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Regioselective Reduction of 2,4-Diacylpyrroles and the Synthesis of a 2,4-Divinylpyrrole

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Reduction of 2,4-diacylpyrroles followed by dehydration to prepare the divinylpyrroles has been studied. The *N*-phenylsulfonyl group exhibited directing ability at the 4-position during the reduction of 2,4-diacylpyrrole and complete regioselectivity was achieved for formations of the 2- and 4-carbinols; several new derivatives, including 2,4-divinylpyrrole, have been prepared.

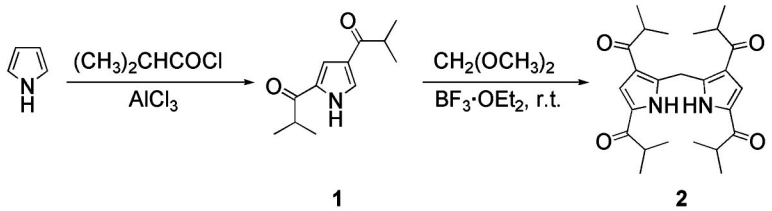
Introduction

C-Vinylpyrroles, such as 2- and 3-vinylpyrroles, are extensively present in natural products such as porphyrins, vitamin B_{12}, chlorophylls and hemoglobin; they are also important building blocks for a variety of compounds.[1] Compared to those of functionalized *C*-vinylpyrroles, where the vinyl substituents are conjugated with aryl, ester and amide groups, the synthesis of unfunctionalized *C*-vinylpyrroles is more challenging due to the considerable reactivity of the unfunctionalized vinyl groups.[2] In addition to Wittig reactions of formyl- or acyl-pyrroles with alkylidenephosphoranes, another effective method to prepare unfunctionalized 2- and 3-vinylpyrroles is reduction of the corresponding acylpyrroles followed by dehydration.[3–8] However, while several pyrroles of unfunctionalized 2,5-divinyl substituents have been prepared by Wittig reactions,[9] there are no reports of the reduction of diacylpyrroles as precursors of *C*-divinylpyrroles. Also, due to the difference in electron densities at the α- and β-positions of pyrrole, the reduction rates of α- and β-acyl substituents should be different, and will presumably give rise to varying regioselectivity. Herein, we have explored the reductions of 2,4-diacylpyrroles to prepare 2,4-divinylpyrrole.

Results and Discussion

According to the literature,[10] 2,4-diisobutyryl)-1*H*-pyrrole (**1**) is easily prepared by a one-pot acylation of pyrrole with isobutyryl chloride in the presence of aluminum chloride (Scheme 1). Using boron boron trifluoride–diethyl ether, diacylpyrrole **1** was treated with dimethoxymethane to produce bis(2,4-diisobutyryl)-1*H*-pyrrol-5-yl) methane (**2**) in moderate yield. Interestingly, this reaction did not proceed with the use of trifluoroacetic acid, although trifluoroacetic acid was reported to catalyze the reactions of 2-alkoxycarbonyl-4-benzoyl)-1*H*-pyrroles with dimethoxymethane to provide the corresponding dipyrromethanes in 25–30% yields.[11]

The reduction of 2- and 3-acylpyrroles is generally carried out using sodium borohydride and 2-propanol or lithium aluminum hydride and ether, but the yields of the resulting carbinols are always low due to over reduction to give the corresponding alkylpyrroles.[3–5,7] We have found that using methanol as solvent for the reduction of diacylpyrrole **1**, and the fractional addition of sodium borohydride at room temperature, produced a single product over



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Scheme 1.

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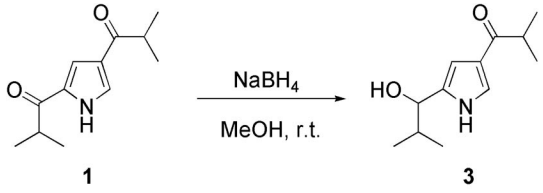
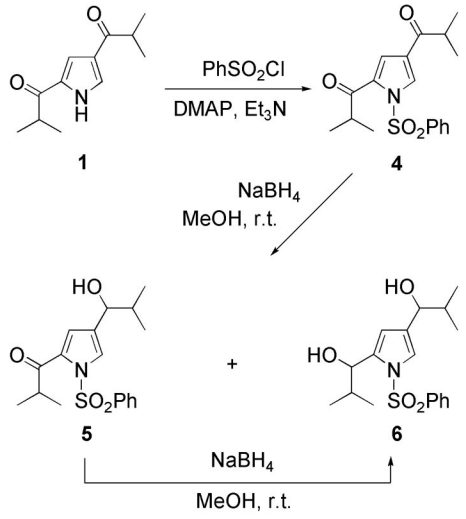
a period of several hours. After work-up and chromatography on silica gel, 2-(1-hydroxyisobutyl)-4-isobutyryl-1*H*-pyrrole (**3**) was obtained in 98% yield (Scheme 2). Carbinol **3** was identified by ^{1}H NMR and H-H NOSY, in which a doublet signal for CHC*H*(OH) appears at δ = 4.49 ppm with integration for a single proton and has interactions with only a single aromatic proton. Although 2,4-dibenzoylpyrrole can be reduced to 2,4-bis(1-hydroxy-benzyl)pyrrole by lithium aluminum hydride,[12] attempts to further reduce the 4-acyl substituent of **3** failed even when a large excess of sodium borohydride or lithium aluminum hydride was used. A similar observation has been reported[7] for the reduction of 3-acetylpyrrole by sodium borohydride, which was unsuccessful even in refluxing dioxane and 2-propanol. On the other hand, reduction of tetraacyldipyrromethane **2**, by sodium borohydride, showed no regioselectivity. A mixture of products identified by mass spectroscopy, as the mono-, di-, tri- and tetra-carbinols were observed but proved to be inseparable by chromatography.

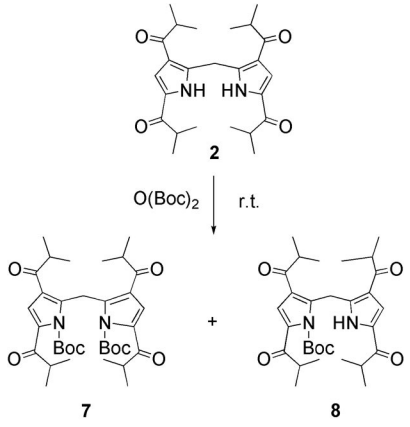


Scheme 2.

It is well known that the *N*-phenylsulfonyl group has a dramatic influence on electrophilic reactions of pyrrole by "sequestering" the nitrogen lone pair resulting in reactions at the β (3)-position for acylation[10,13] and sulfonation.[14] In order to further investigate the reduction of 2,4-diacylpyrroles, diacylpyrrole **1** was treated with phenylsulfonyl chloride in the presence of a catalytic amount of 4-(dimethylamino)pyridine,[15] and 2,4-diisobutyryl-1-(phenylsulfonyl)pyrrole (**4**) was obtained in quantitative yield. Dramatically, the *N*-phenylsulfonyl group preferentially displays directing ability to the 4-position in the reduction of 2,4-diacylpyrrole **4**. When sodium borohydride was added to a solution of diacylpyrrole **4** in methanol at room temperature, 4-(1-hydroxyisobutyl)-2-isobutyryl-1-(phenylsulfonyl)-pyrrole (**5**) was obtained as the major product (Scheme 3). In the ^{1}H NMR and H-H NOSY spectra of carbinol **5**, a doublet signal for CHC*H*(OH) appears at δ = 4.43 ppm with integration for one proton and shows interactions with two aromatic proton signals. The fully reduced compound 2,4-bis(1-hydroxyisobutyl)-1-(phenylsulfonyl)pyrrole (**6**) was also formed in low yield, resulting from the further reduction of **5** since 2-(1-hydroxyisobutyl)-4-isobutyryl-1-(phenylsulfonyl)pyrrole was not observed. Excess sodium borohydride does reduce both **4** and **5** to the dicarbinol **6**. Dicarbinol **6** was separated on a silica gel column as two pairs of racemic stereoisomers **6a** and **6b** in equal yields. They have the same ^{1}H NMR spectra showing two doublet signals for two CHC*H*(OH) protons at δ = 4.5 and 4.3 ppm. Surprisingly, tetraacyldipyrromethane **2** did not react with phenylsulfonyl chloride. When di-*tert*-butyl dicarbonate was used in place of phenylsulfonyl chloride, both bis(1-*tert*-butoxycarbonyl-2,4-diisobutyryl)-1*H*-pyrrol-5-yl)methane (**7**) and [1-(*tert*-butoxycarbonyl)-2,4-diisobutyryl)-1*H*-pyrrol-5-yl](2,4-diisobutyryl)-1*H*-pyrrol-5-yl)methane (**8**) were formed with a ratio of 1:1.2 (Scheme 4). Unfortunately, tetraacyldipyrromethane **7** was deprotected under sodium borohydride reduction condition and provided similar result as in the reduction of **2**.

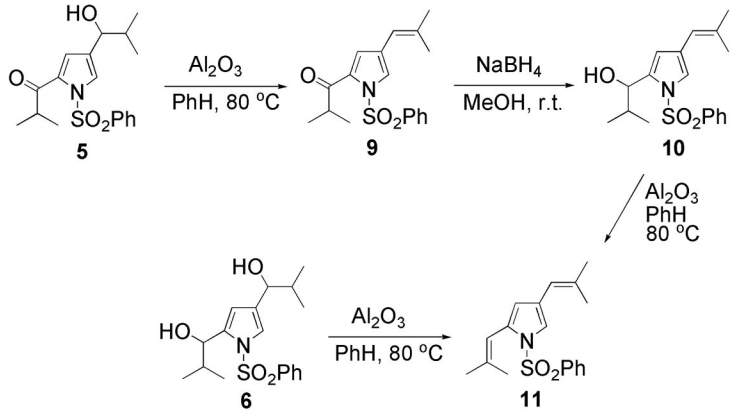


Scheme 3.



Scheme 4.

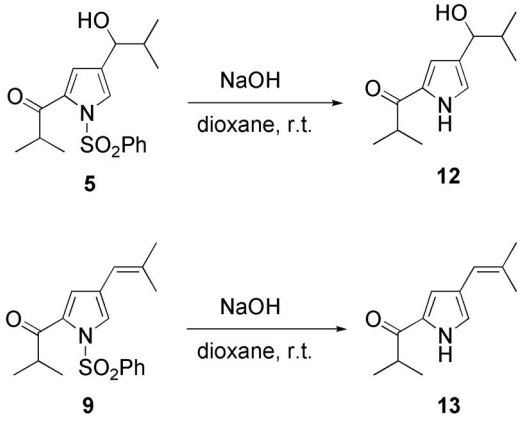
Dehydrations of carbinols at both the 2- and 3-positions are generally carried out in the presence of catalytic amounts of *p*-toluenesulfonic acid[6,16] or at high temperatures.[3,7] Since neither of these conditions are suitable for the carbinols described here we choose to use basic conditions[4] for all dehydrations. Upon refluxing the mixture of carbinol **5** and basic aluminum oxide in benzene with a Dean–Stark trap, **5** was cleanly converted to 4-isobutenyl-2-isobutyryl-1-(phenylsulfonyl)pyrrole (**9**) (Scheme 5). Further reduction of acylpyrrole **9**, with sodium borohydride, gave 2-(1-hydroxyisobutyl)-4-isobutenyl-1-(phenylsulfonyl)-pyrrole (**10**). Dehydration of both **6** and **10** with basic aluminum oxide in refluxing benzene provided 2,4-diisobutenyl-1-(phenylsulfonyl)pyrrole (**11**). In the ^{1}H NMR spec-



Scheme 5.

trum of divinylpyrrole **11**, the doublet signals for CHC*H*(OH) disappear and two singlet signals for two *H*C=CMe$_2$ protons appear at δ = 6.05 and 5.94 ppm.

Hydrolysis of the *N*-(phenylsulfonyl)-1*H*-pyrroles readily gave the corresponding *N*-free pyrroles using previously reported[10] basic conditions. Stirred with 6 N sodium hydroxide, at room temperature, carbinol **5** was converted into 4-(1-hydroxyisobutyl)-2-isobutyryl-pyrrole (**12**) (Scheme 6). Carbinols **3** and **12**, as constitutional isomers, have similar characteristics in their ^{1}H NMR spectra and can be easily identified by H-H NOSY. The formations of carbinols **3** and **12** provide two paths to the mono-reduction of 2,4-diacylpyrroles with complete regioselectivity. Similarly, vinylpyrrole **9** was hydrolyzed to give 4-isobutenyl-2-isobutyryl-pyrrole (**13**). Regrettably, attempts to hydrolyze divinylpyrrole **11** and vinylpyrrole **10** failed as the solutions rapidly decomposed during work-up.



Scheme 6.

Conclusions

A series of reactions, starting from 2,4-diacylpyrroles, including reduction, dehydration, *N*-protection and *N*-deprotection, have been explored and 13 new stable derivatives are reported in this work. The *N*-phenylsulfonyl group, a 3-directing group for acylation and sulfonation of pyrrole, displayed directing ability to the 4-position for the mono-reduction of 2,4-diisobutyryl-1-(phenylsulfonyl)pyrrole; complete regioselectivity was achieved since a 2-carbinol was formed directly from the reduction of 2,4-diisobutyryl-pyrrole and a 4-carbinol from 2,4-diisobutyryl-1-(phenylsulfonyl)pyrrole; The 2,4-diisobutenyl-1-(phenylsulfonyl)-pyrrole reported here is the first example of a *C*-divinylpyrrole synthesized by reduction of diacylpyrrole followed by dehydration. Further investigation on regioselective reductions of additional 2,4-diacylpyrroles and syntheses of *N*-free stable pyrroles bearing unfunctionalized 2,4-divinyl substituents are underway.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker AVANCE-400INV spectrometer; the chemical shifts (δ, ppm) are quoted relative to tetramethylsilane (TMS). Low and high-resolution EI mass spectra were measured with a Kratos MS50 spectrometer. All reactions were performed under an argon atmosphere. Dichloromethane was pre-dried with calcium hydride and distilled prior to use. Methanol and anhydrous tetrahydrofuran were used as received. Column chromatography was performed using 230–400 mesh silica gel.

2,4-Diisobutyryl-1*H*-pyrrole (1): Under conditions similar to the literature,[10] to a mixture of pyrrole (5.90 mL, 0.084 mol) and anhydrous aluminum chloride (13.47 g, 0.101 mol) in dichloromethane (1000 mL) was added isobutyryl chloride (9.98 mL, 0.094 mol) dropwise at room temperature. The mixture was stirred for 30 min to form a clear solution and then another portion of isobutyryl chloride (9.98 mL, 0.094 mol) and anhydrous aluminum chloride (13.47 g, 0.101 mol) was added. Followed by stirring at room temperature for a further 30 min, the resulting solution was refluxed for 24 h. After cooling, ice and saturated aqueous sodium hydrogen carbonate were carefully added. The organic phase was separated and the aqueous phase was extracted with dichloromethane (3 × 300 mL). The combined organic phases were dried with anhydrous sodium sulfate and evaporated under reduced pressure. The residue was chromatographed on silica gel eluting with the mixture of ethyl acetate and hexane (1:1) to provide the desired product (11.02 g); yield 63%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.71 (br., 1 H, NH), 7.61–7.59 [q, *J* = 3.24, 1.38 Hz, 1 H, CCHN (pyrrole)], 7.33–7.32 [q, *J* = 2.41, 1.47 Hz, 1 H, CCHC (pyrrole)], 3.35–

3.26 (m, 1 H, $CHMe_2$), 3.26–3.16 (m, 1 H, $CHMe_2$), 1.22 (d, J = 6.85 Hz, 6 H, 2 CH_3), 1.21 (d, J = 6.84 Hz, 6 H, 2 CH_3) ppm. EI MS: m/z (%) = 207 (12) $[M]^+$, 164 (100), 94 (35). HR-EI MS: m/z calcd. for $C_{12}H_{17}NO_2$: 207.1259; found 207.1262.

Bis(2,4-diisobutyryl-1*H*-pyrrol-5-yl)methane (2): To a solution of dimethoxymethane (1.61 mL, 0.013 mol) in dichloromethane (200 mL) was added boron trifluoride–diethyl ether (18.09 mL, 0.144 mol) at room temperature. The solution was stirred for 10 min and then diacylpyrrole **1** (5.00 g, 0.024 mol) was added and stirring continued for a further 48 h; the resulting mixture was poured onto ice-water. The work-up process was similar to that in the procedure for **1**. The evaporated residue was chromatographed on silica gel eluting with the mixture of ethyl acetate and hexane (1:5) to provide the desired product (1.126 g), followed by the unreacted diacylpyrrole **1** (3.70 g); yield 22%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 10.57 (br., 2 H, 2 NH), 7.11 [d, J = 2.50 Hz, 2 H, 2 CCHC (pyrrole)], 4.52 (s, 2 H, CCH_2C), 3.26–3.16 (m, 4 H, 4 $CHMe_2$), 1.18 (s, 6 H, 2 CH_3), 1.16 (s, 12 H, 4 CH_3), 1.14 (s, 6 H, 2 CH_3) ppm. EI MS: m/z (%) = 426 (64) $[M]^+$, 356 (54), 313 (100), 227 (40). HR-EI MS: m/z calcd. for $C_{25}H_{34}N_2O_4$: 426.2519; found 426.2522.

1*H*-2-(1-Hydroxyisobutyl)-4-isobutyryl)-1*H*-pyrrole (3): To a solution of diacylpyrrole **1** (3.31 g, 0.016 mol) in methanol (100 mL) was added sodium borohydride (1.21 g, 0.032 mol) in small portions over 3 h at room temperature. The reaction was monitored by TLC with a developing solution of ethyl acetate and hexane (1:1). After diacylpyrrole **1** disappeared, the reaction mixture was evaporated to dryness and treated with 100 mL of water. The work-up process was similar to that in the procedure for **1**. The evaporated residue was chromatographed on silica gel eluting with a mixture of ethyl acetate and hexane (1:1) to provide the desired product (3.30 g); yield 98%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.76 (br., 1 H, NH), 7.36 [s, 1 H, CCHN (pyrrole)], 6.44 [s, 1 H, CCHC (pyrrole)], 4.49 (d, J = 6.05 Hz, 1 H, C*H*OH), 3.23–3.14 (m, 1 H, CHC=O), 2.04–1.95 (m, 1 H, CHC*H*Me_2), 1.63 (br., 1 H, OH), 1.18 (d, J = 6.81 Hz, 6 H, 2 CH_3), 0.98 (d, J = 6.70 Hz, 3 H, CH_3), 0.89 (d, J = 6.78 Hz, 3 H, CH_3) ppm. EI MS: m/z (%) = 209 (54) $[M]^+$, 166 (100). HR-EI MS: m/z calcd. for $C_{12}H_{19}NO_2$: 209.1416; found 209.1419.

2,4-Diisobutyry-1-(phenylsulfonyl)-1*H*-pyrrole (4): To a solution of diacylpyrrole **1** (4.00 g, 0.019 mol) in dichloromethane (80 mL) were added triethylamine (6.00 mL), 4-(dimethylamino)pyridine (0.240 g, 0.002 mol) and phenylsulfonyl chloride (2.68 mL, 0.021 mol). The mixture was stirred overnight and monitored by TLC with a developing solution of ethyl acetate and hexane (1:2). After **1** disappeared, the reaction mixture was evaporated to dryness under reduced pressure and the residue was chromatographed on silica gel eluting with the mixture of ethyl acetate and hexane (1:2) to provide the desired product (6.60 g); yield 99%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.32 [d, J = 1.77 Hz, 1 H, CCHN (pyrrole)], 8.05–8.02 [q, J = 7.36, 1.48 Hz, 2 H, 2 *o*-HC (phenyl)], 7.64 [d, J = 7.34 Hz, 1 H, *p*-HC (phenyl)], 7.56 [t, J = 7.53 Hz, 2 H, 2 *m*-HC (phenyl)], 7.38 [d, J = 1.76 Hz, 1 H, CCHC (pyrrole)], 3.29–3.13 (m, 2 H, 2 $CHMe_2$), 1.24 (d, J = 6.84 Hz, 6 H, 2 CH_3), 1.09 (d, J = 6.86 Hz, 6 H, 2 CH_3) ppm. EI MS: m/z (%) = 347 (44) $[M]^+$, 304 (100), 141 (28). HR-EI MS: m/z calcd. for $C_{18}H_{21}NO_4S$: 347.1191; found 347.1189.

4-(1-Hydroxyisobutyl)-2-isobutyryl-1-(phenylsulfonyl)-1*H*-pyrrole (5): Prepared using the same procedure as for **3**, using diacylpyrrole **4** (0.347 g, 0.001 mol), sodium borohydride (0.151 g, 0.004 mol) and methanol (20 mL); yield 63% (0.220 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.00–7.97 [q, J = 7.20, 1.28 Hz, 2 H, 2 *o*-HC (phenyl)], 7.70 [d, J = 1.77 Hz, 1 H, CCHN (pyrrole)], 7.59 [d, J = 7.09 Hz, 1 H, *p*-HC (phenyl)], 7.52 [t, J = 7.39 Hz, 2 H, 2 *m*-HC (phenyl)], 6.98 [d, J = 1.76 Hz, 1 H, CCHC (pyrrole)], 4.43 (d, J = 6.19 Hz, 1 H, C*H*OH), 3.18–3.09 (m, 1 H, CHC=O), 1.98–1.89 (m, 1 H, CHC*H*Me_2), 1.67 (br., 1 H, OH), 1.08 (d, J = 6.84 Hz, 3 H, CH_3), 1.06 (d, J = 6.85 Hz, 3 H, CH_3), 0.99 (d, J = 6.71 Hz, 3 H, CH_3), 0.90 (d, J = 6.78 Hz, 3 H, CH_3) ppm. EI MS: m/z (%) = 349 (18) $[M]^+$, 306 (100), 141 (16). HR-EI MS: m/z calcd. for $C_{18}H_{23}NO_4S$: 349.1348; found 349.1342.

2,4-Bis(1-hydroxyisobutyl)-1-(phenylsulfonyl)-1*H*-pyrrole (6): 6a and **6b** were obtained in 28% yield (0.098 g) during the procedure to prepare carbinol **5** or prepared in 79% yield, using the same procedure and a 1:8 molar ratio of diacylpyrrole **4** and sodium borohydride.

6a: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.77 [d, J = 7.32 Hz, 2 H, 2 *o*-HC (phenyl)], 7.59 [t, J = 4.81 Hz, 1 H, *p*-HC (phenyl)], 7.49 [t, J = 7.54 Hz, 2 H, 2 *m*-HC (phenyl)], 7.19 [d, J = 1.12 Hz, 1 H, CCHN (pyrrole)], 6.24 [d, J = 1.62 Hz, 1 H, CCHC (pyrrole)], 4.51 (d, J = 8.09 Hz, 1 H, C*H*CHMe_2), 4.31 (d, J = 6.25 Hz, 1 H, C*H*CHMe_2), 2.39 (br., 1 H, OH), 2.09–1.99 (m, 1 H, CHC*H*Me_2), 1.90–1.81 (m, 1 H, CHC*H*Me_2), 1.79 (br., 1 H, OH), 0.99 (d, J = 6.59 Hz, 3 H, CH_3), 0.91 (d, J = 6.70 Hz, 3 H, CH_3), 0.80 (d, J = 6.78 Hz, 3 H, CH_3), 0.67 (d, J = 6.70 Hz, 3 H, CH_3) ppm. EI MS: m/z (%) = 351 (6) $[M]^+$, 308 (100), 141 (8). HR-EI MS: m/z calcd. for $C_{18}H_{25}NO_4S$: 351.1504; found 351.1507.

6b: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.77 [d, J = 7.19 Hz, 2 H, 2 *o*-HC (phenyl)], 7.59 [t, J = 6.81 Hz, 1 H, *p*-HC (phenyl)], 7.48 [t, J = 7.54 Hz, 2 H, 2 *m*-HC (phenyl)], 7.18 [d, J = 1.31 Hz, 1 H, CCHN (pyrrole)], 6.25 [d, J = 1.66 Hz, 1 H, CCHC(pyrrole)], 4.52 (d, J = 8.07 Hz, 1 H, C*H*CHMe_2), 4.31 (d, J = 6.22 Hz, 1 H, C*H*CHMe_2), 2.20 (br., 1 H, OH), 2.09–1.98 (m, 1 H, CHC*H*Me_2), 1.92–1.81 (m, 1 H, CHC*H*Me_2), 1.80 (br., 1 H, OH), 0.99 (d, J = 6.59 Hz, 3 H, CH_3), 0.90 (d, J = 6.71 Hz, 3 H, CH_3), 0.80 (d, J = 6.79 Hz, 3 H, CH_3), 0.67 (d, J = 6.70 Hz, 3 H, CH_3) ppm.

Bis(1-*tert*-butoxycarbonyl-2,4-diisobutyryl-1*H*-pyrrol-5-yl)methane (7): To a solution of tetraacyldipyrromethane **2** (0.253 g, 0.593 mmol) in dichloromethane (20 mL) were added di-*tert*-butyl dicarbonate (0.284 g, 1.305 mmol) and 4-(dimethylamino)pyridine (0.014 g, 0.118 mmol). The mixture was stirred overnight and then evaporated under reduced pressure. The residue was chromatographed on silica gel eluting with a mixture of ethyl acetate and hexane (1:4). Unreacted tetraacyldipyrromethane **2** was recovered first and then product **7** was obtained in 36% yield (0.134 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.01 [s, 2 H, CCHC (pyrrole)], 5.17 (s, 2 H, CCH_2C), 3.32–3.04 (m, 4 H, 4 $CHMe_2$), 1.44 [s, 18 H, 2 $(CH_3)_3C$], 1.15 [d, J = 6.90 Hz, 12 H, 2 $(CH_3)_2CH$], 1.08 [d, J = 6.71 Hz, 12 H, 2 $(CH_3)_2CH$] ppm. ESI MS: m/z (%) = 649 (100) $[M]^+$. HR-ESI MS: m/z calcd. for $C_{35}H_{50}N_2O_8 + Na^+$: 649.3465; found 649.3455.

(1-*tert*-Butoxycarbonyl-2,4-diisobutyryl-1*H*-pyrrol-5-yl)(2,4-diisobutyryl-1*H*-pyrrol-5-yl)methane (8): Obtained in 43% yield (0.132 g) during the procedure to prepare tetraacyldipyrromethane **7**. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.63 (br., 1 H, NH), 7.18 [s, 1 H, CCHC (pyrrole)], 7.16 [s, 1 H, CCHC (pyrrole)], 4.77 (s, 2 H, CCH_2C), 3.32–3.06 (m, 4 H, 4 $CHMe_2$), 1.46 [s, 9 H, $(CH_3)_3C$], 1.23–1.15 [m, 24 H, 4 $(CH_3)_2CH$] ppm. EI MS: m/z (%) = 526 (2) $[M]^+$, 426 (58), 383 (23), 356 (53), 313 (100). HR-EI MS: m/z calcd. for $C_{30}H_{42}N_2O_6$: 526.3043; found 526.3064.

4-Isobutenyl-2-isobutyryl-1-(phenylsulfonyl)-1*H*-pyrrole (9): A mixture of carbinol **5** (1.53 g, 4.384 mmol) and basic aluminum oxide (4.40 g) in benzene (100 mL) was refluxed for 2 h using a Dean–

Stark trap protected with anhydrous calcium chloride. After cooling, the mixture was evaporated to dryness under reduced pressure and the aluminum oxide residue was poured onto the top of a silica gel column. Elution with a mixture of ethyl acetate and hexane (1:4) gave the desired product in 82% yield (1.19 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.99 [d, J = 7.16 Hz, 2 H, 2 *o*-HC (phenyl)], 7.66 [s, 1 H, CCHN (pyrrole)], 7.58 [d, J = 7.11 Hz, 1 H, *p*-HC (phenyl)], 7.52 [t, J = 7.37 Hz, 2 H, 2 *m*-HC (phenyl)], 6.95 [d, J = 1.55 Hz, 1 H, CCHC (pyrrole)], 5.98 (s, 1 H, CH=CMe_2), 3.18–3.09 (m, 1 H, $CHMe_2$), 1.90 [s, 6 H, $(CH_3)_2C$=C], 1.08 [d, J = 6.86 Hz, 6 H, $(CH_3)_2CH$] ppm. EI MS: *m*/*z* (%) = 331 (55) $[M]^+$, 288 (100). HR-EI MS: *m*/*z* calcd. for $C_{18}H_{21}NO_3S$: 331.1242; found 331.1246.

2-(1-Hydroxyisobutyl)-4-isobutenyl-1-(phenylsulfonyl)-1*H*-pyrrole (10): Prepared using the same procedure as for **3**, using acylpyrrole **9** (1.19 g, 3.595 mmol), sodium borohydride (0.544 g, 0.014 mol) and methanol (50 mL); yield 73% (0.873 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.75 [d, J = 7.22 Hz, 2 H, 2 *o*-HC (phenyl)], 7.50 [d, J = 7.10 Hz, 1 H, *p*-HC (phenyl)], 7.41 [t, J = 7.35 Hz, 2 H, 2 *m*-HC (phenyl)], 7.14 [s, 1 H, CCHN (pyrrole)], 6.26 [s, 1 H, CCHC (pyrrole)], 5.90 (s, 1 H, CH=CMe_2), 4.55 (d, J = 7.79 Hz, 1 H, C*H*OH), 2.60 (br., 1 H, OH), 2.06–1.96 (m, 1 H, $CHMe_2$), 1.81 [s, 6 H, $(CH_3)_2C$=C], 0.97 (d, J = 6.50 Hz, 3 H, CH_3CH), 0.67 (d, J = 6.60 Hz, 3 H, CH_3CH) ppm. EI MS: *m*/*z* (%) = 333 (23) $[M]^+$, 290 (100), 148 (40). HR-EI MS: *m*/*z* calcd. for $C_{18}H_{23}NO_3S$: 333.1399; found 333.1389.

2,4-Diisobutenyl-1-(phenylsulfonyl)-1*H*-pyrrole (11): Prepared using the same procedure as for **9**, using dicarbinol **6** (1.30 g, 3.705 mmol), basic aluminum oxide (3.70 g) and benzene (100 mL); yield 67% (0.781 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.73 [d, J = 7.79 Hz, 2 H, 2 *o*-HC (phenyl)], 7.54 [t, J = 7.37 Hz, 1 H, *p*-HC (phenyl)], 7.43 [t, J = 7.75 Hz, 2 H, 2 *m*-HC (phenyl)], 7.18 [s, 1 H, CCHN (pyrrole)], 6.33 [s, 1 H, CCHC (pyrrole)], 6.05 (s, 1 H, HC=CMe_2), 5.94 (s, 1 H, HC=CMe_2), 1.86 [s, 6 H, $(CH_3)_2C$], 1.85 (s, 3 H, CH_3C), 1.52 (s, 3 H, CH_3C) ppm. EI MS: *m*/*z* (%) = 315 (100) $[M]^+$, 174 (69). HR-EI MS: *m*/z calcd. for $C_{18}H_{21}NO_2S$: 315.1293; found 315.1301.

1*H*-4-(1-Hydroxyisobutyl)-2-isobutyryl)-1*H*-pyrrole (12): Using similar conditions to those reported in the literature,[10] to a solution of carbinol **5** (20.1 mg, 0.057 mmol) in dioxane (4 mL) was added 6 N sodium hydroxide (1 mL). The resulting mixture was stirred for 30 h at room temperature and then poured into water (20 mL). The aqueous solution was extracted with chloroform (3 × 20 mL). The combined organic phase was dried with anhydrous sodium sulfate and evaporated under reduced pressure. The residue was chromatographed on silica gel eluting with a mixture of ethyl acetate and hexane (1:3) to provide the desired product (11.3 mg); yield 94%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.61 (br., 1 H, NH), 6.94 [t, J = 1.36 Hz, 1 H, CCHN (pyrrole)], 6.86 [s, 1 H, CCHC (pyrrole)], 4.38 (d, J = 6.57 Hz, 1 H, C*H*OH), 3.30–3.21 (m, 1 H, CHC=O), 2.00–1.91 (m, 1 H, CHC*H*Me_2), 1.70 (br., 1 H, OH), 1.18 [d, J = 6.85 Hz, 6 H, $(CH_3)_2C$], 0.98 (d, J = 6.53 Hz, 3 H, CH_3CH), 0.85 (d, J = 6.76 Hz, 3 H, CH_3CH) ppm. EI MS: *m*/*z* (%) = 209 (19) $[M]^+$, 166 (100). HR-EI MS: *m*/*z* calcd. for $C_{12}H_{19}NO_2$: 209.1416; found 209.1416.

1*H*-4-Isobutenyl-2-isobutyryl)-1*H*-pyrrole (13): Prepared using the same procedure as for **12**, using 4-vinylpyrrole **9** (30.0 mg, 0.090 mmol), dioxane (6 mL) and 6 N sodium hydroxide (1.5 mL); yield 89% (15.3 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.27 (s, 1 H, NH), 6.97 [s, 1 H, CCHN (pyrrole)], 6.87 [s, 1 H, CCHC (pyrrole)], 6.07 (s, 1 H, CH=CMe_2), 3.31–3.24 (m, 1 H, CHC=O), 1.90 [d, J = 6.10 Hz, 6 H, $(CH_3)_2C$=C], 1.22 [d, J = 6.86 Hz, 6 H, $(CH_3)_2CH$] ppm. EI MS: *m*/*z* (%) = 191 (49) $[M]^+$, 147 (100). HR-EI MS: *m*/*z* calcd. for $C_{12}H_{17}NO$: 191.1310; found 191.1305.

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