Synthesis of Pyrrole Derivatives through Functionalization of 3,4-Bis(lithiomethyl)dihydropyrroles

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Bis(2-lithioallyl)amines **2**, substituted at the double bonds, undergo intramolecular carbolithiation of a lithiated double bond in different solvents to afford dilithiated dihydropyrroles **3**. Treatment of these dianions with electrophiles allows the preparation of functionalized pyrrole derivatives **5** and **6**. Interestingly, treatment of these dianions with carboxylic esters selectively affords either keto or hydroxy compounds (**9** or **10**), depending on the conditions. Several experiments have been carried out in order to clarify the mechanism of this selective transformation. Finally, dilithiated dihydropyrrole **3a** could be transformed in a three-step procedure into the corresponding 3,4-bis(bromomethyl) derivative **31**, which can easily be converted into bicyclic pyrrole compounds **32**–**33** by treatment with different nucleophiles.
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Introduction

The development of carbolithiation reactions[1] as a methodology for the preparation of heterocyclic systems[2] has recently emerged as a powerful tool in organic synthesis.[3,4] Moreover, these anionic cyclizations allow the cyclized product to be functionalized by treatment with electrophiles, representing an important advantage over radical cyclizations. This strategy has been used for the preparation of nitrogen heterocycles such as pyrrolidines,[5] indolines,[6] or isoquinolines[7] in a diastereoselective and even enantioselective way.[8] On the other hand, pyrroles are important heterocycles widely used in materials science,[9] they are abundant in nature and are of great interest as subunits for natural products synthesis.[10] In addition, functionalized pyrroles often display biological activity. Substantial attention has therefore been paid to the development of efficient methods for the synthesis of this kind of heterocycles. Many procedures, however, are limited in regard to substituents and substitution patterns. Most known methods for the synthesis of the pyrrole ring afford 2,5-di-,[11] 2,3-di[12] or polysubstituted[13] pyrroles. However, methods for the preparation of 2,5-unsubstituted pyrroles are scarce,[14] although α-free pyrroles are very important precursors for the synthesis of a variety of porphyrinoid dyes and polypyrroles.[15] In connection with our interest in the study of carbolithiation reactions, we have recently reported the first intramolecular carbolithiation of lithiated double bonds[16] and we have applied this methodology to the preparation of some indole and pyrrole derivatives.[17] Here, in continuation of our research into the preparation of *N*-heterocycles through carbolithiation reactions,[18] we would like to report our results in the synthesis of 2,5-unsubstituted 3,4-functionalized pyrrole derivatives.

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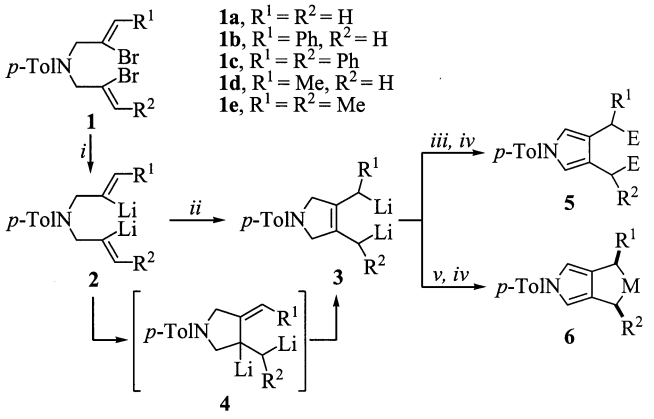
Results and Discussion

Intramolecular Carbolithiation of Substituted *N*,*N*-Bis(2-lithioallyl)amines

As we have recently reported,[16,17] treatment of amine **1a** ($R^1 = R^2 = H$) with 4 equiv. of *tert*-butyllithium in Et_2O at −78 °C gave rise to dianion **2a**, which on addition of 4 equiv. of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) at low temperature and subsequent warming to room temperature afforded 3,4-bis(lithiomethyl)pyrrole derivative **3a**, the methylenepyrrolidine **4a** being a likely intermediate in the reaction. In order to test the scope of this novel transformation with respect to the allyl moieties, we prepared amines **1b**−**e** and treated them under the reaction conditions described previously (4 equiv. of *t*BuLi in Et_2O at −78 °C and then 4 equiv. of TMEDA from −78 to 20 °C). The expected dianions **3** were obtained in all cases except for that of amine **1e** ($R^1 = R^2 = Me$), in which the intramolecular carbolithiation did not work and decomposition products were obtained (Scheme 1). Moreover, we have found that while dianion **2a** is transformed under these reaction conditions into the dilithio derivative **3a** at −50 °C,[17] dianions **2b** and **2c** cyclize at temperatures as low as −78 °C

and the transformation of both intermediates even in the absence of TMEDA takes place at −40 °C. In contrast, dianion **2d** is only converted into **3d** at temperatures over −20 °C and it needs to reach room temperature when the reaction is carried out in the absence of TMEDA. All these observations support the initial formation of intermediate **4** by a carbolithiation reaction, it being necessary that the R^2 substituent is a hydrogen or a group, such as a phenyl moiety, able to stabilize the terminal organolithium moiety in **4**.[19] Finally, an allylic rearrangement in **4** would provide



Scheme 1. Synthesis of functionalized pyrrole derivatives **5** and **6**; reagents and conditions: *i*) *t*BuLi (4 equiv.), Et_2O, −78 °C; *ii*) TMEDA (4 equiv.), −78 to 20 °C; *iii*) E^+ (2.2 equiv., see Table 1), −78 to 20 °C; *iv*) DDQ (CH_2Cl_2, 1 equiv., 15 min); *v*) MCl_2 (1 equiv.), −78 to 20 °C

dilithiated dihydropyrrole derivatives **3** (Scheme 1). The presence of an additional phenyl group (R^1 = Ph) also favors the carbolithiation reaction, probably due to extra stabilization in intermediate **3**. Dilithiated dihydropyrrole derivatives **3** were trapped with different electrophiles (deuterium oxide, silicon chlorides or acetone), giving rise to functionalized dihydropyrrole derivatives which were dehydrogenated by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to give the corresponding functionalized pyrroles **5** and **6**. Interestingly, the functionalized pyrroline intermediates could also be isolated if a fast purification was carried out.[17] In the case of starting amine **1c** (R^1 = R^2 = Ph), diastereoisomeric mixtures were obtained after treatment with electrophiles (Scheme 1 and Table 1). Compound **5d** (R^1 = R^2 = Ph; E = $SiMe_3$) was obtained as a 4:1 mixture of diastereoisomers, but we were unable to establish their stereochemistry. In the case of bicyclic compound **6b** (R^1 = R^2 = Ph; M = $SiMe_2$), however, a 6:1 mixture of diastereoisomers was obtained, and we were able to establish the stereochemistry of the major *meso* diastereoisomer by NOE experiments (Scheme 1).

We have also studied the role played by the solvent in this novel transformation, carrying out different experiments with dianion **2a** in several solvents (Table 2). In Et_2O the cyclization was complete in 45 min at room temperature, whereas in Et_2O/TMEDA the process was complete in 1 h at temperatures ranging between −78 and −50 °C. With respect to other ethereal solvents, we also observed

Table 1. Preparation of pyrrole derivatives **5** and **6** from amines **1**

Starting amine	R^1	R^2	E^+	Product	E/M	Yield (%)[a]
1b	Ph	H	D_2O	**5a**	D	89
1b	Ph	H	Me_3SiCl	**5b**	$SiMe_3$	86
1b	Ph	H	Ph_2SiCl_2	**6a**	$SiPh_2$	81
1c	Ph	Ph	D_2O	**5c**	D	91
1c	Ph	Ph	Me_3SiCl	**5d**	$SiMe_3$	87[b]
1c	Ph	Ph	Me_2SiCl_2	**6b**	$SiMe_2$	81[c]
1d	Me	H	D_2O	**5e**	D	85
1d	Me	H	Me_2CO	**5f**	$Me_2C(OH)$	71

[a] Isolated yield based on the starting amine **1**. [b] A 4:1 mixture of diastereoisomers was obtained. [c] A 6:1 mixture of diastereoisomers was obtained.

that the process worked efficiently in tetrahydropyran. In THF, however, the cyclic product was obtained only in 45% yield after 1 h at room temperature, along with unidentified decomposition products. When toluene or hexane were used as solvents, no transformation of the starting dianion **2a** was observed at 20 °C. Interestingly, though, when TMEDA was added to a solution of **2a** in toluene or hexane, the cyclization was complete in 1 h at room temperature. We can therefore conclude that TMEDA plays an important role both in polar and in non-polar solvents. In the former, the carbolithiation reaction occurs at lower temperatures and the yields are generally higher. In the latter, the reaction only works when TMEDA is present.[20]

Table 2. Intramolecular carbolithiation reactions of dianion **2a** in different solvents

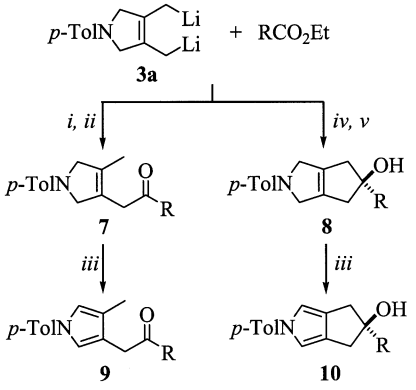
Solvent	Reaction Conditions	Time (min)	Yield (%)[a]
Et_2O	−78 to 20 °C	45−60	91
Et_2O-TMEDA	−78 to −50 °C	60	96
Tetrahydropyran	−78 to 20 °C	60	88
THF	−78 to 20 °C	60	45
Toluene	−78 to 20 °C	60	0
Toluene-TMEDA	−78 to 20 °C	60	92
Hexane-TMEDA	−78 to 20 °C	60	93

[a] Isolated yields of hydrolyzed compound corresponding to **3a** based on the starting amine **1a**.

Reactions of Dianions 3 with Carboxylic Esters

To extend the synthetic scope of this carbolithiation reaction we carried out the functionalization of the dilithiated dihydropyrrole derivatives **3** with different carboxylic esters. Surprisingly, treatment of **3a** with 2 equiv. of ethyl isobutyrate gave rise to a mixture of compounds that was analyzed by GC-MS to show that the major product had incorporated only one equivalent of ester. We therefore treated **3a** with 1 equiv. of ethyl isobutyrate at −78 °C, the mixture then being allowed to come to room temperature and stirred for 1 h. The formation of a mixture of the β,γ-unsaturated ketone **7e** and the bicyclic alcohol **8e** was observed,

but these were isolated as the oxidized pyrrole derivatives **9e** and **10e** (Scheme 2). With the goal of achieving selective formation of each product, several experiments were carried out under different reaction conditions. Finally, we found that the hydroxy bicyclic derivative **8e** was generated exclusively when the reaction mixture was allowed to stir overnight at 20 °C, the corresponding bicyclic pyrrole **10e** being isolated in 77% yield after dehydrogenation of the crude product and further purification by column chromatography (Scheme 2 and Table 3). Moreover, we also observed that if the reaction mixture was stirred for only 1 h at −78 °C, the pyrrole derivative **9e** could be isolated in 78% yield after hydrolysis and further oxidation in air (Scheme 2). It is interesting to note that, despite the strong tendencies of β,γ-unsaturated ketones towards prototropic rearrangements, producing conjugated α,β-unsaturated ketones,[21] no isomerization was observed in our case. In view of the interesting functionalized moieties in the synthesized pyrrole derivatives **7**−**10**, several carboxylic esters were tested as electrophiles with dianion **3a** (Table 3). In all the cases the expected keto or hydroxy derivatives were obtained, depending on the reaction conditions (−78 °C for ketones **7** and **9** or room temperature for alcohols **8** and **10**). With ethyl cyclopropanecarboxylate the dihydropyrroles **7a** and **8a** could be isolated and purified, although they could also be further dehydrogenated to their aromatic counterparts **9a** and **10a** by DDQ.



Scheme 2. Synthesis of functionalized pyrrole derivatives **7**−**10**; reagents and conditions: *i*) Et_2O, −78 °C, 1 h; *ii*) MeOH, −78 to 20 °C; *iii*) DDQ (CH_2Cl_2, 1 equiv., 15 min) or air (CH_2Cl_2, 24 h); *iv*) Et_2O, −78 to 20 °C, 12 h; *v*) H_2O, 20 °C

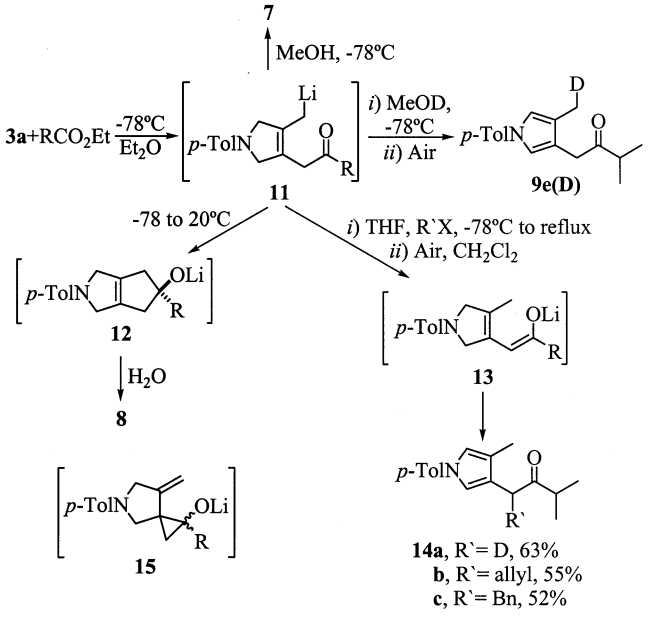
A detailed suggested mechanism for the reactions between intermediate **3a** and carboxylic esters is presented in Scheme 3. The initial attack of **3a** on the ester carbonyl group, followed by elimination of ethoxide anion, would yield monoanion **11**. This is partially supported by the isolation of the deuterated (>90% deuterium incorporated) ketone **9e(D)**, obtained after dehydrogenation, when the reaction mixture was quenched with MeOD at −78 °C after 1 h. To explain the difference in outcome of the reaction depending on the conditions, several experiments were carried out. Surprisingly, we observed that anion **11** was relatively inert towards conventional electrophiles[22] and that its closure to bicyclic alkoxide **12** took place slowly at 0 °C,

Table 3. Preparation of keto and hydroxy pyrrole derivatives **7**−**10** from reactions between dianion **3a** and ethyl carboxylates

Ester	Product	R	Oxidant	Yield (%)[a]
c−$C_3H_5CO_2Et$	**7a**	*c*-C_3H_5		82
c-$C_3H_5CO_2Et$	**8a**	*c*-C_3H_5		80
c-$C_3H_5CO_2Et$	**9a**	*c*-C_3H_5	DDQ	69
$MeCO_2Et$	**9b**	Me	DDQ	68
$EtCO_2Et$	**9c**	Et	Air	75
n$PrCO_2Et$	**9d**	^{n}Pr	DDQ	69
i$PrCO_2Et$	**9e**	*i*Pr	Air	78
$PhCO_2Et$	**9f**	Ph	DDQ	69
c-$C_3H_5CO_2Et$	**10a**	*c*-C_3H_5	DDQ	65
$MeCO_2Et$	**10b**	Me	DDQ	64
$EtCO_2Et$	**10c**	Et	Air	75
n$PrCO_2Et$	**10d**	^{n}Pr	DDQ	68
i$PrCO_2Et$	**10e**	*i*Pr	Air	77
$PhCO_2Et$	**10f**	Ph	DDQ	66

[a] Isolated yields based on the starting amine **1a**.

so the completion of the reaction needed several hours at room temperature. Moreover, if THF was added after the initial reaction between **3a** and the ester, a different pathway occurred and the results were consistent with a translocation of the lithium atom in organolithium **11** to form a more stable lithium enolate **13** (Scheme 3). This process is probably favored by the polar character of THF, which can promote a higher basicity of anion **11**.[23]



Scheme 3. Proposed mechanism for the selective formation of ketones **7** and alcohols **8**

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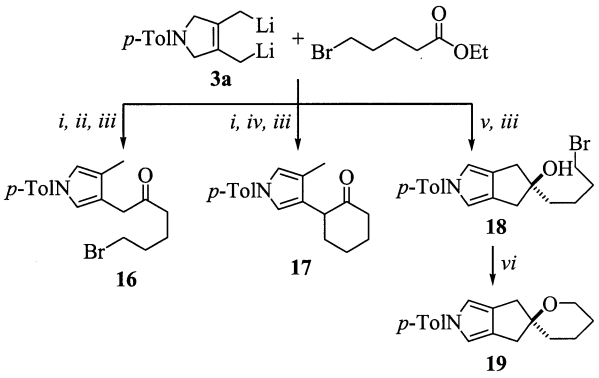
In order to verify the formation of enolate **13** we carried out some experiments. Deuteriolysis of the THF solution of **11e** at −78 °C gave, after oxidation, compound **9e(D)**. However, when the THF solution was allowed to warm to 0 °C before the addition of deuterium oxide, **14a** was obtained exclusively (after air oxidation). Although several ex-

periments at different temperatures were performed, we were not able to determine the exact temperature at which the translocation reaction takes place. Addition of electrophiles other than deuterium oxide, such as allyl bromide or benzyl chloride, to the THF solution of **11** at −78 °C and subsequent warming to room temperature and then heating at reflux gave pyrrole derivatives **14b** and **14c** after oxidation and purification. It is interesting to note that functionalized pyrrole derivatives **14b** and **14c** were obtained from the simple amine **1a**, with the formation of three new C−C bonds in a regioselective way, in good yields without isolation of any intermediates. We also found that if THF was added to **11** and the temperature was then allowed to come to 20 °C, the bicyclic alcohol **8** was not formed but the corresponding ketone **7** was then isolated. All these experiments seem to rule out the possibility of the formation of a lithium cyclopropanolate intermediate such as **15**, generated by intramolecular addition of the allylic organolithium **11** to the ketone carbonyl. These kind of intermediates were proposed by Rieke et al. for the reaction between substituted (2-butene-1,4-diyl)magnesium complexes and carboxylic esters[24] to generate cyclopentenols or β,γ-unsaturated ketones. Those authors also found that soft carbon electrophiles such as imines, ketones and esters reacted regioselectively at the 2-position of the 1,4-diylmagnesium complex, whereas we always found that soft or harder (silicon or tin chlorides) electrophiles reacted at the 1-position in our 3,4-bis(lithiomethyl)dihydropyrrole derivatives.

Furthermore, when a functionalized carboxylate such as ethyl 5-bromovalerate was used as electrophile in the reaction with dianion **3a** and the reaction mixture was quenched at low temperature, the expected ketone derivative **16** was obtained in 69% yield after exposure of the crude product to air in CH_2Cl_2 for 24 h (Scheme 4). According to our proposed mechanism, if THF were added to the reaction mixture after the reaction between intermediate **3a** and the ethyl 5-bromovalerate, cyclic ketone **17** should be generated by intramolecular trapping of the bromide by the intermediate enolate **13** [R = $(CH_2)_4Br$]. Indeed, **17** was obtained in 61% yield after oxidation of the crude product, supporting the pathways outlined in Scheme 3. On the other hand, when the reaction between the ester and the dianion **3a** was carried out at temperatures ranging between −78 and 20 °C, the alcohol **18** was obtained in 45% yield after oxidation and purification, along with the spiro derivative **19** (15%), derived from intramolecular alkylation of the corresponding alkoxide derivative **12** [R = $(CH_2)_4Br$]. However, compound **19** was obtained in 56% yield when compound **18** was treated with NaH in refluxing THF.



Scheme 4. Preparation of pyrroles **16**−**19** by treatment of **3a** with ethyl 5-bromovalerate; reagents and conditions: *i*) Et_2O, −78 °C, 1 h; *ii*) MeOH, −78 to 20 °C; *iii*) air (CH_2Cl_2, 24 h); *iv*) THF, −78 to 20 °C; *v*) Et_2O, −78 to 20 °C, 12 h; *vi*) NaH (1.5 equiv.), THF, reflux, 24 h.

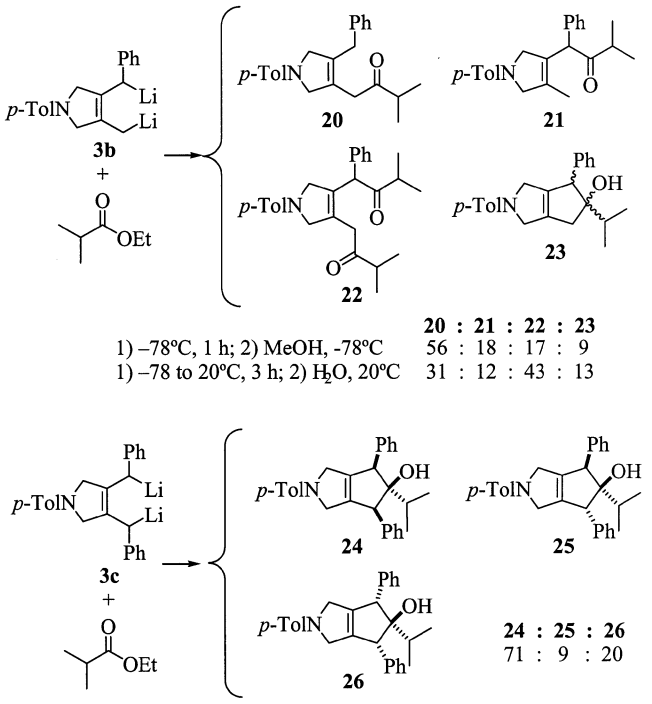
Reactions between Dianions 3b and 3c and Ethyl Isobutyrate

When we extended the reaction to other dianions **3** and other carboxylic esters such as ethyl isobutyrate, different results were obtained, depending on the substituents on the double bonds. Thus, treatment of **3b** with ethyl isobutyrate gave rise to a mixture of four compounds: regioisomeric ketones **20** and **21**, diketone **22** and the hydroxy derivative **23**. When the quenching of the reaction was carried out at −78 °C the overall yield was 58% and the expected monoketone **20** was the main product. When the temperature was allowed to reach 20 °C before quenching, however, the diketone **22** was obtained as the major product and only a small amount of the expected alcohol **23** was generated, with a similar overall yield. Although the process was not useful from a synthetic point of view, the formation of diketone **22** provided additional support for the intermediacy of an anion such as **11**, which in this case mainly reacted intermolecularly with another molecule of ester instead of reacting intramolecularly to afford **23**.

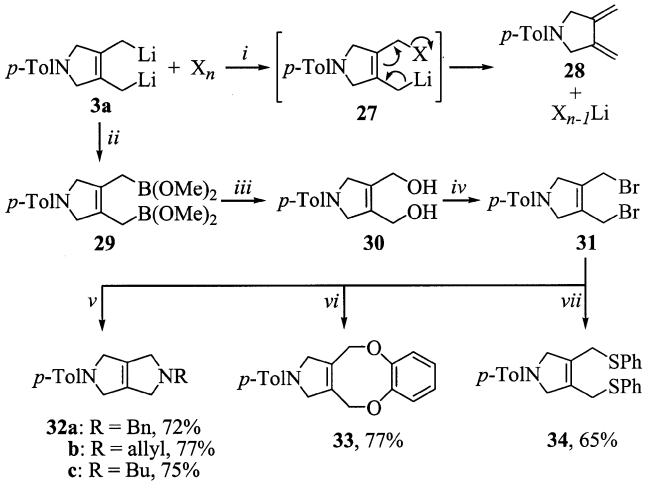
Treatment of dianion **3c** with ethyl isobutyrate, on the other hand, gave rise to a mixture of three diastereoisomeric hydroxy derivatives **24**, **25** and **26** in a 75% overall yield. In this case, the same ratio of isomers was obtained irrespective of the quenching conditions (−78 °C or room temperature). The three diastereoisomers could be separated by column chromatography and their stereochemistry determined by NOESY experiments. Compound **24**, with the two phenyl and the hydroxy groups in a *cis* arrangement, was the major diastereoisomer (53% isolated yield).

Synthesis of Dibromide 31

We had previously reported that treatment of dianions **3** with some electrophiles such as diphenyl disulfide or 1,2-diphenylethanedione did not afford the expected functionalized dihydropyrrole derivatives because a competing conjugated elimination in **27** gave rise to diene **28** (Scheme 6).[17] In addition, we had also observed that the same result was obtained when 1,2-dibromethane or iodine were used as electrophiles. In view of the potential interest of a dibromide compound like **31**, we considered alternative ways to obtain it, and so a three-step sequence was established. Firstly, **3a** was treated with trimethyl borate at temperatures ranging between −78 and 20 °C. The crude borate **29** was oxidized in situ with alkaline hydrogen peroxide



Scheme 5. Reactions between dianions **3b** and **3c** and ethyl isobutyrate; obtention of compounds **20**–**26**



Scheme 6. Transformation of dianion **3a** into dibromide **31** and further functionalization with nucleophiles; synthesis of compounds **32**–**34**; reagents and conditions: *i*) Et_2O, −78 to 20 °C; *ii*) $B(OMe)_3$ (2 equiv.), Et_2O, −78 to 20 °C; *iii*) $NaOH/H_2O_2$ (4 equiv.), 0 °C and then reflux, 30 min; *iv*) HBr (48%); *v*) RNH_2 (1 equiv.), K_2CO_3 (2 equiv.), CH_3CN, reflux; *vi*) catechol (1 equiv.), K_2CO_3 (2 equiv.), $(CH_3)_2CO$, reflux; *vii*) PhSH (2 equiv.), NaOH (0.7 M), H_2O/THF, 20 °C.

to afford the diol **30**, which was isolated and purified. This compound was transformed into the dibromide **31** by treatment with concentrated HBr (Scheme 6). Surprisingly, diol **30** was stable to all the oxidation conditions attempted (air, DDQ and hydrogen peroxide) and the corresponding pyrrole derivative was not obtained. With dibromide **31** to hand, we were able to prepare interesting bicyclic or tricyclic dihydropyrrole derivatives **32** and **33** by treatment of **31** with different nucleophiles such as amines and catechol. It is also interesting to note that treatment of **31** with thiophenol yielded the disulfide **34**, which had been unobtainable by direct treatment of **3a** with diphenyl disulfide.[17]

Conclusion

In summary, we have extended the scope of our previously reported intramolecular carbolithiation reaction of lithiated double bonds. We have also demonstrated a new and unexpected reactivity of the resulting dianions with carboxylic esters, selectively affording β,γ-unsaturated ketone or bicyclic cyclopentenol derivatives, depending on the reaction conditions. With this methodology, it was possible to form up to three new C−C bonds selectively in a one-pot process, to afford functionalized pyrrole derivatives from simple and easily available bis(2-bromoallyl)amines. Finally, the reactivity of the 3,4-bis(lithiomethyl)dihydropyrroles is completed by their conversion into the corresponding dibromides, which allow further functionalization with nucleophiles to give heterofused polycyclic compounds.

Experimental Section

General Remarks: All reactions were carried out under nitrogen in oven-dried glassware. Temperatures are reported as bath temperatures. Diethyl ether, tetrahydrofuran, toluene, hexane and tetrahydropyran were heated continuously at reflux and freshly distilled under nitrogen from sodium or sodium/benzophenone. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine was distilled from potassium/benzophenone in vacuo. Solvents used in extraction and purification were distilled prior to use. TLC was performed on aluminium-backed plates coated with silica gel 60 with F_{254} indicator (Merck) and compounds were viewed by use of UV light (254 nm) or iodine. Flash column chromatography was carried out on silica gel 60, 230−400 mesh (Merck). Melting points were measured on a Büchi−Tottoli apparatus with open capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 (100.6) and 200 (50.3) MHz on Varian spectrometers with $CDCl_3$ (δ = 7.26 ppm in ^{1}H NMR spectra and δ = 76.95 ppm in ^{13}C NMR spectra), C_6D_6 (δ = 7.15 ppm in ^{1}H NMR spectra and δ = 128.02 ppm in ^{13}C NMR spectra), [D$_6$]DMSO (δ = 2.50 ppm in ^{1}H NMR spectra and δ = 39.43 ppm in ^{13}C NMR spectra) and [D$_6$]acetone (δ = 2.05 ppm in ^{1}H NMR spectra and δ = 30.83 ppm in ^{13}C NMR spectra) as internal standards by use of the DEPT pulse sequence. Low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV on an HP-5987 A instrument and the intensities are reported as percentages relative to the base peak after the corresponding *m*/*z* value. Elemental analyses were performed with Perkin−Elmer and LECO elemental analysers. All commercially available reagents were used without further purification unless otherwise indicated and were purchased from Aldrich Chemical Co. or Acros Organics. *t*BuLi was used as 1.5 M solution in pentane. BuLi was used as 2.5 M solution in hexane.

General Procedure for the Preparation of *N*,*N*-Bis(2-bromoallyl)amines 1a, 1c and 1e: A mixture of 4-methylaniline (2.68 g, 25 mmol), K_2CO_3 (6.9 g, 50 mmol), NaI (0.75 g, 5 mmol), and 2 equiv. of the corresponding substituted alkene (2,3-dibromopropene, (*Z*)-2-bro-

mocinnamyl chloride and (*Z*)-methanesulfonic acid 2-bromo-2-butenyl ester) in CH_3CN (50 mL) was heated at reflux overnight. The mixture was extracted with EtOAc (3 × 30 mL), and the combined organic layers were washed with saturated aqueous Na_2CO_3 and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum, and the residue was purified by flash column chromatography to afford amines **1a** and **1e**. In the case of amine **1c**, on the other hand, the solid amine crystallized after the refluxing of the mixture and cooling to room temperature. It was filtered and washed with water to remove the inorganic salts, affording pure **1c**.

***N*,*N*-Bis(2-bromoallyl)-4-methylaniline (1a):** Data are in agreement with our previous report.[17]

***N*,*N*-Bis[(*Z*)-2-bromocinnamyl]-4-methylaniline (1c):** 4-Methylaniline (2.68 g, 25 mmol) was treated with K_2CO_3 (6.9 g, 50 mmol), NaI (0.75 g, 5 mmol) and (*Z*)-2-bromocinnamyl chloride (11.5 g, 50 mmol) in CH_3CN (50 mL). Workup as above yielded amine **1c** (8.08 g, 65%) as a clear brown solid. M.p. 137−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3 H), 4.44 (s, 4 H), 6.76−6.81 (m, 2 H), 6.92 (s, 2 H), 7.09−7.14 (m, 2 H), 7.29−7.41 (m, 6 H), 7.59−7.64 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.2, 60.1, 112.5, 122.1, 126.4, 127.3, 127.9, 128.0, 128.9, 135.0, 144.7 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 116 (100). $C_{25}H_{23}Br_2N$ (497.3): calcd. C 60.38, H 4.66, N 2.82; found C 60.55, H 4.62, N 2.84.

***N*,*N*-Bis[(*Z*)-2-bromo-2-butenyl]-4-methylaniline (1e):** Treatment of 4-methylaniline (2.68 g, 25 mmol), K_2CO_3 (6.9 g, 50 mmol), NaI (0.75 g, 5 mmol) and (*Z*)-methanesulfonic acid 2-bromo-2-butenyl ester (11.4 g, 50 mmol) as above in CH_3CN (50 mL), followed by workup and purification by column chromatography (hexane/EtOAc, 40:1), yielded amine **1e** (7.05 g, 76%) as a 15:1 *Z*/*E* mixture and as a white solid. M.p. 83−85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74 (dt, *J* = 6.6, 1.7 Hz, 6 H), 2.25 (s, 3 H), 4.11−4.14 (m, 4 H), 5.82 (tq, *J* = 6.6, 1.5 Hz, 2 H), 6.55−6.60 (m, 2 H), 7.00−7.05 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.2, 20.2, 58.4, 112.0, 122.6, 123.7, 126.7, 129.6, 144.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 375 (10) [M^+ + 4], 373 (23) [M^+ + 2], 371 (13) [M^+], 220 (100). $C_{15}H_{19}Br_2N$ (373.1): calcd. C 48.28, H 5.13, N 3.75; found C 48.14, H 5.08, N 3.77.

Preparation of *N*-(2-Bromoallyl)-4-methylaniline: A solution of 4-methylaniline (16.05 g, 150 mmol) in THF (50 mL) was treated at −40 °C with BuLi (20 mL of a 2.6 M solution in hexanes, 50 mmol). The reaction mixture was stirred for 15 min at this temperature and was then allowed to come to room temperature, stirring being continued for 45 min. The reaction mixture was cooled to −60 °C, and 2,3-dibromopropene (10 g, 50 mmol) was added. After 15 min at this temperature, the reaction mixture was allowed to warm and stirring was continued for 3 h. The mixture was hydrolyzed with water and extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvents were removed under vacuum. The residue was purified by silica gel column chromatography (hexane/EtOAc, 30:1) to afford *N*-(2-bromoallyl)-4-methylaniline (10.1 g, 90%) as a clear brown oil. R_f = 0.21 (hexane/EtOAc, 30:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 3.98 (s, 2 H), 4.08 (br. s, 1 H), 5.54−5.58 (m, 1 H), 5.84−5.88 (m, 1 H), 6.51−6.60 (m, 2 H), 6.97−7.06 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.3, 52.1, 112.9, 116.4, 127.1, 129.6, 131.2, 144.1 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 227 (30) [M^+ + 2], 225 (31) [M^+], 120 (100). $C_{10}H_{12}BrN$ (226.1): calcd. C 53.12, H 5.35, N 6.19; found C 53.27, H 5.41, N 6.12.

Preparation of *N*-(2-Bromoallyl)amines 1b and 1d: A mixture of *N*-(2-bromoallyl)-4-methylaniline (10.1 g, 45 mmol), K_2CO_3 (6.21 g, 45 mmol), NaI (0.68 g, 4.5 mmol) and the corresponding substituted alkene [(*Z*)-2-bromocinnamyl chloride and (*Z*)-methanesulfonic acid 2-bromo-2-butenyl ester] in CH_3CN (50 mL) was stirred under reflux overnight. The mixture was extracted with EtOAc (3 × 30 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by flash column chromatography to afford amines **1b** and **1d**.

***N*-(2-Bromoallyl)-*N*-[(*Z*)-2-bromocinnamyl]-4-methylaniline (1b):** Treatment of *N*-(2-bromoallyl)-4-methylaniline (10.1 g, 45 mmol), K_2CO_3 (6.21 g, 45 mmol), NaI (0.68 g, 4.5 mmol) and (*Z*)-2-bromocinnamyl chloride (10.42 g, 45 mmol) as above, workup and purification by column chromatography (hexane/EtOAc, 40:1) afforded amine **1b** (13.27 g, 70%) as a white solid. M.p. 65−67 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32 (s, 3 H), 4.27 (s, 2 H), 4.36 (s, 2 H), 5.63−5.68 (m, 1 H), 5.75−5.80 (m, 1 H), 6.68−6.77 (m, 2 H), 6.91 (s, 1 H), 7.07−7.16 (m, 2 H), 7.28−7.46 (m, 3 H), 7.57−7.66 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.2, 58.5, 60.1, 112.3, 116.2, 122.1, 126.3, 127.3, 127.9, 128.0, 128.8, 128.9, 129.8, 135.0, 144.5 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 423 (5) [M^+ + 4], 421 (13) [M^+ + 2], 419 (6) [M^+], 220 (100). $C_{19}H_{19}Br_2N$ (421.2): calcd. C 54.18, H 4.55, N 3.33; found C 54.01, H 4.49, N 3.37.

***N*-(2-Bromoallyl)-*N*-[(*Z*)-2-bromo-2-butenyl]-4-methylaniline (1d):** Treatment of *N*-(2-bromoallyl)-4-methylaniline (10.1 g, 45 mmol), K_2CO_3 (6.21 g, 45 mmol), NaI (0.68 g, 4.5 mmol), and (*Z*)-methanesulfonic acid 2-bromo-2-butenyl ester (10.31 g, 45 mmol) as above, followed by workup and purification by column chromatography (hexane), afforded amine **1d** (11.96 g, 74%) as a colorless oil. R_f = 0.27 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.75 (dt, *J* = 6.6, 1.8 Hz, 3 H), 2.24 (s, 3 H), 4.09−4.11 (m, 2 H), 4.13−4.16 (m, 2 H), 5.54−5.56 (m, 1 H), 5.66−5.68 (m, 1 H), 5.84 (tq, *J* = 6.6, 1.7 Hz, 1 H), 6.58−6.61 (m, 2 H), 7.00−7.03 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ =16.2, 20.2, 58.4, 58.6, 112.1, 116.0, 122.8, 123.6, 126.9, 128.9, 129.7, 144.5 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 361 (15) [M^+ + 4], 359 (39) [M^+ + 2], 357 (19) [M^+], 158 (100). $C_{14}H_{17}Br_2N$ (359.1): calcd. C 46.83, H 4.77, N 3.90; found C 46.89, H 4.73, N 3.94.

General Procedure for the Preparation of Pyrrole Derivatives 5 and 6: A solution of the starting amine **1b**−**d** (2 mmol) in diethyl ether (15 mL) was treated at −78 °C with 4 equiv. of *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol), and the resulting mixture was stirred at this temperature for 30 min. TMEDA (4 equiv., 1.2 mL, 8 mmol) was then added. The mixture was stirred at −78 °C for 1 h, except in the case of amine **1d**, in which the cooling bath was removed and stirring was continued for 1 h. The ethereal suspension of the corresponding dianion **3** was again cooled to −78 °C and either 2.1 equiv. (4.2 mmol) of neat electrophile (deuterium oxide, chlorotrimethylsilane, acetone) or 1.0 equiv. (2 mmol) of metallodichloride (dichlorodiphenylsilane, dichlorodimethylsilane) were added. The mixture was allowed to come to room temperature and the reaction mixture was stirred for 3 h. The mixture was hydrolyzed with water and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvents were removed under vacuum, yielding the corresponding dihydropyrrole derivatives. The solutions of these compounds in CH_2Cl_2 (20 mL) were each treated with dichlorodicyanobenzoquinone (DDQ, 1.0 equiv., 0.46 g, 2 mmol). After the mixture had been stirred for 15 min at room temperature, aqueous NaOH (1 M, 20 mL) was added (alternatively, oxidation was carried out by stirring the solution exposed to the air for 24 h). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed

under vacuum. The resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc) to afford pyrrole derivatives **5** and **6**.

3-(Deuteriomethyl)-4-[(deuteriophenyl)methyl]-1-(4-methylphenyl)-1*H*-pyrrole (5a): Amine **1b** (0.84 g, 2 mmol) was treated with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and TMEDA (1.2 mL, 8 mmol). Addition of deuterium oxide (excess) was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL). Workup as above and purification by column chromatography (hexane/EtOAc, 40:1) yielded **5a** (0.47 g, 89%) as a colorless oil. R_f = 0.27 (hexane/EtOAc, 30:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.11 (s, 2 H), 2.41 (s, 3 H), 3.90 (s, 1 H), 6.78−6.81 (m, 1 H), 6.90−6.94 (m, 1 H), 7.19−7.44 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.0 (t, $J_{C/D}$ = 19.4 Hz), 20.7, 31.5 (t, $J_{C/D}$ = 19.2 Hz), 117.1, 117.3, 119.4, 119.9, 124.2, 125.6, 128.2, 128.6, 129.8, 134.2, 138.3, 141.3 ppm. LRMS (70 eV, EI): *m/z* (%) = 263 (87) [M$^+$], 186 (100). $C_{19}H_{17}D_2N$ (263.4): calcd. C 86.65, H/D 8.03, N 5.32; found C 86.54, H/D 7.95, N 5.28.

1-(4-Methylphenyl)-3-[phenyl(trimethylsilyl)methyl]-4-(trimethylsilylmethyl)-1*H*-pyrrole (5b): Amine **1b** (0.84 g, 2 mmol) was treated with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol). Chlorotrimethylsilane (0.53 mL, 4.2 mmol) was added before treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above and purification by column chromatography (hexane) yielded **5b** (0.70 g, 86%) as a colorless oil. R_f = 0.22 (hexane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.00 (s, 9 H), 0.13 (s, 9 H), 1.73 (s, 2 H), 2.42 (s, 3 H), 3.41 (s, 1 H), 6.75−6.79 (m, 1 H), 7.06−7.39 (m, 10 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = −1.8, −1.5, 13.5, 20.7, 34.4, 115.2, 116.4, 119.2, 122.5, 124.1, 124.4, 127.8, 128.0, 129.8, 133.9, 138.5, 143.4 ppm. LRMS (70 eV, EI): *m/z* (%) = 405 (32) [M$^+$], 332 (100). $C_{25}H_{35}NSi_2$ (405.7): calcd. C 74.01, H 8.70, N 3.45; found. C 74.20, H 8.81, N 3.41.

2,4,5,6-Tetrahydro-2-(4-methylphenyl)-4,5,5-triphenylsilolo[3,4-*c*]-pyrrole (6a): Treatment of amine **1b** (0.84 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol) was followed by addition of dichlorodiphenylsilane (0.50 g, 2 mmol). Treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C, workup as above and purification by column chromatography (hexane/EtOAc, 40:1) yielded **6a** (0.71 g, 81%) as a white solid. M.p. 163−165 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3 H), 2.32 (d, *J* = 17.4 Hz, 1 H), 2.55 (d, *J* = 17.4 Hz, 1 H), 4.19 (s, 1 H), 6.79−6.81 (m, 1 H), 6.91−6.98 (m, 4 H), 7.00−7.06 (m, 2 H), 7.07−7.16 (m, 6 H), 7.18−7.24 (m, 3 H), 7.34−7.43 (m, 3 H), 7.64−7.69 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 9.3, 20.7, 34.1, 114.1, 114.7, 119.6, 124.1, 126.4, 127.2, 127.3, 127.8, 127.9, 129.2, 129.6, 129.8, 130.9, 132.8, 134.5, 134.8, 135.2, 138.7, 143.8 ppm. LRMS (70 eV, EI): *m/z* (%) = 441 (55) [M$^+$], 105 (100)**.** $C_{31}H_{27}NSi$ (441.6): calcd. C 84.31, H 6.16, N 3.17; found. C 84.50, H 6.08, N 3.21.

3,4-Bis(deuteriophenylmethyl)-1-(4-methylphenyl)-1*H*-pyrrole (5c): Treatment of amine **1c** (1.0 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol) was followed by addition of deuterium oxide (excess). Treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C, workup as above and purification by column chromatography (hexane/EtOAc, 40:1) yielded **5c** (0.62 g, 91%) as a white solid. M.p. 74−76 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 3.74 (s, 2 H), 6.73 (s, 2 H), 7.10−7.36 (m, 14 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.7, 31.5 (t, $J_{C/D}$ = 19.5 Hz), 117.7, 119.4, 123.8, 125.7, 128.2, 128.6, 129.8, 134.3, 138.1, 141.1 ppm. LRMS (70 eV, EI): *m/z* (%) = 339 (78) [M$^+$], 262 (100)**.** $C_{25}H_{21}D_2N$ (339.5): calcd. C 88.45, H/D 7.42, N 4.13; found C 88.28, H/D 7.33, N 4.14.

1-(4-Methylphenyl)-3,4-bis[phenyl(trimethylsilyl)methyl]-1*H*-pyrrole (5d): Treatment of amine **1c** (1.0 g, 2 mmol) with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and TMEDA (1.2 mL, 4 mmol) was followed by addition of chlorotrimethylsilane (0.53 mL, 4.2 mmol). Treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C and workup as above, followed by purification by column chromatography (hexane/EtOAc, 40:1), yielded **5d** (0.84 g, 87%), which was isolated as a 4:1 mixture of diastereoisomers. ^{1}H NMR (200 MHz, $CDCl_3$) for the mixture of the two diastereoisomers: δ = 0.16 (s, 9 H maj.), 0.05 (s, 9 H *min*), 2.36 (s, 3 H *min*), 2.39 (s, 3 H maj.), 3.12 (s, 2 H maj.), 3.29 (s, 2 H min.), 6.77−7.33 (m, 16 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$) for the mixture of the two diastereoisomers: δ = −2.0 (maj.), −1.8 (min.), 20.8, 33.9 (maj.), 34.4 (min.), 116.4 (min.), 117.0 (maj.), 119.4 (min.), 119.5 (maj.), 124.0 (min.), 124.1 (maj.), 125.6 (min.), 125.8 (maj.), 127.6 (min.), 127.7 (maj.), 128.0, 129.9 (min.), 130.0 (maj.), 134.1 (min.), 134.2 (maj.), 138.5, 143.5 (min.), 143.6 (maj.) ppm. LRMS (70 eV, EI): *m/z* (%) = maj.: 481 (31) [M$^+$], 408 (100)**;** *min*: 481 (31) [M$^+$], 408 (100). $C_{31}H_{39}NSi_2$ (481.8): calcd. C 77.28, H 8.16, N 2.91; found. C 77.42, H 8.11, N 2.87.

2,4,5,6-Tetrahydro-5,5-dimethyl-2-(4-methylphenyl)-4,6-diphenylsilolo[3,4-*c*]pyrrole (6b): Amine **1c** (1.0 g, 2 mmol) was treated with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and TMEDA (1.2 mL, 8 mmol). Addition of dichlorodimethylsilane (0.24 mL, 2 mmol) was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL). Workup as above and purification by column chromatography (hexane/EtOAc, 40:1) yielded **6b** (0.64 g, 81%) as a mixture of diastereoisomers *cis*/*trans* = 6:1. ^{1}H NMR (400 MHz, $CDCl_3$) for the mixture of diastereoisomers: δ = −0.46 (s, 3 H *cis*), 0.00 (s, 6 H *trans*), 0.50 (s, 3 H, *cis*), 2.38 (s, 3 H *trans*), 2.40 (s, 3 H *cis*), 3.77 (s, 2 H *cis*), 3.82 (s, 2 H *trans*), 6.97 (s, 2 H), 7.12−7.38 (m, 20 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$) for the mixture of diastereoisomers: δ = −6.2 (*cis*), −4.2 (*trans*), −2.4 (*cis*), 20.7, 33.5 (*trans*), 34.5 (*cis*), 114.6, 119.5 (*trans*), 119.6 (*cis*), 124.0 (*trans*), 124.1 (*cis*), 126.5 (*trans*), 126.7 (*cis*), 128.1, 129.9, 130.3 (*cis*), 130.4 (*trans*), 134.5 (*trans*), 134.6 (*cis*), 138.7, 143.9 (*cis*), 144.4 (*trans*) ppm. LRMS (70 eV, EI) = *m/z* (%) = *cis*: 393 (57) [M$^+$], 144 (100)**;** *trans*: 393 (47) [M$^+$], 144 (100). $C_{27}H_{27}NSi$ (393.6): calcd. C 82.49, H 6.90, N 3.56; found C 82.61, H 6.84, N 3.60.

3-(1-Deuterioethyl)-4-(deuteriomethyl)-1-(4-methylphenyl)-1*H*-pyrrole (5e): Treatment of amine **1d** (0.72 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol) was followed by addition of deuterium oxide (excess). Treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C and workup as above, followed by purification by column chromatography (hexane), yielded **5e** (0.34 g, 85%) as a colorless oil. R_f = 0.14 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20−1.23 (m, 3 H), 2.05−2.07 (m, 2 H), 2.32 (s, 3 H), 2.42−2.51 (m, 1 H), 6.78−6.81 (m, 2 H), 7.13−7.23 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 9.8 (t, $J_{C/D}$ = 19.5 Hz), 14.3, 18.2 (t, $J_{C/D}$ = 19.5 Hz), 20.7, 115.6, 116.9, 119.4, 127.3, 129.8, 134.1, 138.4 ppm. LRMS (70 eV, EI) = *m/z* (%) = 201 (49) [M$^+$], 186 (100)**.** $C_{14}H_{15}D_2N$ (201.3): calcd. C 83.53, H/D 9.51, N 6.96; found C 83.29, H/D 9.60, N 7.01.

3-(2-Hydroxy-1,2-dimethylpropyl)-4-(2-hydroxy-2-methylpropyl)-1-(4-methylphenyl)-1*H*-pyrrole (5f): Treatment of amine **1d** (0.72 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol) was followed by addition of acetone (0.24 g, 4.2 mmol). Treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) and workup as above, followed by purification by column chromatography (hexane/EtOAc, 2:1), yielded **5f** (0.45 g, 71%) as a reddish oil. R_f = 0.15 (hexane/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (s, 3 H), 1.22−1.27 (m, 9 H), 1.30 (s, 3 H), 2.07 (br. s, 2

H), 2.36 (s, 3 H), 2.64 (d, J = 14.3 Hz, 1 H), 2.75 (d, J = 14.3 Hz, 1 H), 2.91 (q, J = 7.2 Hz, 1 H), 6.91 (d, J = 2.4 Hz, 1 H), 6.93 (d, J = 2.4 Hz, 1 H), 7.18−7.28 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.7, 20.7, 25.5, 28.3, 28.5, 29.5, 38.8, 40.6, 70.1, 72.8, 116.2, 117.8, 119.5, 120.9, 127.5, 129.9, 134.8, 137.9 ppm. LRMS (70 eV, EI): *m/z* (%) = 238 (100). $C_{20}H_{29}NO_2$ (315.4): C 76.15, H 9.27, N 4.44; found C 76.28, H 9.30, N 4.37.

General Procedure for the Preparation of Dihydropyrrole Derivatives 7: A solution of the starting amine **1a** (0.69 g, 2 mmol) in diethyl ether (15 mL) was treated at −78 °C with *t*BuLi (4 equiv., 5.33 mL of a 1.5 M solution in pentane, 8 mmol). The reaction mixture was stirred for 30 min at this temperature and for 1 h at room temperature. The ethereal suspension of dianion **3a** was again cooled to −78 °C, and 1.0 equiv. of one of the different neat carboxylic esters was added. The mixture was then stirred for 1 h at this temperature, quenched with methanol and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 10:1), yielding the dihydropyrrole derivatives **7**.

3-(2-Cyclopropyl-2-oxoethyl)-2,5-dihydro-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (7a): Amine **1a** (0.69 g, 2 mmol) was treated with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol). Addition of ethyl cyclopropanecarboxylate (0.23 g, 2 mmol) and workup as above yielded **7a** (0.42 g, 82%) as a colorless oil. R_f = 0.25 (hexane/EtOAc, 10:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.85−0.99 (m, 2 H), 1.02−1.12 (m, 2 H), 1.82 (s, 3 H), 1.93−2.07 (m, 1 H), 2.27 (s, 3 H), 3.39 (s, 2 H), 4.05 (s, 4 H), 6.40−6.50 (m, 2 H), 7.01−7.11 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.0, 11.5, 19.6, 20.0, 41.5, 57.5, 58.9, 110.7, 124.4, 129.5, 131.2, 144.7, 207.4 ppm. LRMS (70 eV, EI): *m/z* (%) = 255 (33) [M^+], 184 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 80.11, H 8.22, N 5.38.

General Procedure for the Preparation of Hydroxy-dihydropyrrole Derivatives 8: A solution of the starting amine **1a** (0.69 g, 2 mmol) in diethyl ether (15 mL) was treated at −78 °C with *t*BuLi (4 equiv., 5.33 mL of a 1.5 M solution in pentane, 8 mmol). The reaction mixture was stirred for 30 min at this temperature and for 1 h at room temperature. The ethereal suspension of dianion **3a** was again cooled to −78 °C and 1.0 equiv. of one of the different neat esters was added. The mixture was then allowed to come to room temperature and was stirred overnight. The mixture was hydrolyzed with water and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, the solvent was removed under vacuum, and the resulting residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 5:1) to afford the dihydropyrrole derivatives **8**.

5-Cyclopropyl-2-(4-methylphenyl)-1,2,3,4,5,6-hexahydrocyclopenta-[*c*]pyrrol-5-ol (8a): Amine **1a** (0.69 g, 2 mmol) was treated with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol). Addition of ethyl cyclopropanecarboxylate (0.23 g, 2 mmol) and workup as above yielded **8a** (0.41 g, 80%) as a white solid. M.p. 133−135 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.34−0.57 (m, 4 H), 1.17−1.32 (m, 1 H), 1.76 (br. s, 1 H), 2.25 (s, 3 H), 2.34 (d, J = 15.9 Hz, 2 H), 2.54 (d, J = 15.9 Hz, 2 H), 3.88 (s, 4 H), 6.38−6.48 (m, 2 H), 6.99−7.09 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 1.2, 20.1, 20.5, 42.8, 52.0, 86.4, 110.6, 124.1, 129.6, 138.3, 145.5 ppm. LRMS (70 eV, EI): *m/z* (%) = 255 (100) [M^+]. $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 79.84, H 8.35, N 5.43.

General Procedure for the Preparation of Pyrrole Derivatives 9, 10, 16 and 18: Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and the corresponding ester (2 mmol) was carried out as described above. The crude product was dehydrogenated with an equimolar amount of DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL). After the mixture had been stirred for 15 min at room temperature, aqueous NaOH (1 M, 20 mL) was added (alternatively, oxidation could be performed by stirring the solution exposed to the air for 24 h). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum. The resulting residue was purified by flash column chromatography [silica gel, hexane/EtOAc, 10:1 (for compounds **9** and **16**) or 5:1 (for compounds **10** and **18**)] to afford compounds **9**, **10, 16** and **18**.

3-(2-Cyclopropyl-2-oxoethyl)-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (9a): Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and ethyl cyclopropanecarboxylate (0.23 g, 2 mmol) for 1 h at −78 °C, was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **9a** (0.35 g, 69%) as a yellowish oil. R_f = 0.23 (hexane/EtOAc, 10:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.69−0.80 (m, 2 H), 0.89−1.00 (m, 2 H), 1.89−2.03 (m, 4 H), 2.24 (s, 3 H), 3.56 (s, 2 H), 6.72−6.76 (m, 1 H), 6.82−6.86 (m, 1 H), 7.00−7.16 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.1, 11.0, 19.3, 20.6, 40.7, 117.2, 117.4, 117.9, 119.4, 120.0, 129.8, 134.5, 138.1, 209.0 ppm. LRMS (70 eV, EI): *m/z* (%) = 253 (13) [M^+], 184 (100). $C_{17}H_{19}NO$ (253.3): calcd. C 80.60, H 7.56, N 5.53; found C 80.49, H 7.62, N 5.54.

3-Methyl-1-(4-methylphenyl)-4-(2-oxopropyl)-1*H*-pyrrole (9b): Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and EtOAc (0.20 mL, 2 mmol) for 1 h at −78 °C was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **9b** (0.31 g, 68%) as a yellowish solid. M.p. 67−69 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 2.20 (s, 3 H), 2.36 (s, 3 H), 3.56 (s, 2 H), 6.83−6.87 (m, 1 H), 6.91−6.94 (m, 1 H), 7.15−7.25 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.1, 20.7, 28.8, 41.0, 117.3, 117.4, 117.9, 119.6, 119.9, 129.9, 134.7, 138.1, 207.3 ppm. LRMS (70 eV, EI): *m/z* (%) = 227 (16) [M^+], 184 (100). $C_{15}H_{17}NO$ (227.3): calcd. C 79.26, H 7.54, N 6.16; found C 79.41, H 7.49, N 6.17.

3-Methyl-1-(4-methylphenyl)-4-(2-oxobutyl)-1*H*-pyrrole (9c): Amine **1a** was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl propionate (0.23 mL, 2 mmol) for 1 h. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **9c** (0.36 g, 75%) as a yellow solid. M.p. 40−42 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.3 Hz, 3 H), 2.07 (s, 3 H), 2.36 (s, 3 H), 2.53 (q, J = 7.3 Hz, 3 H), 3.55 (s, 2 H), 6.82−6.86 (m, 1 H), 6.91−6.95 (m, 1 H), 7.14−7.27 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 7.8, 10.1, 20.6, 34.5, 39.7, 117.3, 117.5, 117.8, 119.5, 119.9, 129.8, 134.5, 138.0, 209.8 ppm. LRMS (70 eV, EI): *m/z* (%) = 241 (19) [M^+], 184 (100). $C_{16}H_{19}NO$ (241.3): calcd. C 79.63, H 7.94, N 5.80; found C 79.57, H 8.01, N 5.69.

3-Methyl-1-(4-methylphenyl)-4-(2-oxopentyl)-1*H*-pyrrole (9d): Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and ethyl butyrate (0.27 mL, 2 mmol) for 1 h at −78 °C was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **9d** (0.35 g, 69%) as a clear brown solid. M.p. 46−48 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.4 Hz, 3 H), 1.42−1.61 (m, 2 H), 1.95 (s, 3 H), 2.24 (s, 3 H), 2.37 (t, J = 7.4 Hz, 2 H), 3.42 (s, 2 H), 6.71−6.75 (m, 1 H), 6.80−6.84 (m, 1 H), 7.03−7.16 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.1, 13.6, 17.2, 20.6, 40.0, 43.3, 117.3,

117.4, 117.8, 119.5, 119.9, 129.8, 134.5, 138.0, 209.2 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 255 (14) [M$^+$], 184 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 80.10, H 8.19, N 5.42.

3-Methyl-4-(3-methyl-2-oxobutyl)-1-(4-methylphenyl)-1*H*-pyrrole (9e): Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol) for 1 h. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **9e** (0.40 g, 78%) as a yellow oil. R_f = 0.34 (hexane/EtOAc, 10:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 7.0 Hz, 6 H), 1.93 (s, 3 H), 2.22 (s, 3 H), 2.69 (hept, *J* = 7.0 Hz, 1 H), 3.49 (s, 2 H), 6.70−6.74 (m, 1 H), 6.79−6.83 (m, 1 H), 7.02−7.15 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.0, 18.3, 20.5, 37.7, 39.3, 117.2, 117.8, 119.4, 119.9, 129.8, 134.4, 138.2, 212.1 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 255 (9) [M$^+$], 184 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 79.80, H 8.39, N 5.46.

3-Deuteriomethyl-4-(3-methyl-2-oxobutyl)-1-(4-methylphenyl)-1*H*-pyrrole [9e(D)]: Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol) for 1 h. The mixture was quenched with MeOD. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **9e(D)** (0.38 g, 74%) as a yellow oil. R_f = 0.34 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 6.9 Hz, 6 H), 2.01−2.05 (m, 2 H), 2.35 (s, 3 H), 2.80 (hept, *J* = 6.9 Hz, 1 H), 3.60 (s, 2 H), 6.82−6.84 (m, 1 H), 6.90−6.92 (m, 1 H), 7.16−7.24 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 9.9 (t, $J_{C/D}$ = 19.6 Hz), 18.4, 20.7, 37.8, 39.4, 117.3, 117.4, 117.9, 119.5, 119.9, 129.8, 134.5, 138.1, 212.1 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 256 (18) [M$^+$], 185 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.65, H/D 8.65, N 5.46; found C 79.76, H/D 8.59, N 5.44.

3-Methyl-1-(4-methylphenyl)-4-(2-oxo-2-phenylethyl)-1*H*-pyrrole (9f): Treatment of amine **1a** (0.69 g, 2 mmol) at −78 °C with *t*BuLi (5.33 mL, 8 mmol) and ethyl benzoate (0.30 g, 2 mmol) for 1 h was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **9f** (0.40 g, 69%) as a reddish solid. M.p. 82−84 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.00 (s, 3 H), 2.23 (s, 3 H), 4.04 (s, 2 H), 6.73−6.77 (m, 1 H), 6.79−6.83 (m, 1 H), 7.00−7.15 (m, 4 H), 7.30−7.51 (m, 3 H), 7.92−7.99 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.3, 20.7, 35.7, 117.3, 117.4, 118.0, 119.5, 120.0, 128.4, 128.5, 129.8, 132.8, 134.5, 136.7, 138.1, 197.9 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 289 (14) [M$^+$], 184 (100). $C_{20}H_{19}NO$ (289.4): calcd. C 83.01, H 6.62, N 4.84; found C 82.87, H 6.55, N 4.88.

3-(6-Bromo-2-oxohexyl)-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (16): Treatment of amine **1a** (0.69 g, 2 mmol) at −78 °C with *t*BuLi (5.33 mL, 8 mmol) and ethyl 5-bromovalerate (0.42 g, 2 mmol) for 1 h, was followed by exposure of a CH_2Cl_2 (20 mL) solution to the air at 20 °C. Workup as above yielded **16** (0.48 g, 69%) as a colorless oil. R_f = 0.20 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.59−1.68 (m, 2 H), 1.69−1.78 (m, 2 H), 1.95 (s, 3 H), 2.26 (s, 3 H), 2.43 (t, *J* = 7.2 Hz, 2 H), 3.27 (t, *J* = 6.6 Hz, 2 H), 3.44 (s, 2 H), 6.74−6.76 (m, 1 H), 6.81−6.83 (m, 1 H), 7.06−7.16 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.1, 20.7, 22.2, 31.9, 32.2, 40.0, 40.1, 117.1, 117.4, 117.8, 119.5, 119.9, 129.9, 134.7, 138.0, 208.5 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 349 (4) [M$^+$ + 2], 347 (4) [M$^+$], 184 (100). $C_{18}H_{22}BrNO$ (348.3): calcd. C 62.07, H 6.37, N 4.02; found C 62.15, H 6.28, N 3.99.

5-Cyclopropyl-2-(4-methylphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]-pyrrol-5-ol (10a): Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and ethyl cyclopropanecarboxylate (0.23 g, 2 mmol) at 20 °C overnight was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **10a** (0.33 g, 65%) as a white solid. M.p. 132−134 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.33−0.43 (m, 4 H), 1.05−1.23 (m, 1 H), 1.94 (br. s, 1 H), 2.24 (s, 3 H), 2.53 (d, *J* = 15.6 Hz, 2 H), 2.73 (d, *J* = 15.6 Hz, 2 H), 6.62 (s, 2 H), 7.01−7.15 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 1.3, 19.5, 20.6, 39.1, 88.1, 111.8, 119.9, 128.5, 129.8, 134.4, 138.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 253 (16) [M$^+$], 184 (100). $C_{17}H_{19}NO$ (253.3): calcd. C 80.60, H 7.56, N 5.53; found C 80.48, H 7.47, N 5.50.

5-Methyl-2-(4-methylphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-5-ol (10b): Treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and EtOAc (0.20 mL, 2 mmol) at 20 °C overnight was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **10b** (0.29 g, 64%) as a white solid. M.p. 140−142 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.54 (s, 3 H), 2.13 (br. s, 1 H), 2.25 (s, 3 H), 2.75 (d, *J* = 15.4 Hz, 2 H), 2.87 (d, *J* = 15.4 Hz, 2 H), 6.74 (s, 2 H), 7.14−7.24 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.7, 27.4, 41.6, 86.2, 112.0, 120.1, 128.9, 129.9, 134.6, 138.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 227 (16) [M$^+$], 184 (100). $C_{15}H_{17}NO$ (227.3): calcd. C 79.26, H 7.54, N 6.16; found C 79.21, H 7.45, N 6.20.

5-Ethyl-2-(4-methylphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-5-ol (10c): Amine **1a** (0.69 g, 2 mmol) was treated at 20 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl propionate (0.23 mL, 2 mmol) overnight. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **10c** (0.36 g, 75%) as a clear brown solid. M.p. 126−128 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.4 Hz, 3 H), 1.81 (q, *J* = 7.4 Hz, 2 H), 2.06 (br. s, 1 H), 2.26 (s, 3 H), 2.67 (d, *J* = 15.8 Hz, 2 H), 2.84 (d, *J* = 15.8 Hz, 2 H), 6.72 (s, 2 H), 7.11−7.25 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 8.8, 20.7, 33.2, 39.5, 89.3, 112.0, 120.0, 128.8, 129.8, 134.5, 138.9 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 241 (24) [M$^+$], 184 (100). $C_{16}H_{19}NO$ (241.3): calcd. C 79.63, H 7.94, N 5.80; found C 79.74, H 7.99, N 5.72.

2-(4-Methylphenyl)-5-propyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-5-ol (10d): Treatment of amine **1a** (0.69 g, 2 mmol) at 20 °C with *t*BuLi (5.33 mL, 8 mmol) and ethyl butyrate (0.27 mL, 2 mmol) overnight, was followed by treatment with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL) at 20 °C. Workup as above yielded **10d** (0.35 g, 68%) as a pale yellow solid. M.p. 98−100 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.1 Hz, 3 H), 1.32−1.55 (m, 2 H), 1.60−1.73 (m, 2 H), 2.03 (br. s, 1 H), 2.24 (s, 3 H), 2.59 (d, *J* = 15.5 Hz, 2 H), 2.75 (d, *J* = 15.5 Hz, 2 H), 6.63 (s, 2 H), 7.02−7.16 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.6, 17.8, 20.6, 40.0, 43.0, 88.9, 111.9, 120.0, 128.8, 129.8, 134.4, 138.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 255 (13) [M$^+$], 184 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 80.10, H 8.33, N 5.42.

5-Isopropyl-2-(4-methylphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]-pyrrol-5-ol (10e): Amine **1a** (0.69 g, 2 mmol) was treated at 20 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol) overnight. Exposure of a CH_2Cl_2 solution (20 mL) to the air and workup as above yielded **10e** (0.39 g, 77%) as a yellowish solid. M.p. 115−117 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.9 Hz, 6 H), 1.72 (br. s, 1 H), 1.89 (hept, *J* = 6.9 Hz, 1 H), 2.27 (s, 3 H), 2.58 (d, *J* = 15.6 Hz, 2 H), 2.81 (d, *J* = 15.6 Hz, 2 H), 6.68 (s, 2 H), 7.06−7.20 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 17.6, 20.6, 36.7, 38.6,

91.6, 111.8, 119.9, 128.0, 129.7, 134.3, 138.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 255 (11) [M$^+$], 184 (100). $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 79.88, H 8.28, N 5.47.

2-(4-Methylphenyl)-5-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-5-ol (10f): Treatment of amine **1a** (0.69 g, 2 mmol) at 20 °C with *t*BuLi (5.33 mL, 8 mmol) and ethyl benzoate (0.30 g, 2 mmol) overnight was followed by treatment at 20 °C with DDQ (0.46 g, 2 mmol) in CH_2Cl_2 (20 mL). Workup as above yielded **10f** (0.38 g, 66%) as a yellowish solid. M.p. 133−135 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 2.40 (br. s, 1 H), 2.94 (d, *J* = 15.6 Hz, 2 H), 3.21 (d, *J* = 15.6 Hz, 2 H), 6.70 (s, 2 H), 7.02−7.56 (m, 9 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.1, 43.2, 89.6, 112.5, 120.5, 125.4, 127.3, 128.8, 128.9, 130.3, 135.0, 139.3, 146.1 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 289 (12) [M$^+$], 184 (100). $C_{20}H_{19}NO$ (289.4): calcd. C 83.01, H 6.62, N 4.84; found C 83.06, H 6.65, N 4.81.

5-(4-Bromobutyl)-2-(4-methylphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-5-ol (18): Treatment of amine **1a** (0.69 g, 2 mmol) at 20 °C with *t*BuLi (5.33 mL, 8 mmol) and ethyl 5-bromovalerate (0.42 g, 2 mmol) overnight was followed by exposure of a CH_2Cl_2 (20 mL) solution to the air. Workup as above yielded **18** (0.31 g, 45%) as a white solid. M.p. 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63−1.73 (m, 2 H), 1.79−1.85 (m, 2 H), 1.90−1.98 (m, 2 H), 2.10 (br. s, 1 H), 2.36 (m, 3 H), 2.73 (d, *J* = 15.5 Hz, 2 H), 2.87 (d, *J* = 15.5 Hz, 2 H), 3.46 (t, *J* = 6.8 Hz, 2 H), 6.76 (s, 2 H), 7.17−7.25 (m, 4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.7, 23.3, 33.1, 33.7, 39.6, 40.1, 88.7, 112.1, 120.1, 128.5, 129.9, 134.7, 138.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 349 (2) [M$^+$ + 2], 347 (4) [M$^+$], 184 (100). $C_{18}H_{22}BrNO$ (348.3): calcd. C 62.07, H 6.37, N 4.02; found C 61.97, H 6.28, N 4.07.

Preparation of 3-(1-Deuterio-3-methyl-2-oxobutyl)-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (14a): Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol). After the solution had been stirred for 1 h at this temperature, THF (20 mL) was added. The cooling bath was removed and the mixture was allowed to come to room temperature and was quenched with D_2O. Extraction with EtOAc (3 × 20 mL) and workup as described above, followed by exposure to the air and purification by silica gel column chromatography (hexane/EtOAc, 30:1) afforded compound **14a** (0.32 g, 63%) as a yellow oil. R_f = 0.34 (hexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (d, *J* = 7.0 Hz, 6 H), 2.05 (s, 3 H), 2.36 (s, 3 H), 2.81 (hept, *J* = 7.0 Hz, <1 H), 3.57−3.61 (m, 1 H), 6.83−6.85 (m, 1 H), 6.91−6.93 (m, 1 H), 7.16−7.24 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.2, 18.3, 18.4, 20.7, 37.5 (t, $J_{C/D}$ = 19.2 Hz), 39.5, 117.3, 117.9, 119.6, 120.0, 129.8, 134.6, 138.2, 212.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 256 (6) [M$^+$], 186 (100).

Preparation of Substituted Pyrrole Derivatives 14b and 14c: Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol). After the solution had been stirred for 1 h at this temperature, THF (20 mL) and alkyl halide (2 mmol) were added. The cooling bath was removed, and the mixture was allowed to come to room temperature and was then heated at reflux until reaction was complete. Extraction with EtOAc (3 × 20 mL) and workup as described above, followed by exposure to the air, afforded compounds **14b** and **14c**, which were purified by silica gel column chromatography (hexane/EtOAc, 30:1).

3-(1-Allyl-3-methyl-2-oxobutyl)-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (14b): Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol) for 1 h. THF (20 mL) and allyl bromide (0.174 mL, 2 mmol) were added, and the mixture was heated to reflux. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **14b** (0.32 g, 55%) as a yellowish oil. R_f = 0.30 (15:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01 (d, *J* = 6.4 Hz, 3 H), 1.09 (d, *J* = 7.2 Hz, 3 H), 2.12 (s, 3 H), 2.35 (s, 3 H), 2.37−2.45 (m, 1 H), 2.69−2.80 (m, 2 H), 3.81 (dd, *J* = 8.2, 6.6 Hz, 1 H), 4.97−5.01 (m, 1 H), 5.05−5.11 (m, 1 H), 5.73−5.84 (m, 1 H), 6.79−6.84 (m, 2 H), 7.16−7.23 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.3, 18.3, 18.9, 20.7, 36.9, 39.1, 47.9, 116.0, 117.0, 117.3, 119.3, 121.8, 129.8, 134.6, 136.6, 138.0, 213.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 295 (7) [M$^+$], 224 (100). $C_{20}H_{25}NO$ (295.4): calcd. C 81.31, H 8.53, N 4.74; found C 81.43, H 8.61, N 4.69.

3-(1-Benzyl-3-methyl-2-oxobutyl)-4-methyl-1-(4-methylphenyl)-1*H*-pyrrole (14c): Amine **1a** (0.69 g, 2 mmol) was treated at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and ethyl isobutyrate (0.27 mL, 2 mmol) for 1 h. THF (20 mL) and benzyl chloride (0.23 mL, 2 mmol) were added, and the mixture was heated to reflux. Exposure of a CH_2Cl_2 (20 mL) solution to the air and workup as above yielded **14c** (0.36 g, 52%) as a yellowish oil. R_f = 0.23 (25:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 6.9 Hz, 3 H), 0.86 (d, *J* = 6.9 Hz, 3 H), 1.92 (s, 3 H), 2.26 (s, 3 H), 2.50 (hept, *J* = 6.9 Hz, 1 H), 2.78 (dd, *J* = 13.4, 5.9 Hz, 1 H), 3.23 (dd, *J* = 13.4, 8.8 Hz, 1 H), 3.91 (dd, *J* = 8.8, 5.9 Hz, 1 H), 6.71 (s, 2 H), 7.03−7.18 (m, 9 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.1, 18.0, 18.4, 20.7, 39.4, 39.9, 50.0, 117.0, 117.3, 119.3, 119.4, 122.0, 125.9, 128.1, 129.0, 129.9, 134.7, 138.0, 140.5, 213.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 345 (4) [M$^+$], 274 (100). $C_{20}H_{25}NO$ (345.5): calcd. C 83.44, H 7.88, N 4.05; found C 83.31, H 8.00, N 4.03.

Synthesis of 3-Methyl-1-(4-methylphenyl)-4-(2-oxocyclohexyl)-1*H*-pyrrole (17): Dianion **3a,** formed by treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) as described above, was treated at −78 °C with ethyl 5-bromovalerate (0.42 g, 2 mmol). After the solution had been stirred for 1 h at this temperature, THF (40 mL) was added. The mixture was allowed to come to room temperature and stirring was continued for 3 h. The mixture was quenched with water and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and solvents were removed under vacuum. The residue was exposed to the air as described above. Purification by column chromatography (hexane/EtOAc, 10:1) yielded **17** (0.33 g, 61%) as a yellowish solid. M.p. 92−94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66−1.80 (m, 2 H), 1.84−1.98 (m, 5 H), 2.00−2.12 (m, 1 H), 2.23−2.32 (m, 4 H), 2.34−2.51 (m, 2 H), 3.48 (dd, *J* = 12.0, 5.4 Hz, 1 H), 6.76−6.81 (m, 2 H), 7.06−7.17 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.5, 20.6, 25.4, 27.9, 34.3, 41.9, 48.8, 116.5, 117.2, 119.5, 119.8, 122.4, 129.7, 134.3, 138.2, 210.5 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 267 (100) [M$^+$]. $C_{18}H_{21}NO$ (267.4): calcd. C 80.86, H 7.92, N 5.24; found C 81.02, H 7.98, N 5.22.

Synthesis of Spiro Compound 19: NaH (18 mg, 0.75 mmol) was added to a solution of **18** (175 mg, 0.5 mmol) in THF (10 mL). The resulting mixture was heated at reflux for 24 h. Water was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. Purification of the residue by column chromatography (hexane/EtOAc, 10:1) afforded compound **19** (75 mg, 56%) as a white solid. M.p. 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54−1.65 (m, 2 H), 1.69−1.81 (m, 4 H), 2.36 (s, 3 H), 2.79 (d, *J* = 15.2 Hz, 2 H), 2.98 (d, *J* = 15.2 Hz, 2

H), 3.78 (t, J = 5.4 Hz, 2 H), 6.72 (s, 2 H), 7.15−7.25 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.6, 20.7, 25.9, 35.4, 37.0, 63.4, 90.0, 111.6, 120.1, 128.5, 129.8, 134.4, 139.0 ppm. LRMS (70 eV, EI): *m/z* (%) = 267 (100) [M$^+$]. $C_{18}H_{21}NO$ (267.4): calcd. C 80.86, H 7.92, N 5.24; found C 81.00, H 7.87, N 5.25.

Treatment of Dianion 3b with Ethyl Isobutyrate: Ethyl isobutyrate (0.27 mL, 2 mmol) was added at −78 °C to a solution of dianion **3b**, prepared by treatment of amine **1b** (0.84 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) and TMEDA (1.2 mL, 8 mmol) as described above. If the reaction mixture was stirred for 1 h at −78 °C and then hydrolyzed with MeOH, a 56:18:17:9 mixture of **20**, **21**, **22** and **23** was obtained after the usual workup. On the other hand, if the reaction mixture was stirred overnight at 20 °C after the addition of the ester and was then hydrolyzed with water, a 31:12:43:13 mixture of **20**, **21**, **22** and **23** was obtained after the usual workup. These compounds were separated and purified by silica gel column chromatography (hexane/EtOAc, 40:1 to 10:1). Alcohol **23** could not be characterized.

3-Benzyl-2,5-dihydro-4-(3-methyl-2-oxobutyl)-1-(4-methylphenyl)-1*H*-pyrrole (20): White solid. M.p. 89−91 °C. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.11 (d, J = 6.8 Hz, 6 H), 2.17 (s, 3 H), 2.79 (hept, J = 6.8 Hz, 1 H), 3.56 (s, 2 H), 3.60 (s, 2 H), 3.88−3.92 (m, 2 H), 4.04−4.08 (m, 2 H), 6.33−6.37 (m, 2 H), 6.94−6.98 (m, 2 H), 7.18−7.32 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 19.6, 21.3, 34.3, 39.7, 42.1, 58.7, 59.6, 112.7, 125.6, 128.0, 130.3, 130.4, 131.4, 135.4, 140.9, 147.0, 207.1 ppm. LRMS (70 eV, EI): *m/z* (%) = 333 (8) [M$^+$], 260 (100). $C_{23}H_{27}NO$ (333.5): calcd. C 82.84, H 8.16, N 4.20; found C 83.01, H 8.11, N 4.14.

2,5-Dihydro-3-methyl-1-(4-methylphenyl)-4-(3-methyl-2-oxo-1-phenylbutyl)-1*H*-pyrrole (21): White solid. M.p. 93−95 °C. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.05 (d, J = 6.9 Hz, 3 H), 1.12 (d, J = 6.9 Hz, 3 H), 1.89−1.92 (m, 3 H), 2.17 (s, 3 H), 2.84 (hept, J = 6.9 Hz, 1 H), 3.81−3.89 (m, 1 H), 3.92−4.05 (m, 2 H), 4.18−4.26 (m, 1 H), 5.31 (s, 1 H), 6.35−6.40 (m, 2 H), 6.94−7.00 (m, 2 H), 7.25−7.39 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 12.9, 19.7, 20.0, 21.4, 41.8, 56.0, 57.8, 60.9, 112.7, 125.7, 128.9, 130.4, 130.5, 130.8, 131.4, 132.7, 139.4, 146.9, 207.1 ppm. LRMS (70 eV, EI): *m/z* (%) = 333 (8) [M$^+$], 262 (100). $C_{23}H_{27}NO$ (333.5): calcd. C 82.84, H 8.16, N 4.20; found C 82.95, H 8.09, N 4.23.

2,5-Dihydro-3-(3-methyl-2-oxobutyl)-1-(4-methylphenyl)-4-(3-methyl-2-oxo-1-phenylbutyl)-1*H*-pyrrole (22): White solid. M.p. 109−111 °C. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.04 (d, J = 6.9 Hz, 3 H), 1.09 (d, J = 6.9 Hz, 3 H), 1.11 (d, J = 6.9 Hz, 6 H), 2.17 (s, 3 H), 2.77 (hept, J = 6.9 Hz, 1 H), 2.84 (hept, J = 6.9 Hz, 1 H), 3.62 (d, J = 17.0 Hz, 1 H), 3.70 (d, J = 17.0 Hz, 1 H), 3.85−3.93 (m, 1 H), 3.99−4.11 (m, 2 H), 4.24−4.32 (m, 1 H), 5.34 (s, 1 H), 6.35−6.39 (m, 2 H), 6.94−7.00 (m, 2 H), 7.20−7.40 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 19.5, 19.6, 19.7, 19.9, 21.4, 39.9, 41.9, 42.2, 56.0, 57.8, 59.7, 112.7, 125.8, 129.0, 130.5, 130.6, 130.9, 131.4, 134.3, 139.2, 146.9, 207.1, 211.7 ppm. LRMS (70 eV, EI): *m/z* (%) = 403 (3) [M$^+$], 330 (100). $C_{23}H_{27}NO$ (403.6): calcd. C 80.36, H 8.24, N 3.47; found C 80.22, H 8.17, N 3.50.

Treatment of Dianion 3c with Ethyl Isobutyrate: Ethyl isobutyrate (0.27 mL, 2 mmol) was added at −78 °C to a solution of dianion **3c**, formed by treatment of amine **1c** (1.0 g, 2 mmol) with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol) and TMEDA (1.2 mL, 8 mmol) as described above. A 71:9:20 mixture of compounds **24, 25** and **26** was obtained irrespective of whether the reaction mixture was stirred for 1 h at −78 °C and then hydrolyzed with MeOH or allowed to reach 20 °C and stirred overnight at this temperature before the quenching with water. In both cases, after the usual workup, these compounds were separated and purified by silica gel column chromatography (hexane/EtOAc, 20:1 to 5:1).

(4*R*,5*S*,6*S*)-5-Isopropyl-2-(4-methylphenyl)-4,6-diphenyl-1,2,3,4,5,6-hexahydrocyclopenta[*c*]pyrrol-5-ol (24): White solid. M.p. 76−78 °C. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.14 (d, J = 6.8 Hz, 6 H), 1.55 (s, 1 H), 2.15 (hept, J = 6.8 Hz, 1 H), 2.19 (s, 3 H), 3.86−3.95 (m, 2 H), 3.99−4.07 (m, 2 H), 4.13 (s, 2 H), 6.39−6.43 (m, 2 H), 6.96−7.01 (m, 2 H), 7.19−7.24 (m, 2 H), 7.29−7.37 (m, 8 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 18.9, 21.4, 41.1, 53.2, 55.9, 92.1, 112.8, 125.7, 128.4, 129.8, 131.5, 131.9, 140.6, 144.5, 147.7 ppm. LRMS (70 eV, EI): *m/z* (%) = 409 (30) [M$^+$], 338 (100). $C_{29}H_{31}NO$ (409.6): calcd. C 85.04, H 7.63, N 3.42; found C 84.96, H 7.55, N 3.38.

(4*R,6*R**)-5-Isopropyl-2-(4-methylphenyl)-4,6-diphenyl-1,2,3,4,5,6-hexahydrocyclopenta[*c*]pyrrol-5-ol (25):** White solid. ^{1}H NMR (400 MHz, C_6D_6): δ = 0.62 (d, J = 6.8 Hz, 3 H), 0.74 (d, J = 6.8 Hz, 3 H), 1.36 (br. s, 1 H), 1.78 (hept, J = 6.8 Hz, 1 H), 2.20 (s, 3 H), 3.60−3.87 (m, 4 H), 3.91−3.97 (m, 2 H), 6.20−6.24 (m, 2 H), 6.99−7.15 (m, 12 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 19.1, 19.2, 21.3, 36.3, 52.9, 53.3, 56.4, 62.8, 94.3, 112.7, 125.7, 128.3, 128.5, 129.6, 130.0, 131.1, 131.4, 132.5, 140.3, 141.3, 144.8, 145.5, 147.7 ppm. LRMS (70 eV, EI): *m/z* (%) = 409 (35) [M$^+$], 338 (100). $C_{29}H_{31}NO$ (409.6): calcd. C 85.04, H 7.63, N 3.42; found C 85.11, H 7.55, N 3.45.

(4*R*,5*R*,6*S*)-5-Isopropyl-2-(4-methylphenyl)-4,6-diphenyl-1,2,3,4,5,6-hexahydrocyclopenta[*c*]pyrrol-5-ol (26): White solid. M.p. 190−192 °C. ^{1}H NMR (400 MHz, C_6D_6): δ = 0.75 (d, J = 6.7 Hz, 6 H), 1.80 (hept, J = 6.7 Hz, 1 H), 1.89 (br. s, 1 H), 2.21 (s, 3 H), 3.61−3.75 (m, 6 H), 6.20−6.25 (m, 2 H), 6.99−7.21 (m, 12 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 19.5, 21.3, 33.2, 53.2, 64.3, 97.6, 112.7, 125.7, 128.5, 130.0, 131.4, 131.7, 141.8, 143.9, 147.7 ppm. LRMS (70 eV, EI): *m/z* (%) = 409 (40) [M$^+$], 338 (100). $C_{29}H_{31}NO$ (409.6): calcd. C 85.04, H 7.63, N 3.42; found C 85.14, H 7.70, N 3.40.

Treatment of Dianion 3a with Iodine or 1,2-Dibromoethane. Preparation of 3,4-Bismethylene-*N*-(4-methylphenyl)pyrrolidine (28): Either iodine (1.07 g, 4.2 mmol) or 1,2-dibromoethane (0.36 mL, 4.2 mmol) was added at −78 °C to a suspension of **3a** in diethyl ether, prepared by treatment of amine **1a** at −78 °C with *t*BuLi (5.33 mL of a 1.5 M solution in pentane, 8 mmol), followed by warming up to 20 °C. The mixture was stirred and allowed to come to room temperature, and was then hydrolyzed with water. After the usual workup, the crude **28** obtained could not be purified. ^{1}H NMR (200 MHz, $CDCl_3$) for crude **28**: δ = 2.19 (s, 3 H), 3.99 (s, 4 H), 4.99 (m, 2 H), 5.47 (m, 2 H), 6.39−6.46 (m, 2 H), 6.86−7.04 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$) for crude **28**: δ = 20.1, 53.7, 104.1, 112.1, 125.6, 129.5, 143.0, 145.1 ppm. LRMS (70 eV, EI): *m/z* (%) = 185 (77) [M$^+$], 184 (100).

Preparation of 2,5-Dihydro-3,4-bis(hydroxymethyl)-1-(4-methylphenyl)-1*H*-pyrrole (30): A solution of dianion **3a**, generated by treatment of amine **1a** (0.69 g, 2 mmol) with *t*BuLi (5.33 mL, 8 mmol) as described above, was treated at −78 °C with trimethyl borate (2 equiv., 0.47 mL, 4 mmol). The resulting mixture was stirred at this temperature for 30 min, the cooling bath was removed, and the stirring was continued for 1 h at room temperature (addition of 5 mL of THF was necessary because of the low solubility of the reaction mixture in diethyl ether). The reaction mixture was cooled to 0 °C and a solution made up of hydrogen peroxide (4 equiv., 0.8 mL of a 10 M solution in water, 8 mmol) and sodium

hydroxide (4 equiv., 2.7 mL of a 3 M solution in water, 8 mmol) was added dropwise. After addition was complete, the reaction mixture was heated at reflux for 30 min. Boron salts were separated by filtration, the filtrate was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the resulting yellowish solid was purified by column chromatography (EtOAc), yielding diol **30** (0.33 g, 75%) as a white solid. M.p. 154−156 °C. ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ = 2.15, (s, 3 H), 4.04 (s, 4 H), 4.12 (d, *J* = 5.2 Hz, 4 H), 4.79 (t, *J* = 5.2 Hz, 2 H), 6.32−6.41 (m, 2 H), 6.92−7.01 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ = 19.9, 55.4, 56.4, 110.8, 123.4, 129.6, 133.2, 144.9 ppm. $C_{13}H_{17}NO_2$ (219.3): calcd. C 71.21, H 7.81, N 6.39; found C 71.07, H 7.76, N 6.35.

Preparation of 3,4-Bis(bromomethyl)-2,5-dihydro-1-(4-methylphenyl)-1*H*-pyrrole (31): A solution of diol **30** (0.44 g, 2 mmol) in hydrobromic acid (48%, 4 mL) was heated for 2 h under reflux. The resulting mixture was cooled to 0 °C and neutralized with aqueous sodium hydroxide (3 M). The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum, and the resulting residue was purified by column chromatography (hexane/EtOAc, 25:1), affording dibromide **31** (0.58 g, 84%) as a white solid. M.p. 203−205 °C (decomp). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.27 (s, 3 H), 4.12 (s, 4 H), 4.26 (s, 4 H), 6.42−6.48 (m, 2 H), 7.02−7.07 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.2, 22.8, 57.1, 111.4, 125.8, 129.8, 133.5, 144.1 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 184 (100). $C_{13}H_{15}Br_2N$ (345.1): calcd. C 45.25, H 4.38, N 4.06; found C 45.41, H 4.29, N 4.03.

Treatment of Dibromide 31 with Primary Amines. Preparation of Diazabicyclic Compound 32. A solution of dibromide **31** (0.69 g, 2 mmol) and the corresponding primary amine (benzylamine, allylamine or butylamine, 2 mmol) in CH_3CN (20 mL) was treated with K_2CO_3 (0.55 g, 4 mmol). The resulting mixture was stirred under reflux for 3 h. Water was added and the organic product was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The resulting residues were purified by column chromatography, affording compounds **32**.

2-Benzyl-1,2,3,4,5,6-hexahydro-5-(4-methylphenyl)pyrrolo[3,4-*c*]-pyrrole (32a): Dibromide **31** (0.69 g, 2 mmol) was treated with benzylamine (0.19 mL, 2 mmol) and K_2CO_3 (0.55 g, 4 mmol) in CH_3CN (20 mL). Workup as above, followed by purification by column chromatography (hexane/EtOAc, 1:1), yielded **32a** (0.42 g, 72%) as a yellowish solid. M.p. 136−138 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.17 (s, 3 H), 3.49 (s, 4 H), 3.84 (s, 2 H), 3.91 (s, 4 H), 6.29−6.38 (m, 2 H), 6.91−7.00 (m, 2 H), 7.09−7.34 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.2, 51.1, 56.1, 60.5, 110.7, 124.4, 127.0, 128.3, 128.5, 129.7, 138.9, 139.3, 145.4 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 290 (88) [M$^+$], 170 (100). $C_{20}H_{22}N_2$ (290.4): calcd. C 82.72, H 7.64, N 9.65; found C 82.79, H 7.61, N 9.59.

2-Allyl-1,2,3,4,5,6-hexahydro-5-(4-methylphenyl)pyrrolo[3,4-*c*]-pyrrole (32b): Dibromide **31** (0.69 g, 2 mmol) was treated with allylamine (0.15 mL, 2 mmol) and K_2CO_3 (0.55 g, 4 mmol) in CH_3CN (20 mL). Workup as above, followed by purification by column chromatography (EtOAc/Et_3N, 50:1), yielded **32b** (0.37 g, 77%) as a yellowish solid. M.p. 156−158 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 3.40 (d, *J* = 6.4 Hz, 2 H), 3.59 (s, 4 H), 4.02 (s, 4 H), 5.11−5.32 (m, 2 H), 5.83−6.05 (m, 1 H), 6.39−6.49 (m, 2 H), 7.01−7.11 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.2, 51.2, 55.8, 59.0, 110.7, 116.8, 124.4, 129.7, 135.8, 138.8, 145.4 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 240 (90) [M$^+$], 170 (100). $C_{16}H_{20}N_2$ (240.3): calcd. C 79.96, H 8.39, N 11.66; found C 80.01, H 8.40, N 11.57.

2-Butyl-1,2,3,4,5,6-hexahydro-5-(4-methylphenyl)pyrrolo[3,4-*c*]-pyrrole (32c): Dibromide **31** (0.69 g, 2 mmol) was treated with butylamine (0.20 mL, 2 mmol) and K_2CO_3 (0.55 g, 4 mmol) in CH_3CN (20 mL). Workup as above, followed by purification by column chromatography (EtOAc/Et_3N, 50:1), yielded **32c** (0.38 g, 75%) as a white solid. M.p. 159−161 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 3 H), 1.26−1.61 (m, 4 H), 2.26 (s, 3 H), 2.73 (t, *J* = 7.3 Hz, 2 H), 3.57 (s, 4 H), 4.02 (s, 4 H), 6.39−6.48 (m, 2 H), 7.01−7.10 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.0, 20.1, 20.4, 31.3, 51.2, 56.2, 110.7, 116.8, 124.4, 129.8, 138.9, 145.5 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 256 (52) [M$^+$], 253 (100). $C_{17}H_{24}N_2$ (256.4): calcd. C 79.64, H 9.44, N 10.93; found C 79.49, H 9.51, N 10.87.

Treatment of Dibromide 31 with 1,2-Dihydroxybenzene. Preparation of 2,3,4,11-tetrahydro-2-(4-methylphenyl)-1*H*-[1,6]benzodioxocino-[3,4-*c*]pyrrole (33): A solution of dibromide **31** (0.69 g, 2 mmol), 1,2-dihydroxybenzene (0.22 g, 2 mmol) and K_2CO_3 (0.55 g, 4 mmol) in acetone (20 mL) was stirred overnight under reflux. Water was added and the organic product was extracted with EtOAc (3 × 20 mL). The organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The resulting product was purified by column chromatography (hexane/EtOAc, 15:1) to afford **33** (0.45 g, 77%) as a white solid. M.p. 151−153 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 4.08 (s, 4 H), 4.98 (s, 4 H), 6.35−6.44 (m, 2 H), 6.99−7.02 (m, 4 H), 7.03−7.11 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.2, 56.4, 68.4, 110.8, 122.7, 123.9, 124.9, 129.7, 133.2, 144.5, 147.8 ppm. LRMS (70 eV, EI): *m*/*z* (%) = 293 (96) [M$^+$], 184 (100). $C_{19}H_{19}NO_2$ (293.4): calcd. C 77.79, H 6.53, N 4.77; found C 77.90, H 6.54, N 4.72.

Preparation of 2,5-dihydro-1-(4-methylphenyl)-3,4-bis(phenylthiomethyl)-1*H*-pyrrole (34). Thiophenol (0.41 mL, 4 mmol) was added to aqueous sodium hydroxide (0.7 M, 0.16 g in 5.7 mL H_2O, 4 mmol). Dibromide **31** (0.69 g, 2 mmol), dissolved in 15 mL of THF, was added to the resulting solution. The mixture was stirred for 48 h at room temperature. Water was added and the organic product was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The resulting residue was purified by column chromatography (hexane/EtOAc, 20:1), yielding **34** (0.52 g, 65%) as a white solid. M.p. 107−109 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.25 (s, 3 H), 3.29 (s, 4 H), 4.12 (s, 4 H), 6.37−6.45 (m, 2 H), 7.00−7.09 (m, 2 H), 7.11−7.39 (m, 10 H) ppm. ^{13}C NMR (50.5 MHz, $CDCl_3$): δ = 20.2, 30.8, 56.8, 111.0, 124.7, 127.1, 128.8, 129.7, 131.3, 131.5, 135.1, 144.7. $C_{25}H_{25}NS_2$ (403.6): calcd. C 74.40, H 6.24, N 3.47; found C 74.56, H 6.31, N 3.52.

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