Heteroaromatic organolithium addition to a congested ketone: conformational isomerism in (*N*-alkylpyrrol-2-yl)di(1-adamantyl)-methanols

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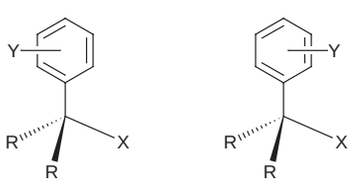
Tertiary alcohols have been prepared by reaction of 2-lithio-*N*-methylpyrrole and 2-lithio-*N*-ethylpyrrole with di(1-adamantyl)ketone. The conformations of the *N*-methyl derivatives have been determined by single crystal X-ray diffraction studies. The *N*-alkylpyrrol-2-yl derivatives are synthesized as the *anti* isomers which upon heating undergo rotation about the sp^2–sp^3 C–C bond to give the more stable, *syn* isomers with activation energies in benzene of 31.0 (Me) and 30.7 (Et) kcal mol^{-1}. Semi-empirical (AM1) and *ab initio* (3-21G*//AM1) calculations indicate that the energy difference between the two rotamers is of the order of 5 kcal mol^{-1}. Ionic hydrogenation of *anti*-(*N*-methylpyrrol-2-yl)diadamantylmethanol in dichloromethane–TFA–triethylsilane gives the *anti* isomer of (*N*-methylpyrrol-2-yl)diadamantyl-methane, accompanied by substantial amounts of diadamantylketone. The barrier to *anti*→*syn* rotation in the deoxygenation product is about 4 kcal mol^{-1} higher than for the corresponding alcohol.

The phenomenon of conformational isomerism (atropisomerism) involving rotation, or lack thereof, about sp^2–sp^3 carbon–carbon bonds has been to a large extent concerned with species where sp^2 carbon is part of a benzenoid aromatic system.[1] This is true of 9-arylfluorenes[1] and aryldi(*tert*-alkyl)methyl derivatives, **1**, where Y is a *meta* or *ortho* substituent.[2–7] In this latter case the rotation barrier can be as high as 45 kcal mol^{-1} † when R is 1-adamantyl, Y is *o*-methyl and X is OH.[4]



1A **1S**

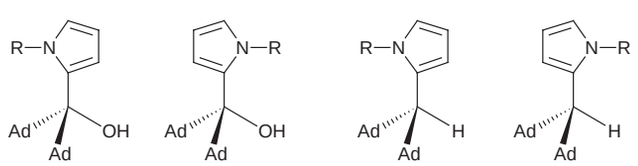
Previous work has shown that 1-adamantyl groups are much more effective in blocking rotation than *tert*-butyls,[2] raising the barrier for *anti*-*o*-tolyldi(alkyl)methanol from 29 to 39 kcal mol^{-1}. In a search for new systems showing atropisomerism we therefore chose to examine the reactions of a number of heteroaromatic organolithium derivatives with di(1-adamantyl)-ketone. Work on *N*-alkylpyrrol-2-yl derivatives will be reported here.

Results and discussion

Alcohol synthesis and structure

Organolithium derivatives of many heteroaromatic systems, such as pyridine,[8] furan,[9] thiophene,[9,10] *N*-alkylpyrroles,[9] *etc*. can be prepared by direct lithiation of the parent compound or exchange with a bromo derivative by *n*-butyllithium. Direct lithiation gives almost exclusively the 2-lithio compounds, the 3-lithio compounds being generally more difficult to prepare, even from the 3-bromo derivative.[11] In this work 2-lithio compounds were prepared directly from the parent compounds which were taken in excess, in order to reduce dilithiation, and a large excess of organolithium reagent with respect to ketone was used. *tert*-Butyllithium was used in preference to *n*-butyllithium–TMEDA[9] as the latter gave only an *n*-butyl derivative.

2-Lithio-*N*-methylpyrrole and 2-lithio-*N*-ethylpyrrole react with the very congested diadamantylketone giving good yields of the corresponding alcohols, **2** and **3**, respectively. (Attempts to perform the same reaction with the *N*-isopropyl derivative were unsuccessful.) Inspection of the aromatic carbon or hydrogen NMR signals indicates that only one isomer is formed; upon heating, a more stable rotamer is obtained. The ^1H and ^{13}C NMR spectra of the new alcohols could be fully attributed on the basis of the proton–proton coupling constants, spectrum simulation by means of the gNMR program[12] and heteronuclear correlation. The isomers obtained initially are unstable in chloroform, probably due to traces of acid, and undergo partial decomposition to regenerate diadamantylketone; all NMR spectra were therefore recorded in benzene. The IR spectra of the rotamers reveal the same difference as was reported for *anti*- and *syn*-*o*-tolyldi(*tert*-butyl)methanols,[13] the less stable isomers showing two bands in the OH stretching region, the more stable only a single band. This strongly suggests that the first-formed isomer is *anti* (**2A** and **3A**) and that



2A: R = Me **3A:** R = Et **2S:** R = Me **3S:** R = Et **4A:** R = Me **4S:** R = Me

the stable isomer has the *syn* geometry (**2S** and **3S**) in which one conformation with respect to rotation about the C–O bond is excluded due to the proximity of the methyl group.

Good crystals of both isomers of the *N*-methylpyrrol-2-yl derivative, **2**, were obtained and their structures determined by single crystal X-ray crystallography (Figs. 1 and 2). This establishes unambiguously that the addition reaction gives the *anti* isomer, **2A**, which is thermally isomerized to the *syn* rotamer, **2S**.

† 1 cal = 4.184 J.

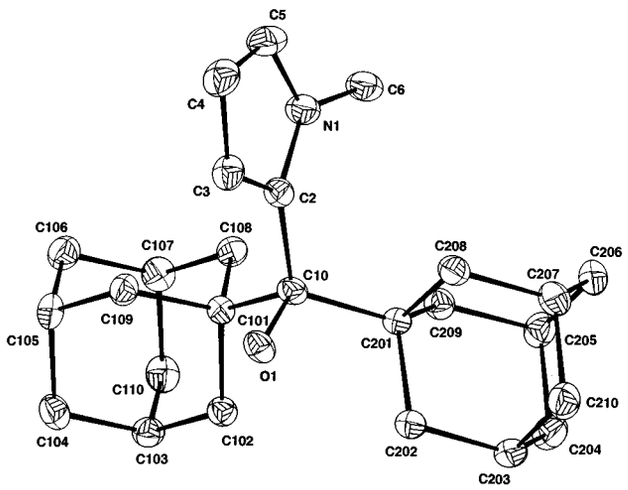


Fig. 1 CAMERON diagram of *anti*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)methanol, **2A**, showing 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

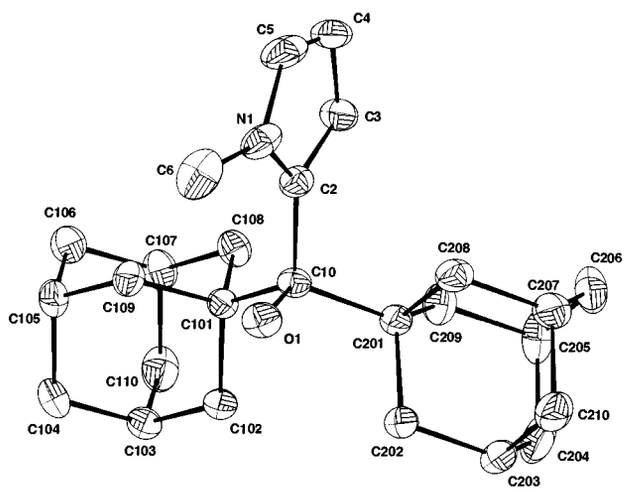


Fig. 2 CAMERON diagram of *syn*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)methanol, **2S**, showing 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

The main structural features of the two *N*-methylpyrrol-2-yl alcohols (Table 1) are very similar in general outline to results on the aromatic analogues.[5–7,14] Bonds to the C–OH carbon are uniformly long; the heteroaromatic ring roughly bisects the very large Ad–C–Ad angles; nevertheless, the two adamantyl groups are distinct as regards their orientation with respect to the sp^2–sp^3 bond; the heteroaromatic rings are slightly non-planar, the nitrogen atoms being 0.006 Å (*anti*) and 0.016 (*syn*) out of the plane defined by the carbon atoms. This non-planarity shows up also in the torsion angles of N1 and C3 with respect to, for example, the oxygen atom; these should be complementary but in fact there is a difference of 6.5° (*anti*) and 8.5° (*syn*) between the sum of the angles and 180°. The methyl group carbons, C6, are substantially more distant from the pyrrole carbon plane, being 0.146 Å (*anti*) and 0.207 Å (*syn*) out-of-plane. The pyrrole rings are also slightly deformed in the plane, but the internal angles do not depart greatly from the values found in less strained systems.[15] The bonds to nitrogen are slightly longer than usual; the very short C4–C5 bond (*ca*. 1.335 Å) is not exceptional. The pyrrole rings are very similar in the two isomers, the major difference being in the 'tilt' with respect to the C2–C10 bond, the angle to N1 (*anti*) or C3 (*syn*) opening so as to reduce interactions with the adamantyl groups. In both cases the N1–C6 bond is 'bent' so as to reduce strain, the angle subtended to C5 being substantially less than that to C2; a similar deviation is found in a much less strained 2-substituted *N*-methylpyrrole.[15d]

Table 1 Selected bond lengths, bond angles and torsion angles for *anti*- and *syn*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)methanols, **2A** and **2S**. Comparison of X-ray crystallographic data and AM1 calculations

	anti		*syn*	
	X-ray	AM1	X-ray	AM1
Bond lengths/Å				
N(1)–C(2)	1.391(4)	1.403	1.394(3)	1.404
N(1)–C(5)	1.377(4)	1.401	1.367(4)	1.393
N(1)–C(6)	1.458(4)	1.428	1.450(4)	1.429
C(2)–C(3)	1.375(5)	1.417	1.377(4)	1.413
C(3)–C(4)	1.401(5)	1.427	1.398(4)	1.429
C(4)–C(5)	1.337(5)	1.396	1.334(5)	1.400
C(10)–C(2)	1.554(4)	1.524	1.532(3)	1.518
C(10)–C(101)	1.595(5)	1.576	1.595(3)	1.577
C(10)–C(201)	1.619(4)	1.577	1.613(4)	1.578
Bond angles/°				
C(2)–N(1)–C(5)	108.6(3)	108.6	107.8(3)	109.0
C(2)–N(1)–C(6)	131.5(3)	131.1	131.4(3)	127.4
C(5)–N(1)–C(6)	119.4(3)	120.1	120.3(3)	123.7
N(1)–C(2)–C(3)	106.1(3)	107.1	106.4(2)	107.1
C(2)–C(3)–C(4)	108.6(3)	108.5	108.8(3)	108.1
C(3)–C(4)–C(5)	107.8(3)	106.7	106.6(3)	107.0
C(4)–C(5)–N(1)	108.9(3)	109.2	110.4(3)	108.8
N(1)–C(2)–C(10)	130.2(3)	132.2	124.4(2)	125.6
C(3)–C(2)–C(10)	123.2(3)	120.6	128.9(2)	127.2
C(2)–C(10)–C(101)	109.4(3)	109.3	109.3(2)	108.5
C(2)–C(10)–C(201)	114.9(3)	113.7	109.7(2)	109.6
C(101)–C(10)–C(201)	119.6(3)	120.3	119.7(2)	119.7
Torsion angles/°				
N(1)–C(2)–C(10)–O(1)	175.9(3)	172.0	−8.1(3)	−6.4
N(1)–C(2)–C(10)–C(101)	−74.9(4)	−79.8	107.1(3)	108.1
N(1)–C(2)–C(10)–C(201)	62.8(4)	57.8	−120.0(3)	−119.6
C(3)–C(2)–C(10)–O(1)	−12.6(4)	−11.5	165.4(3)	172.7
C(3)–C(2)–C(10)–C(101)	96.5(4)	96.7	−79.4(4)	−72.8
C(3)–C(2)–C(10)–C(201)	−125.7(3)	−125.7	53.5(4)	59.6
C(2)–C(10)–C(101)–C(102)	−171.8(3)	−175.6	−176.8(2)	174.5
C(2)–C(10)–C(101)–C(108)	64.8(4)	60.2	52.7(3)	50.6
C(2)–C(10)–C(101)–C(109)	−54.2(3)	−58.4	−64.9(3)	−67.3
C(2)–C(10)–C(201)–C(202)	146.3(3)	146.8	157.5(2)	153.8
C(2)–C(10)–C(201)–C(208)	30.7(4)	30.8	42.0(3)	37.6
C(2)–C(10)–C(201)–C(209)	−91.6(3)	−91.9	−80.2(3)	−82.9

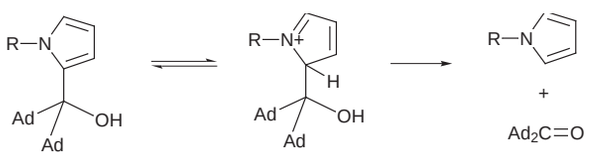
The crystallographically determined coordinates were taken as starting points for optimized AM1 calculations[16a] on the two rotamers, giving a (gas phase) energy difference of 6.3 kcal mol^{-1} in favour of the *syn* isomer. The crystallographic geometries are fairly well reproduced by the AM1 calculations. The bond distances in the pyrrole rings are, however, much more uniform and the long bonds to C10 substantially shorter than those found experimentally. On the other hand, bond and torsion angles are in good agreement with the experimental values. Non-optimized *ab initio* (3-21G* basis set) calculations[16b] based on the AM1 geometries gave a slightly smaller energy difference of 4.3 kcal mol^{-1}. The energy difference between the deoxygenated analogues (see below), according to AM1 calculations, is somewhat smaller (4.8 kcal mol^{-1}) than that for the alcohols, as has been found by molecular mechanics calculations (MM2) on the corresponding *o*-tolyl derivatives.[3]

The fact that the two rotamer alcohols differ in energy by about 5 kcal mol^{-1} and that the thermodynamically less stable isomer is formed by the reaction of the organolithium reagent with diadamantylketone is in all respects comparable to what is found in the addition of *o*-tolyllithium to hindered ketones.[2,3] The mechanism of this addition and a transition state model were discussed at length in a previous publication,[3] without it being clear just why one obtains the less stable rather than the more stable isomer. One possibility is that the transition state is early and that the steric course of the reaction is determined by the predominance of attractive interactions between the methyl and adamantyl groups.

Ionic hydrogenation

In previous work it has been shown that the carbocation generated by protonation–dehydration of a congested aryl-substituted tertiary alcohol by trifluoroacetic acid in dichloromethane can be reduced stereoselectively by hydrosilanes or sodium borohydride, approach of the hydride donor being determined by its steric requirements and those of substituents on the ring.[14]

The *N*-methylpyrrol-2-yl derivative, **2A**, behaves unexpectedly, giving a product consisting largely of diadamantylketone and a very minor amount of a deoxygenation product (Scheme 1). Clearly, carbocation formation is competing with nucleophilic substitution at the heterocyclic nucleus; protonation at the 2-position of the pyrrole ring is followed by loss of diadamantylketone, the protiodealkylation being driven by relief of steric strain.



Scheme 1

The NMR spectra of the deoxygenation product isolated showed it to consist of a single isomer, identified by NOE experiments as the *anti*, **4A**.‡ This behaviour is consistent with that of the *o*-tolyl analogue,[4,14] where the hydride donor approaches the carbocation from the side remote from the methyl group, unless there is also a bulky group in the 5-position. Qualitative experiments indicated that the rotation barrier was substantially higher than in the corresponding alcohol, about 30% conversion to the *syn* isomer occurring in 8 h at 150 °C.

Rotation barriers

The (*N*-alkylpyrrol-2-yl)diadamantylmethanols were obtained in the less stable, *anti* form, **2A** and **3A**, and were found to rotate smoothly to **2S** and **3S** at moderate temperatures. Kinetic study of this rotation in benzene in the 113–157 °C range gave activation energies of 31.0 (R = Me) and 30.7 (R = Et) kcal mol^{-1} at 135 °C, the activation entropies of about −5 cal mol^{-1} K^{-1} being consistent with previous values.[3,4] These activation energies lie between previous values for the *meta*-substituted phenyl[4] and *o*-tolyl[3] analogues, about 27.5 (at 100 °C) and 39 (at 200 °C) kcal mol^{-1}, respectively. This seems reasonable insofar as the replacement of a six-membered aromatic ring by a five-membered heteroaromatic ring will, on purely geometric grounds, somewhat withdraw the alkyl group from the proximity of the bulky adamantyl substituents. It would appear that the resulting modifications of the steric energy of the system are more pronounced in the rotation transition state than in the initial *anti* isomer. In alcohols of this type, increasing strain in the initial state always goes hand-in-hand with enhanced rotation barriers.[2,3,13]

The deoxygenation product, (*N*-methylpyrrol-2-yl)diadamantylmethane, **4A**, yields the *syn* isomer, **4S**, very slowly on heating at 150 °C. The rotation rate constants, measured in benzene between 150 and 195 °C lead to an activation energy of 34.9 kcal mol^{-1} (172 °C), *i.e.* almost 4 kcal mol^{-1} higher than for the corresponding alcohol, and a slightly more negative activation entropy (−8 compared to −5 cal mol^{-1} K^{-1}). These results are in qualitative agreement with results on the *o*-tolyl analogue,[5] where there is a difference of about 6 kcal mol^{-1} between the activation energies for rotation in the alcohol and the alkane. This was explained in terms of variations of the Ad–C–Ad bond angle in the ground and transition states for rotation in these two species.[5] For the corresponding *m*-tolyl derivatives, where the difference is negligible (0.5 kcal mol^{-1}), modelling the rotation by molecular mechanics (MMP2) gave an estimate (1.4 kcal mol^{-1}) in good agreement with what is found.[4]

‡ In the past[3–5,14] we have systematically used the same conformational descriptor, *anti* or *syn*, for an alcohol and the alkane obtained by removal of the oxygen atom, despite the fact that OH and H do not have the same priority with respect to carbon.[17] This practice, though incorrect, has the advantage that analogous structures bear the same descriptor, and we shall continue to employ it here.

Conclusions

In general, the 2-position of heteroaromatic systems is the easiest to functionalize, and the 2-lithio derivatives are readily accessible. This first study of *N*-alkylpyrrole derivatives shows that they are sufficiently nucleophilic to attack even a highly hindered carbonyl bond. The reaction proceeds stereochemically in the same manner as for *o*-tolyllithium, giving the less stable of the potentially rotameric tertiary alcohol pair. The barrier to rotation about the sp^2–sp^3 bond in the alcohol, though smaller, is of the same order of magnitude as for *o*-tolyldiadamantylmethanol. The energy difference between the *anti* and *syn* rotamers of (*N*-methylpyrrol-2-yl)diadamantylmethanol is very similar to that for the *o*-tolyl analogues. Ionic hydrogenation is stereoselective, giving again the less stable rotamer, which can be converted to the more stable one by a substantially slower rotation about the sp^2–sp^3 bond.

Experimental

General methods

NMR measurements were performed on a Bruker AS 200 FT instrument operating at 200 MHz (proton) or 50 MHz (carbon). Unless otherwise noted all measurements were made in hexadeuteriobenzene (reference values: $\delta_H = 7.16$ for ^{1}H, $\delta_C = 128.0$ for ^{13}C). Carbon and hydrogen shifts of the heterocyclic system are numbered: C2, C3, *etc*. Coupling constants J_{H-H} are given in Hz after the assignments. Generally, the proton signals were assigned on the basis of coupling constants[18] and spectrum simulation by the gNMR program (Cherwell Scientific).[12] The corresponding ^{13}C signals were identified by heteronuclear correlation experiments. NOE experiments were performed in chloroform on a Bruker AM-500 spectrometer at 500 MHz using the NOEMULT pulse sequence. IR spectra were measured in carbon tetrachloride on a Nicolet 60SX FIR spectrometer with 1 cm^{-1} resolution. Gas chromatography was performed on a 30 cm 10% SE30 on Chrompack column. Column chromatography was performed on silica gel 60 (Merck) in light petroleum (b. range 35–60 °C)–dichloromethane mixtures. Melting points were determined in capillary glass tubes on a Mettler FP5 instrument with a heating rate of 3 °C min^{-1}.

Synthesis of (*N*-methylpyrrol-2-yl)di(1-adamantyl)methanol, 2. *N*-Methylpyrrole (1 cm^3, 11.2 mmol) was stirred in sodium–dry ether (20 cm^3) under argon at 0 °C. A solution of *tert*-butyllithium in pentane (1.5 M, 2.5 cm^3, 3.7 mmol) was added dropwise in about 2 min and the cooling bath then removed. After stirring for 0.5–1 h at room temperature a solution of di(1-adamantyl)ketone (0.3 g, 1 mmol) in diethyl ether (30 cm^3) was added in about 5 min. After a further 1–1.5 h the reaction mixture was quenched and worked up as usual. The required alcohol (0.244–0.315 g, 64–83%), isolated by column chromatography and crystallized from hexane–diethyl ether, was identified as **2A** by single crystal X-ray crystallography. The ^{13}C and ^{1}H NMR spectra were determined in hexadeuteriobenzene, the material being unstable in chloroform: mp 198 °C; ν_{OH}/cm^{-1} 3603 and 3633; δ_C 29.7 (6 CH), 37.4 (6 CH_2), 39.5 (6 CH_2), 40.9 (CH_3), 45.1 (2 C_q), 85.4 (COH), 106.6 (C4), 113.3 (C3), 125.9 (C5) and 138.75 (C2); δ_H 1.61 (br s, Ad), 1.72 (OH), 1.93 (br m, Ad), 3.36 (CH_3), 6.30 (H4, *J* 2.7 and 3.7), 6.38 (H5, *J* 2.2 and

2.7) and 6.50 (H3, *J* 2.2 and 3.7) (Found: C, 82.6; H, 9.8; N, 3.6. $C_{26}H_{37}NO$ requires C, 82.27; H, 9.82; N, 3.69%).

A solution of the alcohol (110 mg) in benzene (2 cm^3) in a sealed tube was heated for 3 h at 150 °C to give an isomeric material, **2S** (98 mg, 89%), also identified by single crystal X-ray crystallography: mp 209 °C (hexane–diethyl ether); ν_{OH}/cm^{-1} 3632; δ_C 29.5 (6 CH), 37.35 (6 CH_2), 38.9 (6 CH_2), 40.0 (CH_3), 46.7 (2 C_q), 85.9 (COH), 105.6 (C4), 109.1 (C3), 123.1 (C5) and 131.9 (C2); δ_H 1.58 (br s, Ad), 1.6–2.1 (br m, Ad and OH), 3.63 (CH_3), 6.19 (H3, *J* 1.9 and 3.7), 6.27 (H4, *J* 2.5 and 3.7) and 6.37 (H5, *J* 1.9 and 2.5) (Found: C, 82.7; H, 9.7; N, 3.7. $C_{26}H_{37}NO$ requires C, 82.27; H, 9.82; N, 3.69%).

Synthesis of (*N*-ethylpyrrol-2-yl)di(1-adamantyl)methanol, 3. By the same procedure as for (*N*-methylpyrrol-2-yl)di(1-adamantyl)methanol, excess *N*-ethylpyrrole[19] was lithiated and added to diadamantylketone (0.3 g, 0.1 mmol) to give *anti*-(*N*-ethylpyrrol-2-yl)di(1-adamantyl)methanol, **3A** (0.217 g, 55%): mp 126 °C (hexane–diethyl ether); ν_{OH}/cm^{-1} 3605 and 3631; δ_C 16.9 (CH_3), 29.8 (6 CH), 37.4 (6 CH_2), 39.8 (6 CH_2), 45.3 (2 C_q), 45.4 (CH_2), 85.8 (COH), 107.5 (C4), 111.5 (C3), 121.6 (C5) and 139.1 (C2); δ_H 1.17 (CH_3, *J* 7.2), 1.62 (br s, Ad), 1.87 (OH), 1.93 (br m, Ad), 3.85 (CH_2, *J* 7.2), 6.33 (H4, *J* 2.8 and 3.7), 6.38 (H3, *J* 2.1 and 3.7) and 6.62 (H5, *J* 2.1 and 2.8) (Found: C, 82.4; H, 9.9; N, 3.6. $C_{27}H_{39}NO$ requires C, 82.39; H, 9.99; N, 3.56%).

Heating a solution of the alcohol (95 mg) in benzene (2 cm^3) for 4 h at 150 °C gave the *syn* isomer, **3S** (77 mg, 81%): mp 226 °C (hexane–diethyl ether); ν_{OH}/cm^{-1} 3630; δ_C 18.8 (CH_3), 29.6 (6 CH), 37.3 (6 CH_2), 38.9 (6 CH_2), 46.4 (CH_2), 46.7 (2 C_q), 86.2 (COH), 106.0 (C4), 108.7 (C3), 121.5 (C5) and 131.0 (C2); δ_H 1.36 (CH_3, *J* 7.1), 1.5–2.1 (br m, Ad and OH), 4.17 (CH_2, *J* 7.1), 6.17 (H3, *J* 1.8 and 3.8), 6.32 (H4, *J* 2.7 and 3.8) and 6.49 (H5, *J* 1.8 and 2.7) (Found: C, 82.4; H, 9.8; N, 3.7. $C_{27}H_{39}NO$ requires C, 82.39; H, 9.99; N, 3.56%).

Ionic hydrogenation of (*N*-methylpyrrol-2-yl)di(1-adamantyl)methanol, 2. Trifluoroacetic acid (1.0 cm^3) was added dropwise to a solution of alcohol **2A** (244 mg, 0.64 mmol) and triethylsilane (0.25 cm^3, 1.57 mmol) in dichloromethane (20 cm^3) at about −10 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight before quenching and work-up. By silica gel chromatography diadamantylketone (151 mg, 78%) was separated from a fast-running material (41 mg, 18%), identified by NOE experiments as *anti*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)methane, **4A**: mp 170 °C; δ_C 29.8 (6 CH), 37.3 (6 CH_2), 38.5 (CH_3), 39.1 (2 C_q), 44.0 (6 CH_2), 65.0 (CH), 107.0 (C4), 115.1 (C3), 123.6 (C5) and 134.4 (C2); δ_H 1.5–2.1 (br m, Ad), 2.38 (benzylic H), 3.32 (CH_3), 5.91 (H3, *J* 2.0 and 3.3), 6.28 (H4, *J* 2.8 and 3.3) and 6.42 (H5, *J* 2.0 and 2.8) (Found: C, 85.5; H, 10.2; N, 3.7. $C_{26}H_{37}N$ requires C, 85.89; H, 10.26; N, 3.85%).

Heating this material in octadeuteriotoluene for 8 h in a sealed tube at 150 °C resulted in about 30% conversion to the *syn* isomer, **4S**, with the appearance of new ^{1}H NMR signals in the aromatic region at 6.05, 6.24 and 6.35 ppm, a methyl group at 3.06 ppm and a benzylic CH at 1.96 ppm. Prolonged heating (8 h) in hexadeuteriobenzene at 190 °C resulted in complete conversion: δ_C 29.6 (6 CH), 34.2 (CH_3), 37.4 (6 CH_2), 40.4 (2 C_q), 42.9 (6 CH_2), 58.4 (CH), 106.5 (C4), 108.1 (C3), 120.1 (C5) and 132.9 (C2); δ_H 1.5–2.1 (br m, Ad), 1.96 (benzylic H), 3.03 (CH_3), 6.13 (H3, *J* 1.7 and 3.6), 6.32 (H4, *J* 2.7 and 3.6) and 6.40 (H5, *J* 1.7 and 2.7). The new isomer was not isolated.

Treatment of alcohol **2A** (100 mg) with TFA in dichloromethane under the same conditions as above, but without TES, gave only diadamantylketone (76 mg, 97%).

Rotation kinetics. Aliquots (0.1 cm^3) containing 1.5–2.5 mg of *anti*-(*N*-methylpyrrol-2-yl)diadamantylmethanol, **2A**, *anti*-(*N*-ethylpyrrol-2-yl)diadamantylmethanol, **3A**, or *anti*-(*N*-methylpyrrol-2-yl)diadamantylmethane, **4A**, in hexadeuteriobenzene were sealed under vacuum in 5 mm od glass tubes. Batches of tubes (eight samples per run on average) were thermostated in an oil bath and samples withdrawn at convenient intervals. Each sample was made up to 0.45 cm^3 with hexadeuteriobenzene for ^{1}H NMR analysis, the Me group peaks at 3.36 and 3.63 ppm (**2**, R = Me), those at 3.03 and 3.32 ppm (**4**, R = Me) or the CH_2 group signals at 3.85 and 4.17 ppm (**3**, R = Et) being used to estimate the progress of the reaction. The first-order rate constant was determined from a plot of log(% residual *anti*) *vs.* time. Rate constants were as follows (*T*/°C, *k*/s^{-1}), the indicated errors being the standard deviations on single runs. **2A**: 113.0, $2.65 \pm 0.01 \times 10^{-5}$; 128.1, $1.19 \pm 0.02 \times 10^{-4}$; 142.5, $4.26 \pm 0.05 \times 10^{-4}$; 157.0, $1.45 \pm 0.01 \times 10^{-3}$ giving $\Delta H^{\ddagger} = 29.1 \pm 0.1$ kcal mol^{-1} and $\Delta S^{\ddagger} = -4.5 \pm 0.3$ cal mol^{-1} K^{-1}, with $\Delta G^{\ddagger}$(135 °C) = 31.0 kcal mol^{-1}; **3A**: 113.0, $3.82 \pm 0.02 \times 10^{-5}$; 128.1, $1.58 \pm 0.02 \times 10^{-4}$; 142.5, $5.80 \pm 0.04 \times 10^{-4}$; 157.0, $1.92 \pm 0.01 \times 10^{-3}$ giving $\Delta H^{\ddagger} = 29.7 \pm 0.1$ kcal mol^{-1} and $\Delta S^{\ddagger} = -5.1 \pm 0.3$ cal mol^{-1} K^{-1}, with $\Delta G^{\ddagger}$(135 °C) = 30.7 kcal mol^{-1}; **4A**: 149.9, $1.02 \pm 0.02 \times 10^{-5}$; 164.2, $3.52 \pm 0.05 \times 10^{-5}$; 180.1, $1.32 \pm 0.01 \times 10^{-4}$; 195.0, $4.09 \pm 0.04 \times 10^{-4}$) giving $\Delta H^{\ddagger} = 31.4 \pm 0.1$ kcal mol^{-1} and $\Delta S^{\ddagger} = -7.9 \pm 0.3$ cal mol^{-1} K^{-1}, with $\Delta G^{\ddagger}$(135 °C; 172 °C) = 34.6; 34.9 kcal mol^{-1}.

X-Ray crystallography

Crystal data for *anti*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)-methanol, 2A. $C_{26}H_{37}NO$, $M = 379.6$. Orthorhombic $a = 8.574(2)$, $b = 19.894(4)$, $c = 23.742(4)$ Å, $V = 4050(1)$ $Å^3$ (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, $\lambda = 0.710\ 69$ Å), space group *Pcba*, $Z = 8$, $D_x = 1.24$ g cm^{-3}. Colourless prismatic crystals, μ(Mo-Kα) = 0.69 cm^{-1}.

Crystal data for *syn*-(*N*-methylpyrrol-2-yl)di(1-adamantyl)-methanol, 2S. $C_{26}H_{37}NO$, $M = 379.6$. Monoclinic, $a = 13.143(4)$, $b = 10.434(2)$, $c = 15.365(3)$ Å, $\beta = 98.52(2)°$, $V = 2084(1)$ $Å^3$ (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, $\lambda = 0.710\ 69$ Å), space group $P2_1/a$, $Z = 4$, $D_x = 1.21$ g cm^{-3}. Colourless prismatic crystals, μ(Mo-Kα) = 0.67 cm^{-1}.

Data collection and processing. Enraf-Nonius MACH3 diffractometer, $\omega/2\theta$ mode with ω scan width = 0.8 + 0.345 tan θ, graphite-monochromated Mo-Kα radiation. 4027 (*anti*), 4067 (*syn*) reflections measured ($1 \leqslant \theta \leqslant 25°$), 3545 (*anti*), 3661 (*syn*) unique, giving 1749 (*anti*), 1808 (*syn*) with $I > 3\sigma(I)$.

Structure analysis and refinement. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic; hydrogens located from Fourier difference map with one, overall, refined isotropic thermal parameter (255 refinable parameters). No absorption correction. Final R and R_w (Chebyshev series) values are 0.056 (*anti*), 0.047 (*syn*) and 0.050 (*anti*), 0.044 (*syn*). Program used is the PC version of CRYSTALS[20] for refinements and CAMERON[21] for views.

Full crystallographic details, excluding structure factor tables, for **2S** and **2A** have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors' (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 188/134.

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