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Catalyzed Reaction of 2-Methyl-1,3-Dioxep-4-ene and Halogen Magnesium Salts of Secondary Amines. A New Approach to Allylaminoalcohols.

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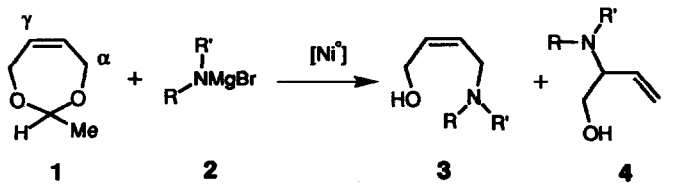
Abstract: In the presence of a catalytic amount of Ni°, 2-methyl-1,3-dioxep-4-ene (**1**) reacts with secondary halogen magnesioamides (**2**) to give mixtures of 4-aminobut-2-enols (**3**) and 2-aminobut-3-enols (**4**), arising from α- or γ- substitution to **1**. The stereo- and regiochemistry of the reaction is closely related to the structures of **2**.

Our recent studies[1-3] indicated that a catalytic amount of $NidppeCl_2$ allows the alkylation of (Z)-1,4-but-2-endiol derivatives by Grignard reagents. Depending on the nature of the precursor, the reaction gives allylic or homoallylic alcohols with a high regio and/or stereocontrol.

In the present paper we report new results obtained, in this Felkin-like[4] reaction, using as nucleophiles halogen magnesium salts of secondary amines instead of Grignard reagents. Such a study has been carried out to establish if allylic or homoallylic aminoalcohols, useful precursors of both biological and natural compounds,[5] could be prepared.

Considering that 2-methyl-1,3-dioxep-4-ene (**1**) is able to convert secondary or tertiary Grignard reagents into the corresponding (Z)-allylic alcohols, the reaction of **1** with **2** in the presence of a catalytic amount of Ni°, should give allylic **3** and/or homoallylic **4** aminoalcohols (Scheme).

Scheme



1 **2** **3** **4**

Preliminary experiments, carried out with Et_2NMgBr[6] (**2a**), indicated that the reaction occurs when a mixture of **1** and the catalyst is treated in THF with an excess of the magnesioamide (**1**/**2**=1/2.2 molar ratio).

The actual catalytic species was prepared by reacting $NidppeCl_2$ with EtMgBr. The data shown in Table 1 indicate that the occurrence and the reproducibility of the reaction depend on the amount of the Grignard reagent used: an excess of the Grignard reagent with respect to $NidppeCl_2$ is necessary to perform the amination of **1** (Table 1, runs 2-4 *vs* run 1).

Table 1. Reaction of **1** with **2a**: Dependence of Products Distribution on the $NidppeCl_2$/EtMgBr Molar Ratio.[a]

Run	[$NidppeCl_2$]/[EtMgBr]	Time (h)[b]	**3**	**4**
1	1 / 2	100	-	-
2	1 / 10	1	72	28
3	1 / 20	0.6	71	29
4	1 / 10	150[c]	67	33

a) Any experiment, repeated at least twice, was performed in THF if not otherwise stated, by using [1] / [Et_2NMgBr] / [$NidppeCl_2$] = 1 / 2.2 / 0.02. b) Required for the quantitative (glc) conversion of **1**. c) Reaction carried out in diethylether; the product distribution is for 79% conversion (glc)

In these reaction conditions, a mixture (70/30) of the expected 4-diethylaminobut-2-enol (**3a**) and 2-diethylaminobut-3-enol (**4a**) was obtained in satisfactory yields (glc).The experimental findings, obtained employing these reaction conditions (Table 1, run 2), are collected in Table 2.

Table 2. Products Distribution in the Reaction of **1** with RR'NMgBr (**2**).

Run	R	R'	Time (h)[a]	Yield (%)[b]	**3**[c]	**4**
1	Et	Et(**a**)	1.5	57	85	15
2	*i*.Bu	*i*.Bu(**b**)	1.0	57	70	30
3	-$(CH_2)_5$-	(**c**)	1.3	70	67	33
4	*i*.Pr	*i*.Pr(**d**)	3.5	10	100[d]	
5	-$(CH_2)_4$-	(**e**)	2.3	54	66	34
6	Me	Bn(**f**)	1.3	56	52	48
7	Me	Ph(**g**)	1.3	55	12	88

a) Referred to a 100% conversion (glc). b) Referred to the recovered mixture of **3** and **4** (see Experimental). c) Only the Z isomer is formed. d) Z/E ratio 68/32.

The data show that in every case quantitative depletion of **1** corresponds to 54-70% yields in mixtures of **3** and **4**; the yield drops dramatically when the poorly nucleophilic amide **2d** (run 4) is used, here the basic nature of the amide causes the degradation of the η^3-allyl intermediate through elimination processes.[7]

Although the reaction is not completely regioselective, its stereoselectivity is noteworthy: compounds (Z)-**3a-c**, **e-g** arise >95% stereoisomerically pure.

The stereocontrol drops only when **2d** is used. In this context it must be emphasized that Pd° mediated allylic amination always gives the corresponding E products.[8]

The regiochemistry of the reaction (α- or γ-substitution) seems to depend on the nature of the η^3-allyl intermediate and on the hardness of the nucleophile[9,10] (Table 2 runs 1-6 *vs* run 7), following a trend similar to that already observed in the reactions between **1** and Grignard reagents in the presence of $NidppeCl_2$.[3]

Any attempts to obtain pure compounds **3** and **4** by distillation, tlc, flash chromatography failed, however chemically pure **3a, e** were obtained by MPLC, **3g, f** and **4g, f** were isolated by semipreparative HPLC.

In conclusion the reaction described here represents one of the few single step methods of obtaining compounds **3** stereospecifically by using a transition metal catalytic system. On the other hand, the reaction offers the possibility of preparing allylaminoalcohols **3** or **4** by employing an inexpensive catalyst more stable than the analogous Pd compounds.

Experimental Section

Materials and instruments. Diethyl ether, hexane and tetrahydrofuran (THF) were purified by standard methods and distilled from $LiAlH_4$ before use. All the amines employed were distilled from KOH under nitrogen before use. Glc analyses were performed on a Perkin Elmer 8500 instrument (both a DB1, 12mx0.22mm or a 25mx0.22mm capillary column was used) equipped with a flame ionization detector and a split-splitless or a PTV injectors, with He as carrier gas. ^1H and ^{13}C NMR (200 and 50 MHz respectively) spectra were recorded on a Varian Gemini 200 spectrometer; all NMR data were obtained using $CDCl_3$ solutions. Chemical shifts (δ ppm) are referred to tetramethylsilane (TMS) (^1H NMR) or $CDCl_3$ (^{13}C NMR) as internal standard. The ^{13}C NMR signals marked with an asterisk are, when possibile, attributable to the minor component of the mixture.

Ir, spectra (ν, cm^{-1}) were recorded on a Perkin Elmer FT-IR, 1760X spectrophotometer, using liquid films. Mass spectra (m/e, I%) were taken on a VG-Analytical 7070 GC-MS instrument. All isolated compounds gave satisfactory elemental analyses (± 0.4%).

Analytical HPLC were performed with a Perkin-Elmer 2.2 apparatus equipped with a Perkin Elmer LC-75 UV detector using a Stacroma (250x4.6mm) Nucleosil-OH (7mμ) column. MPLC separations were carried out with a Lobar apparatus equipped with an RI Knauer detector, using a 31x2.5cm column, packed with a LichroprepDiol phase (24-40mμ, Merck).

General procedure. In a typical run **1** (10 mmol) and $NidppeCl_2$ (0.2 mmol) at 0 °C in 20ml of THF were reacted with EtMgBr (2 mmol) in the same solvent. After 10 min the solution of the suitable amine salt **2** in THF[6] was slowly added at 0 °C. The yellow-red solution was stirred at room temperature until the complete conversion of the precursor was obtained. The solution was then poured, under nitrogen, into a 500ml round-bottom flask containing a 2N aqueous solution of KOH (150ml). Organic products were stream distilled and the double phase obtained, saturated with NaCl, was extracted into $CHCl_3$ (4x100ml). After the elimination of the solvents, at reduced pressure, chemically pure mixtures of **3** and **4** were obtained (glc, NMR).

The reaction time, the recovered yield and the composition of **3/4** mixture, evaluated by glc and by NMR (in brackets) are given below.

*Reaction of **1** with **2a**; preparation of **3a** and **4a***: 1.50 h, 57%, 85(88)/15(12); **3a**: m/e (I%), 143 (M^+, 2.7), 142 (4.1), 128 (40.5), 110 (2.7), 96 (2.7), 86 (27.0), 74 (13.5), 73 (24.3), 72 (16.2), 69 (5.4), 58 (100), 56 (9.5); **4a**: m/e (I%), 142 (M^+-1, 1.0), 128 (1.0), 113 (9.5), 112 (100), 96 (2.7), 84 (14.9), 72 (5.4), 68 (5.4), 58

(17.6), 56 (37.8); **3a, 4a** mixture: ^{1}H NMR (60 °C), 5.98-5.58 (0.12H, CH_2=C<u>H</u>-, m), 5.90 (0.88H, =C<u>H</u>-CH_2OH, dtt, J_1=11.6, J_2=5.1, J_3=1.2), 5.67 (0.88H, =C<u>H</u>CH_2N<, dtt, J_1=11.6, J_2=5.7, J_3=1.3), 5.29-5.07 (0.24H, C<u>H</u>$_2$=CH-, m), 4.50-4.10 (1H, -OH, s), 4.16 (1.76H, =CHC<u>H</u>$_2$OH, dd, J_1=5.1, J_2=1.3), 3.52 (0.24H, >CHC<u>H</u>$_2$OH, d, J=7.6), 3.07 (1.76H, =CHC<u>H</u>$_2$N<, dd, J_1=5.7, J_2=1.2), 2.80-2.20 (0.12H, >C<u>H</u>CH_2OH, m), 2.57 (4H,-N(C<u>H</u>$_2$CH$_3$)$_2$, q, J=7.1), 1.07 (5.28H, -N(CH$_2$C<u>H</u>$_3$)$_2$, t, J=7.1), 1.06 (0.72H, -N(CH$_2$CH$_3$)$_2$, t, J=7.1); ^{13}C NMR, 133.83, 133.38(*), 127.48, 119.04(*), 60.52(*), 59.45, 49.90, 46.32, 43.11(*), 14.03(*), 11.02; Ir, 3391, 3019, 1682, 1642, 1457, 1384, 1197, 1167, 1042, 781.

Chemically pure **3a**, recovered by MPLC (hexane / methanol / methylenechloride = 9/1/1), showed: ^{1}H NMR (50 °C), 5.90 (1H, =C<u>H</u>CH_2OH, dtt, J_1 =11.6, J_2=5.1 , J_3=1.2), 5.67 (1H, =C<u>H</u>CH_2N<, dtt, J_1=11.6, J_2=5.7, J_3=1.3), 5.45-4.95 (1H, -OH, s), 4.16 (2H, =CHC<u>H</u>$_2$OH, ddt, J_1=5.1, J_2=1.3, J_3=1.2), 3.07 (2H, =CHC<u>H</u>$_2$N<, ddt, J_1=5.7, J_2=1.2, J_3=1.2), 2.57 (4H, -N(C<u>H</u>$_2$CH$_3$)$_2$, q, J=7.1), 1.07 (6H, -N(CH$_2$C<u>H</u>$_3$)$_2$, t, J=7.1); ^{13}C NMR, 133.83, 127.48, 59.45, 49.90, 46.32, 11.02; Ir, 3368, 3019, 1679, 1456, 1385, 1196, 1166, 1089, 784.

Reaction of ***1*** *with* ***2b****; preparation of* ***3b*** *and* ***4b***: 1 h, 57%, 70 (71)/30(29); **3b**: m/e (I%), 199 (M^+, 1.6), 184 (1.6), 157 (15.1), 156 (100), 142 (2.4), 129 (3.2), 114 (2.4), 100 (12.7), 86 (31.0), 82 (8.7), 71(6.3), 70 (5.6), 69 (13.5), 57 (23.0), 55 (13.5); **4b**: m/e (I%), 198 (M^+-1, 1.0), 169 (2.9), 168 (100), 157 (1.6), 156 (13.1), 112 (7.4), 86 (9.4), 82 (2.3), 68 (2.3), 57 (7.4), 56 (7.4), 55 (2.3); **3b, 4b** mixture: ^{1}H NMR (60 °C), 5.90-5.50 (0.29H, CH_2=C<u>H</u>-, m), 5.81 (0.71H, =C<u>H</u>CH_2OH, dtt, J_1=11.6, J_2=5.2, J_3 =1.1), 5.63 (0.71H, =C<u>H</u>CH_2N<, dtt, J_1=11.6, J_2=6.1, J_3=1.3), 5.26 (0.29H, H*cis*-CH=CH-, ddd, J_1=10.6, J_2=1.9, J_3=0.7), 5.13 (0.29H, H*trans*-CH=CH-, ddd, J_1=17.1, J_2 =1.9, J_3=0.7), 4.19 (1.42H, =CHC<u>H</u>$_2$OH, dd, J_1=5.2, J_2=1.3), 3.48 (0.58H, >CHC<u>H</u>$_2$OH, dd, J_1=10.3, J_2=5.2), 3.01 (1.42H, =CHC<u>H</u>$_2$N<, dd, J_1=6.1, J_2=1.1), 2.60-2.40 (1H, -OH, s), 2.40 (1.16H, -N(C<u>H</u>$_2$^{i}Pr)$_2$, d, J=6.9), 2.30-2.18 (0.29H, >C<u>H</u>CH_2OH, m), 2.13 (2.84H, -N(C<u>H</u>$_2$^{i}Pr)$_2$, d, J=7.0), 1.95-1.60 (2H, -NCH$_2$(C<u>H</u>Me$_2$)$_2$, m), 0.90 (12H, 4 Me, d, J=6.6); ^{13}C NMR, 132.70, 132.34(*), 128.29, 119.62(*), 69.74, 60.74(*), 59.77, 58.50, 52.64(*), 25.99, 21.17; Ir, 3370, 3076, 1685, 1641, 1467, 1388, 1367, 1198, 1167, 1090, 1035, 695.

Reaction of ***1*** *with* ***2c****; preparation of* ***3c*** *and* ***4c***: 1.30 h, 70%, 67(66)/33 (34); **3c**: m/e (I%), 155 (M^+, 4.3), 154 (10.0), 138 (2.5), 124 (7.9), 110 (7.1), 98 (29.3), 86 (20.0), 85 (57.5), 84 (100), 70 (9.3), 69 (5.7), 68 (6.1), 58 (7.9), 56 (10.4), 55 (14.3); **4c**: m/e (I%), 125 (M^+ -30, 10.7), 124 (100), 96 (9.6), 84 (5.0), 68 (7.1), 56 (7.1), 55 (6.4); **3c, 4c** mixture: ^{1}H NMR (60 °C), 5.95-5.45 (0.34H, CH_2=C<u>H</u>-, m), 5.85 (0.66H, =C<u>H</u>CH_2OH, dtt, J_1=11.7, J_2=5.3, J_3=1.2), 5.60 (0.66H, =C<u>H</u>CH_2N<, dtt, J_1=11.7, J_2=5.8, J_3=1.3), 5.17 (0.34H, H*cis*-CH=CH-, ddd, J_1=14.0, J_2=1.9, J_3=0.9), 5.10 (0.34H, H*trans*-CH=CH-, ddd, J_1=19.9, J_2=1.9, J_3=0.9), 4.08 (1.32H, =CHC<u>H</u>$_2$OH, dd, J_1=5.3, J_2=1.3), 3.70-3.10 (1H, OH, s), 3.42 (0.68H, >CHC<u>H</u>$_2$OH, dd, J_1 =9.1, J_2=7.9), 3.15-2.90 (0.34H, >C<u>H</u>CH_2OH, m), 2.89 (1.32H, =CHC<u>H</u>$_2$N<, dd, J_1=5.8, J_2=1.2), 2.85-2.10 (4H, -C<u>H</u>$_2$(CH$_2$)$_3$C<u>H</u>$_2$-, m), 1.70-1.20 (6H, -CH$_2$(C<u>H</u>$_2$)$_3$CH$_2$-, m); ^{13}C NMR, 134.01, 133.11(*), 127.27, 119.33(*), 68.30(*), 60.16(*), 59.36, 55.40, 54.06, 47.20(*), 26.92, 28.42, 25.65, 24.82(*), 24.60(*), 24.07(*); Ir, 3392, 3077, 1679, 1640, 1454, 1443, 1383, 1155, 1116, 1038, 698.

Reaction of ***1*** *with* ***2d****; preparation of* ***3d*** [Z/E=68/32]: 3.50 h, 10%,100%; m/e (I%), 171 (M^+, 0.8), 170 (0.6), 157 (9.3), 156 (90.4), 114 (12.9), 101 (32.6), 100 (6.2), 96 (20.8), 87 (6.2), 86 (100), 84 (7.3), 72 (7.3), 71 (5.6), 70 (21.3), 69 (39.3), 68 (6.2), 56 (4.5); ^{1}H NMR, 5.76 (0.68H, =C<u>H</u>CH_2OH, dtt, J_1=11.8, J_2= 5.0, J_3=1.2), 5.65-5.43 (1.32H, =C<u>H</u>CH_2N< and *trans* C<u>H</u>=C<u>H</u>, m), 4.08 (1.36H, =CHC<u>H</u>$_2$OH, dd, J_1=5.0, J_2=1.3), 4.01 (0.64H, =CHC<u>H</u>$_2$OH, d, J=4.5), 3.20-2.95 (3H, =CHC<u>H</u>$_2$N< and -OH, m), 2.05-1.85 (1.36H,

-N(C<u>H</u><)$_2$, m), 1.45-1.20 (0.64H, -N(C<u>H</u><)$_2$, m), 1.01 (12H, 4Me, d, J=6.7); ^{13}C NMR, 132.89, 129.13(*), 128.86, 63.54(*), 59.45, 48.06, 41.93(*), 34.24, 19.83; Ir, 3348, 1681, 1462, 1390, 1365, 1199, 1177, 1118, 1031, 972, 701.

Reaction of 1 with 2e; preparation of 3e and 4e: 2.3 h, 54%, 66(65)/34(35); **3e**: m/e (I%), 141 (M$^+$,1.2), 140 (3.8), 110 (9.4), 96 (3.8), 84 (27.0), 72 (39.6), 71 (39.6), 70 (100), 68 (10.1), 55 (5.0); **4e**: m/e (I%), 111 (M$^+$-30, 7.8), 100 (100), 80 (3.8), 70 (8.9), 68 (6.3); **3e, 4e** mixture: ^{1}H NMR, 5.98-5.75 (1H, =C<u>H</u>CH$_2$OH and CH$_2$=C<u>H</u>-, m), 5.69 (0.65H, =C<u>H</u>CH$_2$N<, dtt, J$_1$=11.5, J$_2$=5.9, J$_3$=1.2), 5.32-5.17 (0.70H, C<u>H$_2$</u>=CH-, m), 4.80-4.20 (1H, -OH, s), 4.17 (1.30H, =CHC<u>H$_2$</u>OH, dd, J$_1$=5.2, J$_2$=1.2), 3.61 (0.70H, >CHC<u>H$_2$</u>OH, dd, J$_1$=5.9, J$_2$=1.7), 3.14 (1.30H, =CHC<u>H$_2$</u>N<, dd, J$_1$=5.9, J$_2$=1.1), 2.99 (0.35H, >C<u>H</u>CH$_2$OH, dt, J$_1$=8.5, J$_2$=6.1), 2.70-1.60 (4H, -C<u>H$_2$</u>(CH$_2$)$_2$C<u>H$_2$</u>-, m), 2.00-1.60 (4H, -CH$_2$(C<u>H$_2$</u>)$_2$CH$_2$-, m); ^{13}C NMR, 135.58(*), 133.18, 127.48, 118.64(*), 67.76(*), 63.15(*), 59.30, 53.56, 52.15, 50.08(*), 23.31, 23.13(*); Ir, 3382, 3075, 1644, 1630, 1460, 1371, 1133, 1071, 682.

Chemically pure **3e**, recovered by MPLC (hexane / methanol / methylenechloride = 9/1/1), showed: ^{1}H NMR, 5.85 (1H, =C<u>H</u>CH$_2$OH, dtt, J$_1$=11.5, J$_2$=5.2, J$_3$=1.1), 5.69 (1H, =C<u>H</u>CH$_2$N<, dtt, J$_1$=11.5, J$_2$=5.9, J$_3$=1.2), 4.70-4.22 (1H, -OH, s), 4.17 (2H, =CHC<u>H$_2$</u>OH, dd, J$_1$= 5.2, J$_2$=1.2), 3.14 (2H, =CHC<u>H$_2$</u>N<, dd, J$_1$=5.9, J$_2$=1.1), 2.70-2.40 (4H, -N(C<u>H$_2$</u>CH$_2$)$_2$, m), 2.00-1.60 (4H, -N(CH$_2$C<u>H$_2$</u>)$_2$ m); ^{13}C NMR, 133.18, 127.48, 59.30, 53.56, 52.15, 23.31; Ir, 3354, 3020, 1660, 1461, 1344, 1131, 1036, 704.

Reaction of 1 with 2f; preparation of 3f and 4f: 1.30 h, 56%, 52(50)/48(50); **3f**: m/e (I%), 191 (M$^+$, 1.5), 190 (3.0), 160 (6.1), 134 (6.1), 122 (32.3), 121 (27.7), 120 (47.7), 92 (12.3), 91 (100), 65 (16.9); **4f**: m/e (I%), 161 (M$^+$-30, 8.2), 160 (67.2), 92 (13.1), 91 (100), 65 (18.0); **3f, 4f** mixture: ^{1}H NMR, 7.30 (5H, Ph, s), 6.00-5.60 (0.5H, CH$_2$=C<u>H</u>-, m), 5.93 (0.5H, =C<u>H</u>CH$_2$OH, dtt, J$_1$=11.6, J$_2$=5.2, J$_3$=1.1), 5.71 (0.5H, =C<u>H</u>CH$_2$N<, dtt, J$_1$=11.6, J$_2$=6.0, J$_3$=1.3), 5.34 (0.5H, H*cis*-CH=CH-, dd, J$_1$=10.5, J$_2$=1.8), 5.22 (0.5H, H*trans*-CH=CH-, dd, J$_1$=17.1, J$_2$=1.8), 4.18 (1H, =CHC<u>H$_2$</u>OH, dd, J$_1$=5.2, J$_2$=1.3), 3.74 (1H, >NC<u>H$_2$</u>Ph, s), 3.70-3.40 (2H, >NC<u>H$_2$</u>Ph and >CHC<u>H$_2$</u>OH, m), 3.38-3.12 (0.5H, >C<u>H</u>CH$_2$OH, m), 3.06 (1H, =CHC<u>H$_2$</u>N<, dd, J$_1$=6.0, J$_2$=1.1), 2.20 (3H, >NMe, s), 2.20-2.00 (1H, -OH, s); ^{13}C NMR, 138.75(*), 137.39, 134.44, 131.96(*), 129.38, 128.89(*), 128.47, 128.39(*), 127.44, 127.19, 127.17 (*), 120.30(*), 66.36(*), 61.85, 60.84(*), 59.71, 58.07 (*), 54.13, 41.41, 36.34(*).

Chemically pure **3f** and **4f**, recovered by HPLC (hexane / methanol / methylenechloride = 10/1/1), showed:

3f, ^{1}H NMR, 7.30 (5H, Ph, s), 5.93 (1H, =C<u>H</u>CH$_2$OH, dtt, J$_1$=11.6, J$_2$=5.2, J$_3$=1.1), 5.71 (1H, =C<u>H</u>-CH$_2$N<, dtt, J$_1$=11.6, J$_2$=6.0, J$_3$=1.3), 4.18 (2H, =CHC<u>H$_2$</u>OH, dd, J$_1$= 5.2, J$_2$=1.3), 3.74 (2H, >NC<u>H$_2$</u>Ph, s), 3.06 (2H, =CHC<u>H$_2$</u>N<, dd, J$_1$=6.0, J$_2$=1.1), 2.20 and 2.17 (4H, >NMe and -OH, 2s); ^{13}C NMR, 137.39, 134.44, 129.38, 128.47, 127.44, 127.19, 61.85, 59.71, 54.13, 41.41; Ir, 3368, 3085, 3063, 3026, 1662, 1603, 1495, 1455, 1076, 742, 700;

4f, ^{1}H NMR, 7.30 (5H, Ph, s), 5.80 (1H, CH$_2$=C<u>H</u>-, ddd, J$_1$=17.1, J$_2$=10.5, J$_3$=8.4), 5.34 (1H, H*cis*-CH=CH-, dd, J$_1$=10.5, J$_2$=1.8), 5.22 (1H, H*trans*-CH=CH-, dd, J$_1$=17.1, J$_2$=1.8), 3.80-3.40 (4H, >NC<u>H$_2$</u>Ph and >CHC<u>H$_2$</u>OH, m), 3.40-3.15 (1H, >C<u>H</u>CH$_2$OH, m), 2.80-2.30 (1H, -OH, s), 2.20 (3H, >NMe, s); ^{13}C NMR, 138.75, 131.96, 128.89, 128.39, 127.17, 120.30, 66.36, 60.84, 58.07, 36.34; Ir, 3435, 3064, 3028, 1637, 1604, 1495, 1455, 1076, 738, 700.

Reaction of 1 with 2g; preparation of 3g and 4g: 1.30 h, 55%, 12(6)/88(94); **3g**: m/e (I%), 177 (M$^+$, 18.7), 144 (12.5), 120 (32.8), 107 (100), 106 (42.2), 104 (14.1), 77 (29.7), 51 (10.9); **4g**: m/e (I%), 177 (M$^+$, 27.6), 147 (24.1), 146 (100), 144 (27.6), 131 (65.5), 130 (62.1), 118 (27.6), 106 (20.7), 104 (29.3), 91 (24.1), 77

(67.2), 51 (24.1); **3g, 4g** mixture: ^{1}H NMR, 7.40-7.18 (2H, 2*o*H, m), 6.97-6.70 (3H, 2*m*H and 1*p*H, m), 5.87-5.66 (0.06H, =C<u>H</u>CH$_2$OH, m), 5.76 (0.94H, CH$_2$=C<u>H</u>-, ddd, J_1=17.4, J_2=10.8, J_3=5.7), 5.60 (0.06H, =C<u>H</u>CH$_2$N<, dtt, J_1=11.2, J_2=6.1, J_3=1.2), 5.22 (0.94H, <u>H</u>*cis*-CH=CH-, ddd, J_1=10.8, J_2=1.4, J_3=1.4), 5.14 (0.94H, <u>H</u>*trans*-CH=CH-, ddd, J_1=17.4, J_2=1.5, J_3=1.5), 4.52-4.35 (0.94H, >C<u>H</u>CH$_2$OH, m), 4.28 (0.12H, =CHC<u>H$_2$</u>OH, dd, J_1=6.4, J_2=1.2), 3.95 (0.12H, =CHC<u>H$_2$</u>N<, d, J=6.1), 3.77 (1.88H, >CHC<u>H$_2$</u>OH, dd, J_1=8.5, J_2=6.4), 2.90 (0.18H, >NMe, s), 2.78 (2.82H, >NMe, s), 2.30-1.90 (1H, -OH, s); ^{13}C NMR, 150.89, 133.05, 131.11(*), 129.12, 128.62(*), 118.41, 118.01, 114.95, 113.46(*), 63.39, 61.70, 58.59(*), 49.94(*), 38.24(*), 31.70.

Chemically pure **3g** and **4g**, recovered by HPLC (hexane / methanol / methylenechloride = 9/1/1), showed:

3g, ^{1}H NMR, 7.40-7.18 (2H, 2*o*H, m), 6.97-6.70 (3H, 2*m*H and 1*p*H, m), 5.79 (1H, =C<u>H</u>CH$_2$OH, dtt, J_1=11.2, J_2=6.4, J_3=1.6), 5.60 (1H, =C<u>H</u>CH$_2$N<, dtt, J_1=11.2, J_2=6.1, J_3=1.2), 4.28 (2H, =CHC<u>H$_2$</u>OH, dd, J_1=6.4, J_2=1.2), 3.95 (2H, =CHC<u>H$_2$</u>N<, d, J=6.1), 2.90 (3H, >NMe, s), 1.40-1.20 (1H, -OH, s); ^{13}C NMR, 150.89, 131.11, 129.12, 128.62, 118.01, 113.46, 58.59, 49.94, 38.24; Ir, 3368, 3010, 1599, 1505, 1366, 1201, 1125, 1033, 750, 692;

4g, ^{1}H NMR, 7.40-7.18 (2H, 2*o*H, m), 6.97-6.70 (3H, 2*m*H and 1*p*H, m), 5.76 (1H, CH$_2$=C<u>H</u>-, ddd, J_1=17.4, J_2=10.8, J_3=5.7), 5.22 (1H, <u>H</u>*cis*-CH=CH-, ddd, J_1=10.8, J_2=1.4, J_3=1.4), 5.14 (1H, <u>H</u>*trans*-CH=CH-, ddd, J_1=17.4, J_2=1.5, J_3=1.5), 4.52-4.35 (1H, >C<u>H</u>CH$_2$OH, m), 3.77 (2H, >CHC<u>H$_2$</u>OH, dd, J_1=8.5, J_2=6.4), 2.78 (3H, >NMe, s), 2.50-2.30 (1H, -OH, s); ^{13}C NMR, 150.89, 133.05, 129.12, 118.41, 118.01, 114.95, 63.39, 61.70, 31.70; Ir, 3392, 3024, 3010, 1639, 1598, 1574, 1381, 1212, 1129, 1034, 749, 693.

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