7-CH_{indole}), 63.4 (C(CO_2)), 57.8 (*C*H$_2$N(CH$_3$)$_2$), 45.2 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 45.2 (N(CH$_3$)$_2$), 36.0 (CH$_2$), 0.9 ppm (Si(CH$_3$)$_2$); IR (KBr): $\tilde{\nu}$ = 3434 (br), 3056 (w), 3016 (w), 2941 (br), 2895 (w), 2822 (w), 2772 (w), 1727 (s), 1636 (w), 1487 (m), 1449 (m), 1359 (m), 1326 (w), 1258 (s), 1207 (br), 981 (s), 889 (s), 851 (s), 799 (s), 776 (s), 753 (s), 742 (s), 690 cm^{-1} (w); MS (ESI+): *m*/*z* (%): 967.5 (41) [2*M*+Li$^+$], 961.5 (30) [2*M*+H$^+$], 519.2 (11) [*M*+K$^+$], 487.2 (100) [*M*+Li$^+$], 481.4 (63) [*M*+H$^+$], 425.2 (2) [**1**+H]$^+$; MS (ESI-): *m*/*z* (%): 719.2 (13) [*M*+3·(Si(Me)$_2$O)+OH$^-$], 645.2 (37) [*M*+2·(Si(Me)$_2$O)+OH$^-$], 571.2 (65) [*M*+(Si(Me)$_2$O)+OH$^-$], 497.3 (99) [*M*+OH$^-$], 423.3 (100) [*M*$^-$−(Si(Me)$_2$)+H]; HRMS (ESI+): calcd (*m*/*z*) for $C_{30}H_{33}N_2O_2Si^+$: 481.23058; found: 481.23112; elemental analysis calcd (%) for $C_{30}H_{32}N_2O_2Si$: C 74.96, H 6.71, N 5.83; found: C 75.05, H 6.80, N 5.85. For X-ray structure determination, a single crystal was obtained by recrystallization from methanol.

Spiro[10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5,1′-(4′,4′-diphenyl{3′-oxa-4′-silacyclohexan-2′-one[4′*a*,9′*b*-*b*′]-5′-[2″-(*N,N*-dimethylamino)ethyl]indole})] (5): A 100 mL Schlenk flask was charged with a suspension of 5-{1-[2-(*N,N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (2.0 g, 4.7 mmol) in diethyl ether (20 mL) under an argon atmosphere. A solution of methyllithium in diethyl ether (6.50 mL, 1.6 M, 10.4 mmol, 2.2 equiv) was slowly added by means of a syringe. The reaction mixture was stirred for 16 h at room temperature. The resulting yellow suspension was cooled to −78°C, whereupon a pre-cooled solution of dichlorodiphenylsilane (2.98 g, 2.48 mL, 11.8 mmol) in THF (30 mL) was injected into the flask. The reaction mixture was stirred and allowed to warm to room temperature overnight, yielding a violet suspension. The colorless precipitate was removed by filtration. The remaining violet solution was concentrated in vacuo to give the crude product as a viscous oil. Purification by column chromatography on silica gel (dichloromethane/methanol, 9:1) yielded a yellow solid. It was recrystallized from dichloromethane/methanol and the title compound was obtained as light-yellow crystals (1.29 g, 2.13 mmol). Yield: 45%; R_f = 0.70 (CH_2Cl_2/MeOH, 9:1); m.p. 239°C; ^{1}H NMR (500 MHz, [D_6]DMSO, 25°C): δ = 7.75–7.73 (m, 4H; H_{phenyl}), 7.70–7.67 (m, 2H; H_{phenyl}), 7.63–7.59 (m, 4H; H_{phenyl}), 7.48–7.45 (m, 1H; 7-H_{indole}), 7.25–7.23 (m, 2H; H_{aryl}), 7.13–7.07 (m, 3H; 6-H_{indole}, H_{aryl}), 6.98–6.96 (m, 2H; H_{aryl}), 6.87–6.84 (m, 2H; H_{aryl}), 6.74–6.70 (m, 1H; 5-H_{indole}), 6.59–6.57 (m, 1H; 4-H_{indole}), 4.29 (t, ^3J(H,H) = 7.0 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.63–3.57 (m, 2H; CH$_2$), 3.20–3.14 (m, 2H; CH$_2$), 2.22 (t, ^3J(H,H) = 7.0 Hz, 2H; CH_2N(CH$_3$)$_2$), 1.92 ppm (s, 6H; N(CH$_3$)$_2$); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 7.80–7.75 (m, 4H; H_{phenyl}), 7.61–7.44 (m, 6H; H_{phenyl}), 7.35 (d, $^3J_{H,H}$ = 8.3 Hz, 1H; H_{indole}), 7.20–7.02 (m, 7H; $H_{indole/aryl}$), 6.86–6.67 (m, 4H; $H_{indole/aryl}$), 4.35 (t, ^3J(H,H) = 7.7 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.80–3.69 (m, 2H; CH$_2$), 3.26–3.16 (m, 2H; CH$_2$), 2.35 (t, ^3J(H,H) = 7.7 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.10 ppm (s, 6H; N(CH$_3$)$_2$); ^{1}H NMR (250 MHz, [D_8]THF, 25°C): δ = 7.82–7.78 (m, 4H; H_{phenyl}), 7.62–7.45 (m, 6H; H_{phenyl}), 7.39–7.34 (m, 1H; H_{indole}), 7.17–7.13 (m, 2H; $H_{indole/aryl}$), 7.08–6.97 (m, 5H; $H_{indole/aryl}$), 6.79–6.71 (m, 2H; $H_{indole/aryl}$), 6.66–6.63 (m, 2H; $H_{indole/aryl}$), 4.32 (t, ^3J(H,H) = 7.9 Hz, 2H; CH_2CH$_2$N-(CH$_3$)$_2$), 3.78–3.68 (m, 2H; CH$_2$), 3.21–3.11 (m, 2H; CH$_2$), 2.28 (t, ^3J-(H,H) = 7.9 Hz, 2H; CH_2N(CH$_3$)$_2$), 1.99 ppm (s, 6H; N(CH$_3$)$_2$); ^{13}C{^{1}H} NMR (125 MHz, [D_6]DMSO, 25°C): δ = 170.4 (CO_2), 143.2 (C_{aryl}), 140.1 (7a-C_{indole}), 139.8 (C_{aryl}), 135.1 (CH_{phenyl}), 133.5 (3-C_{indole}), 132.2 (CH_{phenyl}), 131.8 (CH_{aryl}), 130.5 (CH_{aryl}), 129.9 (C_{phenyl}), 128.9 (CH_{phenyl}), 127.5 (2-C_{indole}), 127.1 (CH_{aryl}), 125.9 (CH_{aryl}), 125.6 (3a-C_{indole}), 123.7 (6-CH_{indole}), 120.7 (4-CH_{indole}), 119.5 (5-CH_{indole}), 110.6 (7-CH_{indole}), 63.9 (*C*(CO_2)), 57.8 (*C*H$_2$N(CH$_3$)$_2$), 46.0 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 45.1 (N-(CH$_3$)$_2$), 36.0 ppm (CH$_2$); IR (KBr): $\tilde{\nu}$ = 3450 (br), 3050 (w), 3019 (w), 2942 (w), 2822 (w), 2771 (w), 1733 (s), 1489 (m), 1447 (w), 1430 (m), 1359 (m), 1326 (w), 1174 (s), 1120 (s), 1110 (s), 977 (s), 885 (m), 825 (w), 740 (s), 719 (m), 700 (s), 611 (w), 513 (s), 493 cm^{-1} (m); MS (ESI+): *m*/*z* (%): 722.5 (9), 605.3 (100) [*M*+H$^+$]; MS (ESI-): *m*/*z* (%): 635.3 (44) [*M*$^-$+MeO], 623.3 (62), 591.3 (27), 283.3 (54), 255.2 (100); HRMS (ESI+): calcd (*m*/*z*) for $C_{40}H_{37}N_2O_2Si^+$: 605.26227; found: 605.26243; elemental analysis calcd (%) for $C_{40}H_{36}N_2O_2Si$: C 79.43, H 6.00, N 4.63; found: C 79.14, H 6.04, N 4.70. For X-ray structure determination, a single crystal was obtained by recrystallization from dichloromethane/methanol.

Spiro[10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5,1′-(4′,4′-di-*n*butyl{3′-oxa-4′-stannacyclohexan-2′-one[4′*a*,9′*b*-*b*′]-5′-[2″-(*N,N*-dimethylamino)-ethyl]indole})] (6): A 150 mL Schlenk flask was charged with a suspension of 5-{1-[2-(*N,N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid (4.0 g, 9.4 mmol) in diethyl ether (40 mL) under an argon atmosphere. A solution of methyllithium in diethyl ether (13.0 mL, 1.6 M, 20.7 mmol, 2.2 equiv) was slowly added by means of a syringe. The reaction mixture was stirred for 16 h at room temperature. The resulting yellow suspension was cooled to −78°C, whereupon a pre-cooled solution of dibutyltin dichloride (3.7 g, 12 mmol) in THF (60 mL) was injected into the flask. The reaction mixture was stirred and allowed to warm to room temperature overnight, and then the solvent was removed in vacuo. Diethyl ether was added to the orange

crude product, stirred for a few hours, and filtered. This process was repeated twice more. The nearly colorless powder was recrystallized from methanol to afford the title compound as colorless crystals (4.8 g, 7.3 mmol). Yield: 77%; m.p. 188°C (decomposition); ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25°C): δ = 7.31–7.29 (m, 1H; 7-H$_{indole}$), 7.08–7.05 (m, 2H; H$_{aryl}$), 7.04–7.00 (m, 2H; H$_{aryl}$), 6.94–6.87 (m, 3H; 6-H$_{indole}$, H$_{aryl}$), 6.77–6.69 (m, 2H; H$_{aryl}$), 6.56–6.53 (m, 2H; 4-H$_{indole}$, 5-H$_{indole}$), 4.51–4.49 (m, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.66–3.58 (m, 2H; CH$_2$), 3.18–3.16 (m, 2H; CH_2N(CH$_3$)$_2$), 3.10–3.02 (m, 2H; CH$_2$), 2.50 (s, 6H; N(CH$_3$)$_2$), 1.68–1.58 (m, 4H; SnCH$_2$), 1.43–1.25 (m, 8H; SnCH$_2$CH_2CH_2), 0.82 ppm (t, ^3J(H,H) = 7.2 Hz, 6H, SnCH$_2$CH$_2$CH$_2$CH_3); ^{1}H NMR (250 MHz, CDCl$_3$, 25°C): δ = 7.22–7.15 (m, 1H; H$_{indole}$), 7.10–6.90 (m, 7H; H$_{indole/aryl}$), 6.80–6.65 (m, 4H; H$_{indole/aryl}$), 4.45–4.37 (m, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.83–3.70 (m, 2H; CH$_2$), 3.32–3.25 (m, 2H; CH_2N(CH$_3$)$_2$), 3.19–3.07 (m, 2H; CH$_2$), 2.57 (s, 6H; N(CH$_3$)$_2$), 1.76–1.59 (m, 4H; SnCH$_2$), 1.43–1.29 (m, 8H; SnCH$_2$CH_2CH_2), 0.85 ppm (t, ^3J(H,H) = 7.3 Hz, 6H; SnCH$_2$CH$_2$CH$_2$CH_3); ^{1}H NMR (250 MHz, [D$_8$]THF, 25°C): δ = 7.30–7.28 (m, 2H; H$_{indole/aryl}$), 7.23–7.21 (m, 1H; H$_{indole}$), 7.00–6.98 (m, 2H; H$_{indole/aryl}$), 6.85–6.66 (m, 6H; H$_{indole/aryl}$), 6.42–6.40 (m, 1H; H$_{indole}$), 5.03–5.01 (m, 2H; CH_2CH$_2$N-(CH$_3$)$_2$), 3.79–3.69 (m, 2H; CH$_2$), 3.25–3.15 (m, 2H; CH$_2$), 2.75–2.73 (m, 2H; CH_2N(CH$_3$)$_2$), 2.33 (s, 6H; N(CH$_3$)$_2$), 1.87–1.75 (m, 4H, SnCH$_2$), 1.46–1.28 (m, 8H; SnCH$_2$CH_2CH_2), 0.88 ppm (t, ^3J(H,H) = 7.3 Hz, 6H; SnCH$_2$CH$_2$CH$_2$CH_3); ^{13}C{^{1}H} NMR (75 MHz, [D$_6$]DMSO, 25°C): δ = 175.4 (CO$_2$), 143.7 (C$_{aryl}$), 142.2 (C$_{aryl}$), 140.1 (7a-C$_{indole}$), 134.8 (3-C$_{indole}$), 132.5 (CH$_{aryl}$), 129.2 (CH$_{aryl}$), 126.9 (3a-C$_{indole}$), 125.0 (CH$_{aryl}$), 124.7 (CH$_{aryl}$), 121.0 (4-CH$_{indole}$), 120.3 (6-CH$_{indole}$), 118.2 (5-CH$_{indole}$), 109.2 (7-CH$_{indole}$), 65.9 (*C*(CO$_2$)), 57.4 (*C*H$_2$N(CH$_3$)$_2$), 45.2 (N(CH$_3$)$_2$), 41.7 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 36.2 (CH$_2$), 27.7 (SnCH$_2$), 26.4 (SnCH$_2$*C*H$_2$), 26.4 (SnCH$_2$CH$_2$*C*H$_2$), 13.6 ppm (SnCH$_2$CH$_2$CH$_2$*C*H$_3$), (2-C$_{indole}$Sn) not visible; ^{119}Sn{^{1}H} NMR (112 MHz, CDCl$_3$, 25°C): δ = −142.5 ppm; ^{119}Sn{^{1}H} NMR (112 MHz, CD$_2$Cl$_2$, 25°C): δ = −148.8 ppm; ^{119}Sn{^{1}H} NMR (112 MHz, [D$_6$]DMSO, 25°C): δ = −166.2 ppm; ^{119}Sn{^{1}H} NMR (112 MHz, [D$_5$]pyridine, 25°C): δ = −167.2 ppm; ^{119}S{^{1}H} NMR (112 MHz, [D$_8$]THF, 25°C): δ = −174.6 ppm; IR (KBr): $\tilde{\nu}$ = 3426 (br), 3048 (w), 2954 (s), 2924 (s), 2869 (m), 2854 (m), 1644 (s), 1485 (s), 1465 (s), 1353 (s), 1318 (m), 1281 (s), 1176 (w), 1160 (w), 1016 (w), 813 (m), 779 (w), 752 (s), 738 (s), 720 cm^{-1} (m); MS (ESI+): *m*/*z* (%): 868.5 (7), 695.2 (33) [*M*+K$^+$], 679.2 (28) [*M*+Na$^+$], 657.3 (100) [*M*+H$^+$]; HRMS (ESI+): calcd (*m*/*z*) for C$_{36}$H$_{45}$N$_2$O$_2$Sn$^+$: 657.24975; found: 657.25331; elemental analysis calcd (%) for C$_{36}$H$_{44}$N$_2$O$_2$Sn: C 65.97, H 6.77, N 4.27; found: C 65.28, H 6.83, N 4.15. For X-ray structure determination, a single crystal was obtained by recrystallization from benzene.

Disodium chloride 5-{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylate (7): A mixture of 1-[2-(*N*,*N*-dimethylamino)ethyl]indole (2.00 g, 10.6 mmol) and 5-hydroxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylic acid·0.5(1,4-dioxane) (3.17 g, 10.6 mmol) in glacial acetic acid (30 mL) was heated under reflux conditions for 12 min at 118°C and then cooled rapidly to room temperature. Brine (50 mL) was added to the red solution, and the mixture was stirred for 30 min. The product was extracted with dichloromethane. The combined organic layers were washed five times with brine, and then dried over magnesium sulfate. The organic solvent was removed by rotary evaporation leaving the crude product. Recrystallization from chloroform/diethyl ether gave the title compound as a light-brown powder. The chloroform incorporated into the solid could be removed from the product by stirring in diethyl ether, filtering, and drying in vacuo (3.12 g, 7.35 mmol). Yield: 69%; ^{1}H NMR (250 MHz, [D$_6$]DMSO/1% CF$_3$COOD, 25°C): δ = 7.60–7.53 (m, 1H; H$_{indole}$), 7.31 (s, 1H; 2-H$_{indole}$), 7.18–6.98 (m, 7H; H$_{aryl}$, H$_{indole}$), 6.97–6.87 (m, 2H; H$_{aryl}$, H$_{indole}$), 6.75–6.66 (m, 1H; H$_{indole}$), 6.51–6.42 (m, 1H; H$_{indole}$), 4.71–4.59 (m, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.54–3.39 (m, 2H; CH_2N(CH$_3$)$_2$), 3.21–2.98 (m, 4H; CH$_2$), 2.83 (s, 3H; N(CH$_3$)$_2$), 2.81 ppm (s, 3H; N(CH$_3$)$_2$); elemental analysis found (%): C 65.68, H 5.39, N 5.15.

5-{2-Acetyl-1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene (8): A 50 mL Schlenk flask was charged with a suspension of sodium 5-{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylate (1.00 g, 2.24 mmol) in diethyl ether (15 mL) under an argon atmosphere. A solution of methyllithium in diethyl ether (6.30 mL, 1.6 M, 10.3 mmol, 4.6 equiv) was slowly added by means of a syringe. The reaction mixture was stirred for 16 h at room temperature and then water (5 mL) was added. The resulting suspension was stirred for 15 min and then poured into water (50 mL). The aqueous suspension was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over magnesium sulfate. Dichloromethane was removed by rotary evaporation. The crude product was purified by column chromatography (dichloromethane/methanol, 7:1) and recrystallized from toluene. The title compound was obtained as slightly yellow crystals (248 mg, 0.587 mmol). Yield: 24%; R_f = 0.48 (CH$_2$Cl$_2$/MeOH, 7:1); m.p. 143°C; ^{1}H NMR (300 MHz, CDCl$_3$, 25°C): δ = 7.44–7.40 (m, 1H; 7-H$_{indole}$), 7.32–7.24 (m, 3H; 6-H$_{indole}$, H$_{aryl}$), 7.22–7.12 (m, 4H; H$_{aryl}$), 7.09–7.03 (m, 2H; H$_{aryl}$), 6.97–6.94 (m, 2H; 4-H$_{indole}$, 5-H$_{indole}$), 6.15 (s, 1H; CH), 4.33 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.23–3.02 (m, 4H; CH$_2$), 2.63 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.29 (s, 6H; N(CH$_3$)$_2$), 2.17 ppm (s, 3H; (CO)CH$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$, 25°C): δ = 197.6 (CO), 140.5 (C$_{aryl}$), 140.4 (C$_{aryl}$), 137.2 (7a-C$_{indole}$), 136.4 (2-C$_{indole}$), 130.4 (CH$_{aryl}$), 130.3 (CH$_{aryl}$), 127.5 (3-C$_{indole}$), 127.2 (CH$_{aryl}$), 125.9 (CH$_{aryl}$), 124.0 (6-CH$_{indole}$), 123.4 (4-CH$_{indole}$), 120.2 (5-CH$_{indole}$), 119.5 (3a-C$_{indole}$), 110.1 (7-CH$_{indole}$), 58.9 (*C*H$_2$N(CH$_3$)$_2$), 47.9 (CH), 45.7 (N(CH$_3$)$_2$), 42.9 (*C*H$_2$CH$_2$N(CH$_3$)$_2$), 33.1 (CH$_2$), 31.8 ppm ((CO)*C*H$_3$); IR (KBr): $\tilde{\nu}$ = 3433 (br), 3058 (w), 3016 (w), 2940 (w), 2822 (w), 2784 (w), 1667 (s), 1524 (w), 1485 (w), 1458 (m), 1403 (w), 1349 (m), 1336 (w), 1261 (w), 1206 (w), 1153 (w), 1105 (w), 1029 (w), 769 (m), 751 cm^{-1} (s); MS (ESI+): *m*/*z* (%): 423.2 (100) [*M*+H$^+$], 391.3 (4), 108.2 (6); HRMS (ESI+): calcd (*m*/*z*) for C$_{29}$H$_{31}$N$_2$O$^+$: 423.24309; found: 423.24304; elemental analysis calcd (%) for C$_{29}$H$_{30}$N$_2$O: C 82.43, H 7.16, N 6.63; found: C 81.97, H 7.09, N 6.80. For X-ray structure determination, a single crystal was obtained by recrystallization from toluene.

5-{2-Acetyl-1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-(5-deutero)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene ([D$_1$]8): A 25 mL Schlenk flask was charged with a suspension of sodium 5-{1-[2-(*N*,*N*-dimethylamino)ethyl]indol-3-yl}-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxylate (333 mg, 0.751 mmol) in diethyl ether (5 mL) under an argon atmosphere. A solution of methyllithium in diethyl ether (2.10 mL, 1.6 M, 3.36 mmol, 4.6 equiv) was slowly added by means of a syringe. The reaction mixture was stirred for 16 h at room temperature. Deuterium oxide (2 mL) was then added. The resulting suspension was stirred for 15 min and then poured into water (20 mL). The aqueous suspension was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over magnesium sulfate. The dichloromethane was removed by rotary evaporation. The crude product was purified by column chromatography (dichloromethane/methanol, 7:1) to afford the title compound as slightly yellow crystals (105 mg, 0.248 mmol). Yield: 33%; R_f = 0.49 (CH$_2$Cl$_2$/MeOH, 7:1); ^{1}H NMR (250 MHz, CDCl$_3$, 25°C): δ = 7.44–7.38 (m, 1H; 7-H$_{indole}$), 7.31–7.21 (m, 3H; 6-H$_{indole}$, H$_{aryl}$), 7.18–7.10 (m, 4H; H$_{aryl}$), 7.08–7.00 (m, 2H; H$_{aryl}$), 6.97–6.92 (m, 2H; 4-H$_{indole}$, 5-H$_{indole}$), 4.32 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2CH$_2$N(CH$_3$)$_2$), 3.23–2.99 (m, 4H; CH$_2$), 2.62 (t, ^3J(H,H) = 7.2 Hz, 2H; CH_2N(CH$_3$)$_2$), 2.28 (s, 6H; N(CH$_3$)$_2$), 2.16 ppm (s, 3H; (CO)CH$_3$); MS (ESI+): *m*/*z* (%): 675.7 (33), 424.2 [*M*+H$^+$], 338.3 (49); HRMS (ESI+): calcd (*m*/*z*) for C$_{29}$H$_{30}$DN$_2$O$^+$: 424.24937; found: 424.24901.

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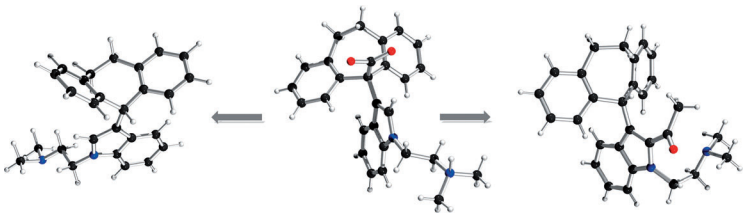

To balance or to unbalance—that is CO_2's question: A facile decarboxylation at room temperature of a zwitterionic amino acid has been observed. The re-carboxylation influences the reaction kinetics (middle to left X-ray structure). Stable silicon and tin spiro derivatives are reported. The detailed mechanism of a carbon chain rearrangement from the sodium carboxylate and excess methyllithium is reported (middle to right structure).

Carboxylate Transformations