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Naphthalene-catalysed Lithiation of *N,N*-Diisopropylbenzamide and its Methoxy Derivatives

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Abstract

The reaction of *N,N*-disubstituted benzamide derivatives **1** with lithium and a catalytic amount of naphthalene (4 mol %) in the presence of carbonyl compounds (Barbier-type conditions) led to the formation of the corresponding 3,4-dihydro-4-substituted benzamides **2**. The presence of a 4-*tert*-butyl group in the starting benzamide changed the position of the electrophilic fragment to give the 3,4-dihydro-3-substituted amide **3**. When the reaction was performed with the corresponding methoxybenzamides **7**, only reductive demethoxylation took place, giving (by reaction with carbonyl compounds) the corresponding substituted benzamides **8**.

Keywords: Lithiation; Arenes; Amides; Reduction

I. Introduction

The reduction of aromatic compounds to give their dihydroderivatives by dissolving metals is one of the most powerful synthetic procedures available to organic chemists [1]. Metals of main groups dissolve readily in liquid ammonia, the resulting solutions of solvated electrons being powerful reducing agents that may be used to perform highly selective reductions. The reduction process of benzenoid substrates having electron withdrawing groups, in the presence

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of a source of protons, may follow two mechanistic pathways: (a) Formation of an anion-radical, protonation on the most reactive position, formation of a stabilised anion, and final reaction of the resulting enolate with different electrophiles, or (b) formation of a dianion and successive reaction with the source of protons and the electrophile [2]. Using this methodology several benzoic acid derivatives have been reduced to the corresponding 1,3-cyclohexadiene derivatives, the intermediate dienolate being alkylated *in situ* with a variety of electrophiles to afford substituted-1,3-cyclohexadiene derivatives [2]. Only in the case of 4-(4-chlorobutyl)benzoic acid was it possible to alkylate the fourth position by an intramolecular reductive process [3]. When the reaction was performed with tertiary benzamides, the main product was benzaldehyde. However, the presence of an electron-donating group in the aromatic ring led the reduction to the corresponding 1,3-cyclohexadiene derivatives [4]. This strategy has been successfully employed to reduce several chiral tertiary methoxybenzamide [5-7] and dihydroisoquinolin-1-one derivatives [8], and to the diastereoselective alkylation of the corresponding enolate intermediates.

On the other hand, in the last few years we have applied an arene-catalysed lithiation [9] to the preparation of very reactive fuctionalised organolithium compounds [10,11] starting from a wide variety of susbstrates.[1] In this paper, we report on the naphthalene-catalysed lithiation of tertiary benzamides and related systems.

II. Results and discussion

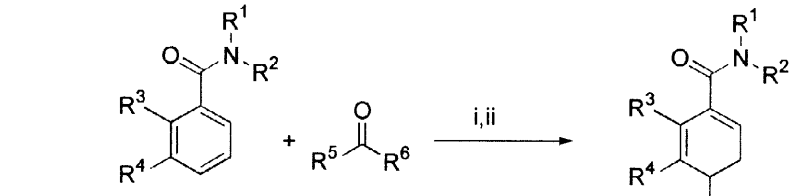
The reaction of *N,N*-disubstituted benzamides **1a-c** with an excess of lithium powder (1:14 molar ratio) and a catalytic amount of naphthalene (4 mol %) in the presence of a carbonyl compound (Barbier-type reaction [18,19]) in THF at –78°C gave after 2 hours, and final hydrolysis with water, the corresponding cyclohexadiene derivatives **2**, according to n.O.e. and ^{1}H-^{1}H correlations (Scheme 1 and Table 1).

Concerning the optimal conditions to carry out the process showed in Scheme 1, we observed that the best yields of compound **2** were obtained after 2 hours. Although at this reaction time a variable amount of starting amide **1** was recovered, longer reaction time afforded lower yields, giving an intractable mixture of products in which neither starting materials **1** nor products **2** were present in an isolable amount.[2] When the amount of lithium was decreased in order to avoid the formation of by-products, the reaction either did not take

[1] For the last papers from our laboratory on an arene-catalysed lithiation of chlorinated material [12], heterocycles [13], thioethers [14], sulfones [15] or unsaturated carbonyl compounds [16], see the corresponding references. For a recent review on the reductive cleavage of heterocycles by this methodology, see reference [17].

[2] Two possible ways to explain the decomposition of amide **2** in the presence of the lithiation mixture could be (a) a further lithiation followed by oligo or polymerization [16] or (b) Diels-Alder type processes [20].

place or the yield of amide **2** was lower than using an excess of lithium. In the case of using pivalaldehyde as electrophile the amide **2a** was isolated as a single diastereoisomer of unknown relative configuration.



1a: $R^1 = R^2 = Pr^i$; $R^3 = R^4 = H$
1b: R^1-R^2 = -$(CH_2)_4$-; $R^3 = R^4 = H$
1c: $R^1 = R^2 = Pr^i$; R^3-R^4 = -(CH=CH)$_2$-

Scheme 1. *Reagents and conditions*: i, Li (excess), $C_{10}H_8$ (4 mol%), R^5COR^6, -78°C, THF; ii, H_2O.

Table 1
Preparation of compounds **2**

	Benzamide	Hydroxyamide 2[a]							
Entry	No.	No.	R^1	R^2	R^3	R^4	R^5	R^6	Yield (%)[b]
1	**1a**	**2a**	Pr^i	Pr^i	H	H	H	Bu^t	52
2	**1a**	**2b**	Pr^i	Pr^i	H	H	Et	Et	51
3	**1a**	**2c**	Pr^i	Pr^i	H	H	Pr^i	Pr^i	46
4	**1b**	**2d**	-$(CH_2)_4$-		H	H	Et	Et	21
5	**1c**	**2e**	Pr^i	Pr^i	-CH=CH-CH=CH-		Et	Et	24[c]

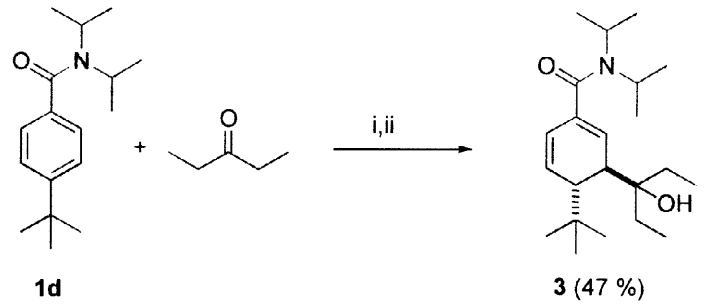
[a] All produts **2** were >95% (GLC and 300 MHz ^{1}H-RMN).
[b] Isolated yield after column chromatography (neutral aluminium oxide, hexane/ethyl acetate) based on the starting benzamide **1**.
[c] Silica gel was used in the choromatographic purification.

When the reaction of amide **1a** was performed in the absence of an electrophile, the only product isolated was isopropyl phenyl ketone (75% yield). Similar products have been reported to be formed as traces through an intramolecular radical rearrangement, when *N,N*-dialkyl arenecarboxamides were treated with lithium powder under sonochemical conditions [21], the main product being the corresponding *N*-dealkylated amide. Our lithiating system seems to show a different behaviour and, in this case the radical rearrangement is the main process in the absence of an electrophile. The *N*-dealkylated benzamide[3] could not be detected by either GLC or ^{1}H NMR spectroscopy on the crude mixture.

The reaction of *N,N*-diisopropyl-4-*tert*-butylbenzamide (**1d**) with 3-pentanone under the above lithiation conditions (Barbier-type conditions) led to the substituted amide **3** as the only isolated product, according to n.O.e. and ^{1}H-^{1}H correlations (Scheme 2). In this case, the

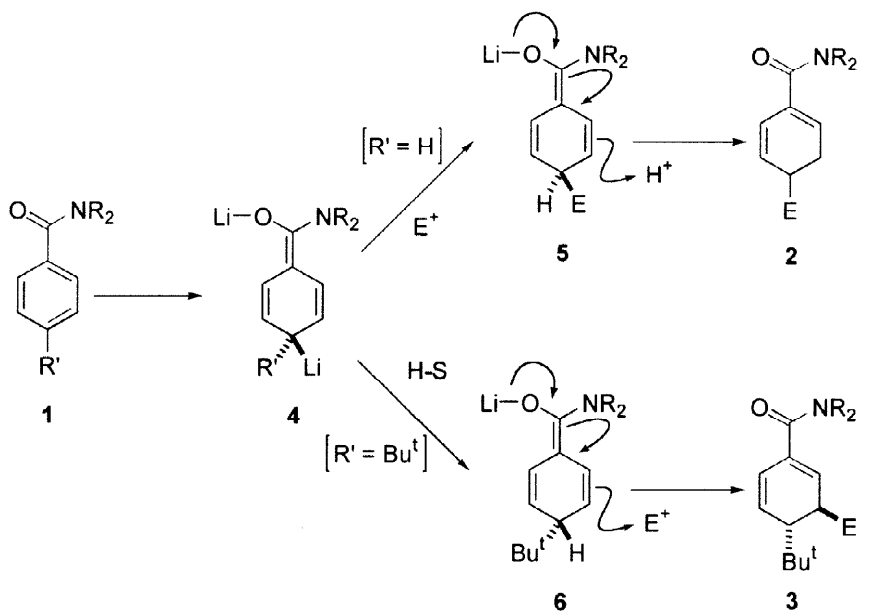
[3] For the use of a naphthalene-catalysed lithiation in the reductive deprotection of carboxamides, see reference [22].

reaction took place at a different position in the ring compared to the unsubstituted benzamides **1a-c** (Scheme 1).



Scheme 2. *Reagents and conditions*: i, Li, $C_{10}H_8$ cat. (4 mol %), -78°C, THF; ii, H_2O.

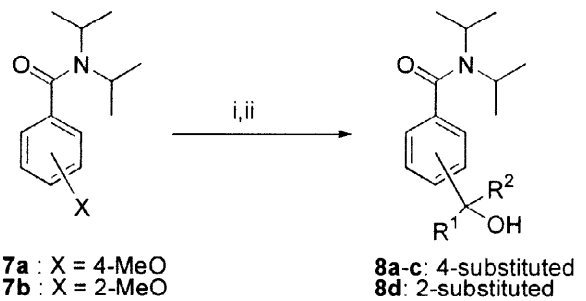
From a mechanistic point of view, the above results may be explained by a double SET process to form firstly the dianion **4**, which reacts with the electrophile depending on its substitution pattern. For non-substituted systems (**1a-c**, R' = H), the dianion reacts with an electrophile at the most reactive position to give the intermediate **5**, and the final hydrolysis gives products **2**.[4] In the case of the 4-*tert*-butylbenzamide derivative **1d** (R' = Bu^t), the most reactive tertiary organolithium intermediate of type **4** is probably quite unstable and rapidly takes a proton from the reaction medium to give the enolate **6**, which reacts with the electrophile on the less hindered face to produce, after hydrolysis, the amide **3** (Scheme 3).



Scheme 3.

[4] Hydrolysis to give the 1,4-cyclohexadiene derivative and further isomerisation in the basic aqueous medium to give the corresponding 1,3-cyclohexadiene **2** can not be ruled out.

The methoxybenzamides **7** were submitted to the above mentioned lithiation conditions with the purpose of improving the yield in the Birch-type reaction as has previously been described [4-7]. Surprisingly, in this case, the isolated products **8** were aromatic, their preparation being explained through a reductive demethoxylation process[5,6] followed by reaction of the corresponding aryllithium intermediate with the electrophile, or by reaction of the corresponding intermediate of type **4** (R' = MeO) with the electrophile and final elimination of lithium methoxyde re-aromatising the intermediate and giving the product **8**[7] (Scheme 4 and Table 2).



Scheme 4. *Reagents and conditions*: i, Li, $C_{10}H_8$ cat. (4 mol %), R^1COR^2, -78 to 20°C, THF; ii, H_2O.

Table 2
Preparation of benzamides **8**

	Starting benzamide		Product			
Entry	No.	X	No.	R^1	R^2	Yield (%)[b]
1	**7a**	4-MeO	**8a**	H	Bu^t	45
2	**7a**	4-MeO	**8b**	H	Ph	43
3	**7a**	4-MeO	**8c**	Et	Et	55
4	**7b**	2-MeO	**8d**	H	Bu^t	52

[a] All produts **8** were >95% (GLC and 300 MHz ^{1}H-RMN).
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting benzamide **7**.

III. Conclusion

As a conclusion, we present in this paper the first example describing a 4-alkylation of tertiary benzamides involving a dearomatisation process (Birch-type reaction). The alkylation is sensitive to the presence of substituents and, in the case of methoxy groups the lithiation

[5] For a review on the reductive cleavage of ethers, see reference [23].
[6] For examples on the reductive demethoxylation of 4-methoxy-1-acetylnaphthyl and 1,2,3-trialkoxyaryl derivatives by lithium, see references [24,25]. For reductive demethylation of anisol by lithium-byphenyl, see reference [26]. For examples where the presence of lithium and catalytic amounts of naphthalene did not affect to alkoxyaryl derivatives, see references [22,27].
[7] We thank the referee for this suggestion.

takes place in a different manner, giving reductive demethoxylation and reaction with an electrophile.

IV. Experimental section

IV.1. General

For general information see reference [28].

IV.2. Preparation of starting amides **1** *and* **7**.

General Procedure [22].- To a solution of the corresponding amine (10 mmol) and triethylamine (1.7 mL, 12 mmol) in CH_2Cl_2 (20 mL) was added dropwise the corresponding acid chloride (10 mmol) at 0°C. After 2h stirring at 20°C the resulting mixture was hydrolysed with water (10 mL), extracted with ethyl acetate (2x20 mL) and successively washed with a 2N HCl solution (2x20 mL) and saturated $NaHCO_3$ (2x20 mL). The organic layer was dried over anhydrous Na_2SO_4. Solvents were evaporated (15 Torr) and the resulting residue containing the title compounds was submitted to the lithiation process without further purification. Yields, physical, spectroscopic and analytical data, as well as literature references for known compounds, follow.

N,N-*Diisopropylbenzamide* (**1a**) [21]:[8] Yield 80%; Pale yellow oil, R_f 0.59 (hexane/ethyl acetate: 1/1); t_r 10.9; mp 67-68°C (hexane/ethyl acetate); ν (melted) 3030 (HC=C), 1627 cm^{-1} (C=O); δ_H 0.90-1.80 (12H, m, 4xCH_3), 3.40-3.90 (2H, m, 2x$CHCH_3$), 7.20-7.45 (5H, m, ArH); δ_C 20.55 (4xCH_3), 41.85, 50.5 (2x$CHCH_3$), 125.4, 128.25, 128.45, 138.75 (ArC); *m/z* 266 (M^++1, <1%), 205 (M^+, 5), 162 (13), 105 (100), 77 (43), 51 (16), 43 (10).

Phenyl-tetrahydro-1H-1-pyrrolymethanone (**1b**): Yield 98%; Pale yellow oil, R_f 0.23 (hexane/ethyl acetate: 1/1); t_r 10.5; ν (film) 1635 cm^{-1} (C=O); δ_H 1.80-2.00 (4H, m, CH_2CH_2), 3.40, 3.64 (2 and 2H, respectively, 2t, *J*=6.4, 2xCH_2N), 7.35-7.50 (5H, m, ArH); δ_C 23.95, 25.9 (CH_2CH_2), 45.65, 49.1 (2xCH_2N), 126.55, 127.75, 129.25, 139.75 (ArC), 169.15 (C=O); *m/z* 177 (M^++2, <1%), 176 (M^++1, 5), 175 (M^+, 32), 174 (20), 146 (14), 105 (100), 104 (12), 77 (72), 51 (36), 50 (10), 43 (15) (Found: M^+, 179.0998. $C_{11}H_{13}NO$ requires 175.0997).

N,N-*Diisopropyl-1-naphthamide* (**1c**) [29]:[8] Yield 87%; White crystals, R_f 0.65 (hexane/ethyl acetate: 1/1); t_r 12.0; mp 161-162°C (hexane/ethyl acetate); ν (melted) 1623 cm^{-1} (C=O); δ_H 1.00, 1.05, 1.65, 1.72 (12H, 4d, *J*=6.7, 4xCH_3), 3.50-3.65 (2H, m, 2x$CHCH_3$), 7.25-7.50, 7.75-7.90 (4 and 3H, respectively, 2m, ArH); δ_C 20.45, 20.55, 20.6, 20.7 (4xCH_3), 45.85, 50.9 (2xCHN), 121.95, 124.8, 125.1, 126.15, 126.5, 128.05, 128.1, 129.45, 133.4, 136.6 (ArC), 169.95 (C=O); *m/z* 257 (M^++2, <1%), 256 (M^++1, 5), 255 (M^+, 27), 212 (18), 156 (22), 155 (100), 128 (11), 127 (65), 126 (12), 43 (12), 42 (11).

N,N-*Diisopropyl-4-(*tert-*butyl)benzamide* (**1d**): Yield 90%; White crystals, R_f 0.74 (hexane/ethyl acetate: 1/1); t_r 13.34; mp 99-100°C (hexane/ethyl acetate); ν (melted) 3030 (HC=C), 1622 cm^{-1}(C=O); δ_H 1.10-1.60 (21H, m, 7xCH_3), 3.20-3.80 (2H, m, 2x$CHCH_3$), 7.24,

[8] No physical and spectroscopic data given in the literature.

7.37 (2 and 2H, respectively, 2d, *J*=8.3, ArH); δ_C 20.7, 31.15 (7xCH_3), 34.6 [*C*(CH_3)], 125.15, 125.45, 135.8, 151.6 (ArC), 171.2 (C=O); *m/z* 262 (M^++1, 2%), 261 (M^+, 13), 218 (32), 162 (22), 161 (100), 146 (11), 118 (16), 91 (15), 43 (15), 42 (10) (Found: C, 78.15; H, 10.49; N, 5.19. $C_{17}H_{27}NO$ requires: C, 78.11; H, 10.41; N, 5.36).

N,N-*Diisopropyl-4-methoxybenzamide* (**7a**): Yield 75%; Pale yellow oil, R_f 0.70 (hexane/ethyl acetate: 1/1); t_r 11.8; ν (film) 1613 (C=O), 1247, 1030 cm^{-1} (CO); δ_H 1.15-1.60 (12H, m, 4x*C*H_3CH), 3.55-3.95 (5H, m with s at 3.81, CH_3O, 2xCHN), 6.89, 7.28 (2 and 2H, respectively, 2d, *J*=8.6, ArH); δ_C 20.65 (4x*C*H_3CH), 55.15 (CH_3O), 48.0, 50.0 (2x*C*HCH$_3$), 113.5, 127.4, 130.85, 159.85 (ArC), 171.0 (C=O); *m/z* 236 (M^++1, <1%), 235 (M^+, 5), 192 (12), 135 (100), 77 (15) (Found: M^+, 235.1573. $C_{14}H_{21}NO_2$ requires 235.1572).

N,N-*Diisopropyl-2-methoxybenzamide* (**7b**): Yield 78%; White crystals, R_f 0.57 (hexane/ethyl acetate: 1/1); t_r 10.6; mp 89-90°C (ethyl acetate); ν (melted) 1621 cm^{-1} (C=O); δ_H 1.03, 1.14, 1.54, 1.56 (3, 3, 3, and 3H, respectively, 4d, *J*=6.7, 6.7, 4.0 and 4.0, respectively, 4x*C*H_3CH), 3.45-3.55, 3.60-3.70 (1 and 1H, respectively, 2m, 2x*C*HCH$_3$), 3.80 (3H, s, CH_3O), 6.85-6.95, 7.10-7.15, 7.25-7.30 (2, 1 and 1H, respectively, 3m, ArH) 6.89, 7.28 (2 and 2H, respectively, 2d, *J*=8.6, ArH); δ_C 20.25, 20.35, 20.55, 20.6 (4x*C*H_3CH), 45.5, 50.7 (2x*C*HCH$_3$), 55.2 (CH_3O), 110.6, 120,65, 126.65, 128.5, 129.25, 154.9 (ArC), 168.4 (C=O); *m/z* 236 (M^++1, <1%), 235 (M^+, 4), 192 (16), 135 (100), 77 (23) (Found: C, 70.39; H, 8.51; N, 5.19. $C_{14}H_{21}NO_2$. 0.25 H_2O requires: C, 70.11; H, 9.04; N, 5.84).

IV.3. Naphthalene-catalysed lithiation of benzamides **1** *and* **7** *in the presence of electrophiles. Isolation of compounds* **2**, **3** *and* **8**.

General Procedure.- To a green suspension of lithium powder (100 mg, 14 mmol) and naphthalene (10 mg, 0.08 mmol) in THF (5 mL) was slowly added (*ca.* 10 min) a solution of the corresponding benzamide **1** or **7** (1 mmol) and the electrophile (1.2 mmol) in THF (2 mL) at –78°C under an argon atmosphere. Stirring was continued for 2 h at the same temperature. In the case of starting material **7** stirring was continued for 12 h allowing the temperature to rise to 0°C. This resulting mixture was then hydrolysed with water (5 mL) and extracted with diethyl ether (2x20 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give a residue, which was purified by column chromatography (neutral aluminium oxide for compounds **2** and **3** or silica gel for compounds **8**, hexane/ethyl acetate) affording the pure title compounds. Yields are included in Tables 1, 2 and text. Physical, spectroscopic and analytical data follow:

N,N-*Diisopropyl-4-(1-hydroxy-2,2-dimethylpropyl)-1,5-cyclohexadiene-1-carboxamide* (**2a**):[9] Pale yellow iol, R_f 0.6 (ethyl acetate); t_r 15.44; ν (film) 3301 (OH), 1611 cm^{-1} (C=O); δ_H 0.95 [9H, s, C(CH_3)$_3$], 1.10-1.50 (13H, m, 4x*C*H_3CH, OH), 2.20-2.40, 2.45-2.60, 2.60-2.75 (1, 1 and 1H, respectively, 3m, CH_2CH), 3.40-3.45 (1H, m, CHO), 3.50-4.00 (2H, m, 2x*C*HCH$_3$), 5.65-5.70, 5.80-5.85, 5.90-6.00 (1, 1 and 1H, respectively, 3m, 3xCH=C); δ_C 20.8 (4xCH_3CH), 23.2 (CH_2), 26.95 [(*C*H_3)$_3$C], 35.15 (*C*HCH$_2$), 35.55 [*C*(CH_3)$_3$], 81.45 (CO), 123.8, 124.05, 131.8, 134.15 (C=CH) 170.55 (C=O); *m/z* 236 (M^+-57, 2%), 207 (37), 206 (100), 164 (20), 122 (11), 107 (15), 105 (30), 79 (16), 77 (18), 57 (12), 44 (12), 43 (32).

[9] For this oil, it was not possible to obtain the corresponding HRMS due to the absence of M^+ signal.

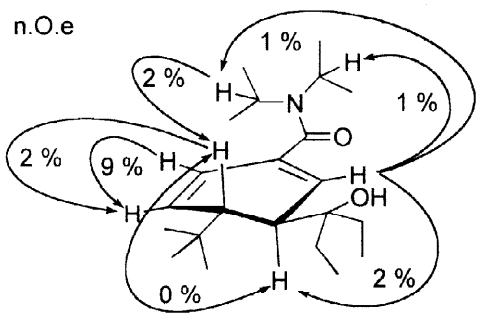
N,N-*Diisopropyl-4-(1-ethyl-1-hydroxypropyl)-1,5-cyclohexadiene-1-carboxamide* (**2b**): White crystals, R_f 0.39 (hexane/ethyl acetate: 1/1); t_r 15.16; mp 87-88°C (ethyl acetate); ν (melted) 3323 (OH), 3042, 1442 (HC=C), 1614 cm^{-1} (C=O); δ_H 0.89, 0.90 (3 and 3H, respectively, 2t, *J*=7.4, 2xCH_3CH_2), 1.00-1.70 (16H, m, 4xCH_3CH, 2xCH_2CH_3), 2.25-2.30, 2.55-2.65 (2 and 1H, respectively, 2m, CH_2CH), 3.20-3.80 (2H, m, 2x$CHCH_3$), 5.75-6.05 (3H, m, 3xCH=C); δ_C 7.5, 7.6 (2xCH_3CH_2), 20.8 (4xCH_3CH), 23.05 (CH_2CH), 28.4, 28.5 (2xCH_2CH_3), 39.55 ($CHCH_2$), 46.0, 48.5 (2x$CHCH_3$), 76.0 (CO), 123.85, 124.2, 127.85, 134.65 (C=CH), 170.5 (C=O); *m/z* 275 (M^+-18, <1%), 232 (27), 207 (24), 206 (64), 176 (11), 175 (68), 176 (34), 164 (15), 147 (14), 119 (29), 115 (11), 107 (10), 106 (11), 105 (100), 104 (12), 91 (42), 87 (18), 86 (27), 84 (11), 79 (20), 78 (12), 77 (43), 58 (25), 57 (34), 55 (17), 51 (12), 45 (26), 44 (26), 43 (83), 42 (24) (Found: C, 73.67; H, 10.91; N, 4.58. $C_{18}H_{30}NO_2$ requires: C, 73.93; H, 10.34; N, 4.79).

1,1-Diisopropyl-4-(1-hydroxy-1-isopropyl-2-methylpropyl)-1,5-cyclohexadiene-1-carboxamide (**2c**): White crystals, R_f 0.26 (hexane/ethyl acetate: 1/1); t_r 16.32; mp 139-140°C (ethyl acetate); ν (melted) 3403 (OH), 3030, 1595 (HC=C), 1624 cm^{-1} (C=O); δ_H 0.95-1.00 (12H, m, 4xCH_3CHC), 1.15-1.45 (13H, m, 4xCH_3CHN, OH), 2.00-2.15, 2.25-2.35, 3.25-3.85 (2, 2 and 1H, respectively, 3m, 2x$CHCH_3$, CH_2CH), 3.30-3.90 (2H, m, 2xNCHCH_3), 5.80-5.95, 6.00-6.10 (2 and 1H, respectively, 2m, 3xCH=C); δ_C 17.9, 18.0, 18.65, 18.7, 20.8 (8xCH_3), 24.6 (CH_2), 32.9, 33.75, 39.1, 45.9, 50.1 (5xCH), 78.25 (CO), 121.95, 123.8, 130.95, 134.8 (CH=C), 170.55 (C=O); *m/z* 321 (M^+, <1%), 278 (22), 260 (12), 207 (40), 206 (100), 203 (14), 164 (14), 115 (18), 105 (40), 100 (17), 91 (11), 79 (14), 77 (18), 71 (56), 55 (18), 45 (12), 44 (17), 43 (86), 42 (10) (Found: C, 73.24; H, 10.98; N, 4.17. $C_{20}H_{34}NO_2$. 0.5 H_2O requires: C, 72.90; H, 10.71; N, 4.25).

*4-(3-Hydroxypentyl)-1,5-cyclohexadienyl-tetrahydro-1*H*-1-pyrrolylmethanone* (**2d**): Pale yellow oil, R_f 0.31 (ethyl acetate); t_r 16.60; ν (film) 3439 (OH), 1651 cm^{-1} (C=O); δ_H 0.80-0.90 (4H, m, 2xCH_2CH_2), 1.85-1.95 (4H, m, 2xNCH_2CH_2), 2.25, 2.35, 2.50-2.60 (2, 1 and 1H, respectively, s, s and m, respectively, CH_2CH), 3.45-3.50 (4H, m, 2xCH_2N), 5.85-5.95, 6.10-6.20 (1 and 2H, respectively, 2m, 3xCH=C); *m/z* 244 (M^+-18, 11%), 177 (32), 176 (100), 175 (13), 173 (10), 105 (39), 99 (17), 98 (30), 91 (11), 87 (19), 77 (23), 71 (14), 57 (25), 56 (17), 55 (31), 45 (30), 43 (18) (Found: M^+-18, 244.1690. $C_{16}H_{22}NO$ requires 244.1701).

N,N-*Diisopropyl-1-(1-ethyl-1-hydroxypropyl)-1,2-dihydro-4-naphththalenecarboxamide* (**2e**): Pale yellow oil, R_f 0.48 (hexane/ethyl acetate: 1/1); t_r 18.95; ν (film) 3427 (OH), 1620 cm^{-1} (C=O); δ_H 0.70-2.30 (23H, m, 4xCH_3CH, 2xCH_2CH_3, OH), 3.05-3.15, 3.85-4.00 (1 and 4H, respectively, 2m, 2x$CHCH_3$, CH_2CHCO), 6.90-7.35 (5H, m, ArH); δ_C 7.70, 7.9 (2xCH_3CH_2), 20.65, 20.7, 20.95, 21.45 (4xCH_3CH), 26.65, 27.15, 29.2 (3xCH_2), 43.9, 44.0, 45.65 (2xCHN, $CHCH_2$), 77.6 (CO), 125.65, 126.3, 126.75, 131.4, 136.7, 139.65 (ArC), 160.0 (C=O); *m/z* 325 (M^+-18, 2%), 258 (10), 257 (60), 256 (100), 214 (15), 155 (37), 129 (38), 128 (45), 127 (30), 100 (12), 87 (26), 86 (36), 58 (42), 57 (52), 45 (39), 44 (21), 43 (94), 42 (14) (Found: M^+-H_2O, 325.2398. $C_{22}H_{31}NO$ requires 325.2405).

N,N-*Diisopropyl-4-*tert-*butyl-3-(1-ethyl-1-hydroxypropyl)-1,5-cyclohexadiene-1-carboxamide* (**3**): Pale yellow oil, R_f 0.67 (hexane/ethyl acetate: 1/1); t_r 15.30; ν (film) 3394 (OH), 3038 (HC=C), 1621 cm^{-1} (C=O); δ_H 0.85-0.95 (6H, m, 2xCH_3CH_2), 1.04 [9H, s, $(CH_3)_3C$], 1.15-1.40 (12H, m, 4xCH_3CH), 1.50-1.70 (4H, m, 2xCH_2CH_3), 2.05 (1H, br. s, OH), 3.30-3.50 (2H, m with dd at 3.41, J=13.5, 3.3, $CHCH_3$, CHCO), 3.62 [1H, dt, J=13.5, 2.8, $CHC(CH_3)_3$], 4.05-4.25 (1H, m, $CHCH_3$), 5.25-5.35 (1H, m, OCC=CH), 5.42 (1H, dd, J=9.8, 2.8, OCCC*H*=CH), 6.05-6.15 (1H, m, OCCCH=C*H*); δ_C 7.15, 8.05, 20.7, 20.8 (2xCH_3CH_2, 4xCH_3CH), 28.75 [$(CH_3)_3C$], 28.95, 29.3 (CH_2), 33.85 [$C(CH_3)_3$], 39.65, 42.1, 46.05, 48.5 (4xCH), 76.35 (CO), 117.8, 123.6, 125.15, 141.85 ($CH=CH_2$), 174.5 (C=O); *m/z* 320 (M^+-29, 2%), 161 (16), 147 (22), 129 (17), 128 (81), 119 (12), 114 (13), 91 (15), 87 (37), 86 (106), 72 (18), 70 (11), 58 (18), 57 (63), 45 (39), 44 (18), 43 (38), 42 (17) (Found: M^+-29, 320.2580. $C_{20}H_{34}NO_2$ requires 320.2589).



N,N-*Diisopropyl-4-(2,2-dimethyl-1-hydroxypropyl)benzamide* (**8a**): White crystals, R_f 0.46 (hexane/ethyl acetate: 1/1); t_r 16.62; mp 147-148°C (ethyl acetate); ν (melted) 3430 (OH), 1645 cm^{-1} (C=O); δ_H 0.90 [9H, s, $(CH_3)_3$], 1.05-1.60 (12H, m, 4xCH_3CH), 2.45-2.55 (1H, br. s, OH), 3.40-3.90 (2H, m, 2xCHN), 4.36 (1H, s CHO), 7.23, 7.30 (2 and 2H, respectively, 2d, J=7.9, ArH); δ_C 20.65 (4xCH_3CH), 25.6 [$(CH_3)_3C$], 35.6 [$(CH_3)_3C$], 46.05, 50.9 (2xCHN), 81.85 (CO), 124.8, 127.6, 137.45, 142.8 (ArC), 171.0 (C=O); *m/z* 293 (M^++2, <1%), 292 (M^++1 , 3), 291 (M^+, 17), 248 (36), 235 (40), 234 (63), 192 (26), 191 (100), 175 (18), 173 (21), 135 (40), 134 (42), 133 (36), 107 (51), 106 (53), 105 (40), 102 (41), 100 (17), 86 (19), 79 (33), 78 (20), 77 (45), 70 (14), 58 (45), 57 (90), 51 (15), 44 (52), 43 (95), 42 (36) (Found: C, 73.55; H, 9.97; N, 4.23. $C_{18}H_{29}NO_2$ requires: C, 74.18; H, 10.03; N, 4.81).

N,N-*Diisopropyl-4-(1-hydroxy-1-phenylmethyl)benzamide* (**8b**): White crystals, R_f 0.43 (hexane/ethyl acetate: 1/1); t_r 19.65; mp 163-164°C (ethyl acetate); ν (melted) 3383 (OH), 3058, 3029, 1688 (HC=C), 1606 cm^{-1} (C=O); δ_H 1.00-1.70 (12H, m, 4xCH_3), 3.30-3.90 (3H, m, 2xCHN, OH), 5.70 (1H, s, CHO), 7.15-7.35 (9H, m, ArH); δ_C 20.6 (4xCH_3), 45.75, 50.5 (2xCHN), 75.55 (CO), 125.6, 126.5, 126.55, 127.4, 128.3, 137.45, 143.75, 144.7 (ArC), 170.95 (C=O); *m/z* 312 (M^++1, <1%), 311 (M^+, 1), 268 (25), 212 (15), 211 (10), 209 (14), 165 (19), 105 (61), 79 (13), 77 (40), 51 (11), 43 (22), 42 (13) (Found: C, 77.29; H, 8.28; N, 4.37. $C_{20}H_{25}NO_2$ requires: C, 77.14; H, 8.09; N, 4.50).

N,N-*Diisopropyl-4-(1-hydroxy-1-ethylpropyl)benzamide* (**8c**): Pale yellow oil, R_f 0.57 (hexane/ethyl acetate: 1/1); t_r 16.22; ν (film) 3422 (OH), 1630 cm^{-1} (C=O); δ_H 0.76 (6H, t, J=7.4, 2xCH_3CH_2), 1.00-1.70 (12H, m, 4xCH_3CH), 1.75-1.95 (5H, m, 2xCH_2CH_3, OH), 3.30-3.90 (2H, m, 2x$CHCH_3$), 7.28, 7.33 (2 and 2H, respectively, 2d, J=6.5 ArH); δ_C 7.75 (2xCH_3CH_2), 20.75 (2xCH_2), 34.85 (2xCHN), 77.25 (CO), 125.45, 125.55, 136.75, 146.45 (ArC), 171.1 (C=O); *m/z* 292 (M^++1, 1%), 291 (M^+, 8), 262 (11), 248 (27), 230 (11), 192 (13), 191 (100), 173 (67), 162 (10), 161 (10), 134 (20), 115 (12), 105 (15), 91 (12), 86 (15), 77 (15), 70 (10), 57 (59), 44 (14), 43 (76), 42 (18) (Found: M^+, 291.2197. $C_{18}H_{29}NO_2$ requires 291.2198).

N,N-*Diisopropyl-2-(1-hydroxy-2,2-dimethylpropyl)benzamide* (**8d**): Pale yellow oil, R_f 0.59 (hexane/ethyl acetate: 1/1); t_r 14.79; ν (film) 3452 (OH), 3035, 1596 (C=CH), 1623 cm^{-1} (C=O); δ_H (*ca.* 1:1 rotameric mixture) 0.95, 1.00 [9H, 2s, 2x(CH_3)$_3$C], 1.02, 1.10 (3H, 2d, *J*=6.6, CH_3CH), 1.16, 1.23 (3H, 2d, *J*=6.6, CH_3CH), 1.51, 1.55 (3H, 2d, *J*=6.7, CH_3CH), 1.55, 1.57 (3H, 2d, *J*=6.7, CH_3CH), 2.30-2.40 (1H, m, OH), 3.40-3.65 (2H, m, 2xC*H*CH_3), 4.40-4.45, 4.75-4.80 (1H, 2m, CHO), 7.05-7.55 (4H, m, ArH); δ_C 20.2, 20.35, 20.45, 20.55, 20.65, 20.7, 21.1 (4xCH_3), 26.4, 26.9 [(CH_3)$_3$C], 35.6, 36.4 [(CH_3)$_3$*C*], 45.7, 46.0, 50.55, 50.9 (2xCHN), 77.2, 78.95 (CO), 124.95, 125.45, 126.3, 127.6, 127.75, 127.85, 128.3, 129.45, 137.45, 138.05, 138.2, 141.5 (ArC), 170.25, 171.0 (C=O); *m/z* 291 (M^+, <1%), 234 (14), 192 (31), 189 (17), 134 (26), 133 (100), 105 (27), 102 (13), 86 (25), 77 (22), 58 (11), 57 (16), 44 (52), 43 (39), 42 (16) (Found: M^+, 291.2196. $C_{18}H_{29}NO_2$ requires 291.2198).

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VI. References

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