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Reaction of Dianion β-Enamino Ketones with Electrophiles. Part. 4.# Synthesis of β'- and δ-Hydroxy-β-enamino Ketones.

Giuseppe Bartoli,[a]* Marcella Bosco,[b] Cristina Cimarelli,[a] Renato Dalpozzo,[b] Gianni Palmieri.[a]

[a] *Dipartimento di Scienze Chimiche, Via S.Agostino 1, I-62032 Camerino (MC), Italy*
[b] *Dipartimento diChimica Organica "A.Mangini",Viale Risorgimento 4, I-40136, Bologna, Italy*

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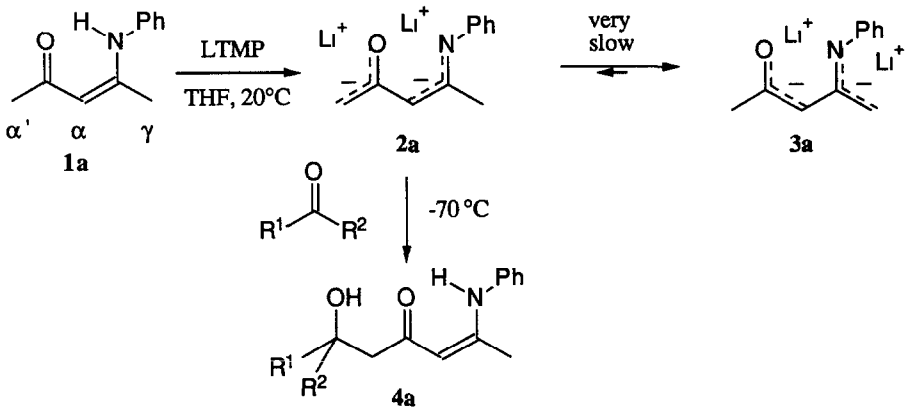
Abstract Selective generation techniques of α' and γ dianions of β-enamino ketones allow an almost complete regiocontrol in the reaction with aldehydes and ketones for the synthesis of β'- and δ-hydroxy-β-enamino ketones An important role is also displayed by bulkiness of the substituent at the nitrogen atom The reaction gives good to high yields even with enolizable carbonylic compounds α,β-insaturated aldehydes and ketones generally undergo 1,2-addition process except in the case of high sterically hindered compounds

1,3-Diketones and their derivatives are important building blocks for the construction of a large variety of heterocyclic compounds[1] as well as useful intermediates for the synthesis of many biologically active molecules [2] The introduction of an alkyl side chain containing an hydroxyl function at the α'- or γ-position of a 1,3-diketone represents an important synthetic goal since the added functionality would increase the synthetic scope of these intermediates However the classical approach *ie* the reaction of 1,3-diketone dianion with aldehydes and ketones suffers of some drawbacks due to an intrinsic impossibility of regiocontrol in unsymmetrical systems and to very poor yields obtained with enolizable substrates [3] Analogous unsatisfactory results were found when using closely related systems such as dipotassium or disodium salts of the enaminone [4] We have recently shown that in the case of acyclic β-(monoalkylamino)-α,β-unsaturated ketones appropriate generation techniques of the dianion allow an actual regiodirected control of the attack to α'- or γ-position in the reaction with alkyl halides,[5] oxiranes[6] and nitriles [7] We wish to report now an application of this procedure to the reaction with aldehydes and ketones for an efficient and regiocontrolled synthesis of β'- and δ-hydroxy-β-enamino ketones

Synthesis of β'-hydroxy-β-enaminoketones. Treatment of a β-enamino ketone of type **1ab** (see schemes of Tables 1 and 2) with 2 5 equivalent of a strong lithium base in THF produce both α'- (**2**) and/ or γ-dianion (**3**) The former product is the kinetically favoured isomer being, in the initially formed monoanion, the γ protons shielded from attack of the base by the substituent at the nitrogen atom Moreover, in the absence of a lithium complexating agent the α'-dianion is generated in a geometry which does not permit a rapid intramolecular isomerisation into the more stable γ-isomer [5b] Thus, the optimum conditions for generation of **2**

for Part 3, see reference 7

Table 1 - Synthesis of β'-hydroxy-β-enamino ketones **4aa-am** from reaction of **aldehydes or** ketones with the α'-dianion (**2a**) generated from 4-anilino-pent-3-en-2-one (**1a**) by treatment with 2 5 eq of LTMP in THF

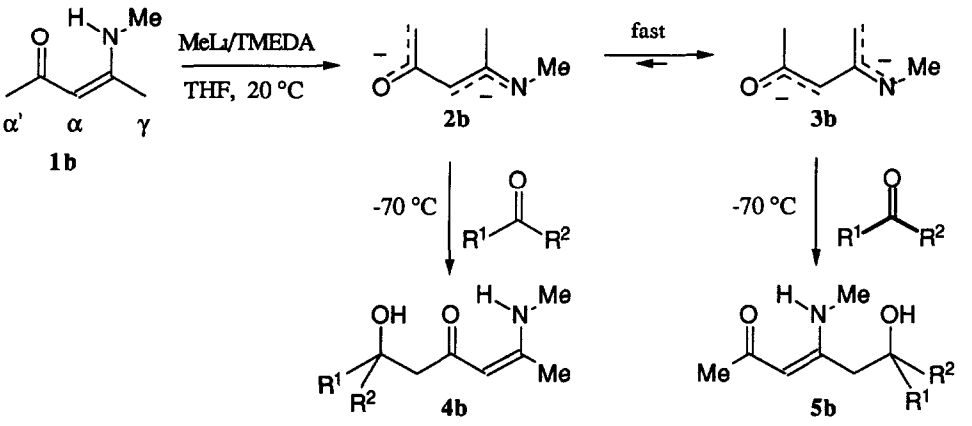


Entry	R^1	R^2	4a	Yield(%)[a]
1	H	Pr	**4aa**	85
2	H	Bu^t	**4ab**	82
3	H	n-C_6H_{13}	**4ac**	58
4	H	Ph	**4ad**	79
5	H	CH=CH-Ph	**4ae**	86
6	Me	Me	**4af**	90
7	Me	Ph	**4ag**	97
8	Me	$(CH_2)_2$-Ph	**4ah**	98
9	Ph	Ph	**4ai**	93
10	Me	CH=CH-Ph	**4al**	93
11	Ph	CH=CH-Ph	**4am**	41[b]

[a] Yields given for pure isolated products
[b] together a 51% of yield of 1,4-addition product.

requires the use of a strongly hindered base such as lithium tetramethylpiperidide (LTMP) as well as the presence of a bulky substituent (*e g* phenyl group) at the nitrogen atom (see scheme of Table 1) When 4-anilino-pent-3-en-2-one (**1a**) was treated with LTMP (2 5 eq) at 0° C in THF for 2 hours, followed by addition of an excess of the appropriate carbonylic compound at -70 °C, the usual work up gave the expected β'-hydroxy-β–enamino ketone (**4aa-am**) not contaminated by the presence of the corresponding δ-isomer The reaction shows general applicability, good to high yields being obtained for a large variety of aldehydes and ketones It is noteworthy that excellent yields were found even with high sterically hindered substrates(*e g*

Table 2 - Synthesis of δ-hydroxy-β-enamino ketones **5ba-bl** and β'-hydroxy-β-enamino ketones **4ba-bl** from reaction of **aldehydes or ketones** with the α'-(**2b**) and γ-dianions (**3b**) generated from 4-methylamino-pent-3-en-2-one (**1a**) by treatment with MeLi/TMEDA



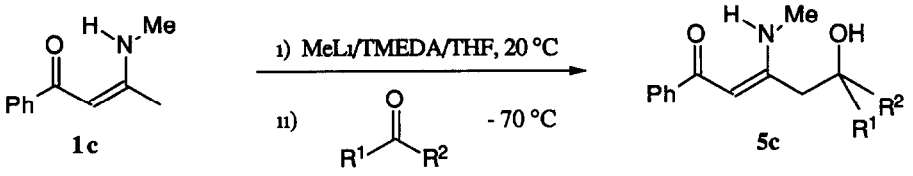
Entry	R^1	R^2	4b	Yield (%) [a]	5b	Yield (%) [a]
12	H	Pr	**4ba**	9	**5ba**	47
13	H	Bu^t	**4bb**	15[b]	**5bb**	80
14	H	n-C_6H_{13}	**4bc**	16	**5bc**	67
15	H	Ph	**4bd**	6	**5bd**	73
16	H	CH=CH-Ph	**4be**	18	**5be**	53
17	Me	Me	**4bf**	7	**5bf**	75
18	Me	Ph	**4bg**	11[b]	**5bg**	60
19	Me	$(CH_2)_2$-Ph	**4bh**	20	**5bh**	60
20	Ph	Ph	**4bi**	39	**5bi**	55
21	Me	CH=CH-Ph	**4bl**	28	**5bl**	65

[a] Yields given for pure isolated products except otherwise mentioned.
[b] Yields obtained by GC-MS analysis

tetramethylacetaldehyde and benzophenone, entries 2 and 9) and easily enolizable ketones (*e g* acetophenone, entry 7) α,β-Unsaturated compounds gave the 1,2 addition product (entries 5 and 10) except in the case of highly sterically hindered ketones such as 1,3-diphenil-2-propen-1-one where the 1,2 and 1,4 addition products account for the 41% and 51% yields of the reaction, respectively

Synthesis of δ-hydroxy-β-enaminoketones. When metallation of enaminones is carried out with MeLi in the presence of an equimolecular amount of TMEDA, the kinetically favoured α'-dianion **2** is generated in a geometry suitable for rapid intramolecular equilibration into the more stable γ-isomer **3** (see

Table 3 - Synthesis fo δ-hydroxy-β-enamino ketones **5cd-co** from reaction of **aldehydes or ketones** with the γ-dianion (**3c**) generated from 1phenyl-3-methylamino-but-3-en-1-one (**1c**) by treatment with MeLi/TMEDA



Entry	R^1	R^2	5c	Yield (%)[a]
22	H	Ph	**5cd**	95
23	H	Et	**5cm**	61
24	H	c-C_6H_{11}	**5cn**	85
25	Me	Me	**5cf**	96
26	Me	Ph	**5cg**	94
27	Et	Et	**5co**	96

[a] Yields given for pure isolated products

scheme of Table 2) Under these condition alkylation with primary halides exclusively occurs at the γ position independently from the size of the substituent at nitrogen atom [5b] Otherwise, preliminary experiments with aldehydes and ketones showed that bulky substituents at nitrogen (*e g* phenyl group as in **1a**) favour the formation of the α' product. Theoretical calculations allowed to assert that in any possible conformation of the dianion **3b** the N-substituent is in a *syn* position with respect to the γ carbon atom and by consequence there is a difficult access to the reaction centre of hindered electrophiles such as cabonylic derivatives. So the more reactive α' dianion (**2**), although present in negligible concentration, can reacts competitively since its amount is quickly restored by fast equilibrium existing between **2** and **3** Therefore it is necessary to carry out the reaction with enaminones bearing N-substituent of moderate size for regiodirecting the attack to the γ position (see scheme of Table 2) The results from the reaction of 4-(N-methylamino)-pent-2-en-1-one (**1b**) with various aldehydes and ketones are summarized in table 2 In all cases good to high yields were obtained The isolated amount of undesired α'-hydroxy derivative is generally low except in the case of the high sterically hindered benzophenone (entry 20) Finally we wanted to re-examine the reactivity of 1-phenyl-3-(N-monoalkylamino)-but-2-en-1-one system In a previous communication we reported that the dianion of the N-isopropyl derivative generated by treatment with 2 5 equivalent of LTMP in THF gave very unsatisfactory results [5a] For example, the reaction with acetone did not exceed 28% yields In the light of the findings discussed above that failure must be ascribed both to an unappropriate choice of the substituent at the nitrogen atom as well as to the metallation conditions employed In fact, the dianion generated from the N-methyl

derivative **1c**, under the same procedure adopted for **1b**, reacts with a large variety of carbonylic compounds to affords the expected addition products in very high yields (see table 3) For example, the reaction with highly enolizable ketones such as acetone and acetophenone is almost quantitative (96% and 94% yields respectively)

In conclusion the reaction of α' and γ-dianions of β-enamino ketones with aldehydes and ketones provides an efficient and regiodirected synthesis of β'- and δ-hydroxy derivatives respectively The high efficiency of the reaction with respect to previously known procedures must be ascribed to the choice of appropriate selective techniques to generate the dianion It is noteworthy that the reaction works well even with highly enolizable carbonylic compounds

EXPERIMENTAL

^1H and ^{13}C-NMR spectra were recorded with a Varian VXR 300 instrument Chemical shifts are given in ppm downfield from Me_4Si in $CDCl_3$ solution Coupling constants are given in Hertz IR spectra were recorded with a Perkin-Elmer 257 spectrometer GC-MS analyses were performed with an HP 59970 workstation formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector THF were dried by refluxing over sodium wires until the blue colour of benzophenone ketyl persisted and then distilling into a dry receiver under nitrogen atmosphere Commercial methyllithium and butyllithium solutions (Aldrich) were employed under dry atmosphere Commercial TMEDA and TMP (Aldrich) were distilled and dried before use Lithium tetramethylpiperidide (LTMP) was prepared from equimolecular amounts of butyllithium and amine in THF at 0 °C Starting β-enamino ketones (**1a-c**) were synthesized by the condensation of the appropriate 1,3-diketone and primary amine according to Singh and Tandon's procedure [8]

Synthesis of β'-hydroxy-β-enamino ketones* 4aa-am *from reaction of aldehydes or ketones with the α'-dianion* (2a) *generated from 4-anilino-pent-3-en-2-one* (1a) *by treatment with LTMP/THF A solution of LTMP (5 mmol in THF, 6ml) was dropped into a stirred solution of **1a** (2 mmol in THF, 6ml) at 0 °C under nitrogen The temperature was allowed to rise to 20 °C and the mixture stirred at this temperature for 1 hour The mixture was cooled at -70 °C then a solution of the appropriate carbonyl compound (6 mmol in THF, 3ml) was slowly added (30 min) The temperature was allowed to rise to 20 °C and the mixture stirred at this temperature for 1 hour further Then the solution was poured into saturated aqueous ammonium chloride (5 ml) and extracted with diethyl ether, the organic layer was dried, evaporated under reduced pressure and submitted to a chromatographic separation on a silica gel column (hexane ethyl acetate from 5 1 to1 1 as eluent) Yields of isolated pure β'-hydroxy-β-enamino ketones **4aa-am** are reported in Table 1 Physical data follows

6-Hydroxy-2-(N-Phenylamino)-non-2-en-4-one (**4aa**) Oil (Found C, 72 89, H, 8 51, N, 5 74 $C_{15}H_{21}NO_2$ requires C, 72 84, H, 8 56, N, 5 66 %), ^1H-NMR δ 0 92 (t, J=7 0, 3H, $(CH_2)_2C\underline{H}_3$), 1 57-1 32 (m, 4H, $(C\underline{H}_2)_2CH3$), 1 98 (s, 3H, g-CH3), 2 37 (dd, J=15 4, 8 8, 1H, α'-CH_2,Ha), 2 50 (dd, J=15 4, 2 9, 1H, α'-CH2,Hb), 3 97-4 03 (m, 1H, C$\underline{H}$OH), 4 09 (bs, 1H, OH), 5 14 (s, 1H, CH), 7 00-7 40 (m, 5H, Ph), 12 45 (bs, 1H, NH) ^{13}C-NMR δ 13 99 (q), 18 64 (t), 19 77 (q), 38 99 (t), 47 25 (t), 68 80 (d), 97 53 (d), 124 68 (d), 125 79 (d), 129 03 (d), 138 05 (s), 161 14 (s), 198 04 (s) IR ν_{max}(film) 3370(broad), 1575, 1545, 1305, 1135, 735, 685 cm^{-1} MS m/z (%) 247 (M+,25), 176 (46), 160 (100), 132 (66), 118 (51), 77 (45)

7,7-Dimethyl-6-hydroxy-2-(N-Phenylamino)-oct-2-en-4-one (**4ab**) Mp 63-65 °C (dichloromethane /hexane), (Found C, 73 69, H, 8 73, N, 5 54 $C_{16}H_{23}NO_2$ requires C, 73 53, H, 8 87, N, 5 36 %), ^{1}H-NMR δ 0 92 (s, 9H, $3CH_3$), 1 98 (s, 3H, γ-CH_3), 2 29 (dd, J=15 1, 10.4, 1H, α'-CH2,Ha), 2 52 (dd, J=15 1, 2 0, 1H, α'-CH_2,Hb), 3 68 (dd, J=10 4, 2 0, 1H, C<u>H</u>OH), 4 03 (bs, 1H, OH), 5.18 (s, 1H, CH), 7 00-7 45 (m, 5H, Ph), 12 45 (bs, 1H, NH) ^{13}C-NMR δ19 47 (q), 25 33 (q), 34 00 (s), 41 96 (t), 76 30 (d), 97 28 (d), 124 36 (d), 125 48 (d), 128 72 (d), 137 92 (s), 161 04 (s), 198 39 (s) IR ^{13}C-NMR ν_{max} (nujol) 3340 (broad), 1555, 1525, 1210, 1100, 710, 660 cm^{-1} MS m/z (%) 261 (M^+,8), 204 (17), 176 (27), 160 (100), 132 (15), 77 (13)

6-Hydroxy-2-(N-Phenylamino)-dodec-2-en-4-one (**4ac**) Oil (Found C, 74 83, H, 9.52, N, 4 75 $C_{18}H_{27}NO_2$ requires C, 74 70, H, 9 40, N, 4 84 %), ^{1}H-NMR δ 0 83-0 94 (m, 3H, $(CH_2)_5C\underline{H}_3$), 1 20-1 89 (m, 10H, $(C\underline{H}_2)_5CH_3$), 1 99 (s, 3H, γ-CH_3), 2 37 (dd, J=15 5, 8 9, 1H, α'-CH_2,Ha), 2 52 (dd, J=15 5, 2 7, 1H, α'-CH_2,Hb), 3 96-4 06 (m, 1H, C<u>H</u>OH), 4 08 (bs, 1H, OH), 5 14 (s, 1H, CH), 7 08-7 39 (m, 5H, Ph), 12 50 (bs, 1H, NH) ^{13}C-NMR δ 14 08 (q), 19 88 (q), 22 60 (t), 25 51 (t), 29 30 (t), 31 83 (t), 36 99 (t), 47 29 (t), 69 32 (d), 97 63 (d), 124 79 (d), 125 91 (d), 129 13 (d), 138 30 (s), 161 52 (s), 198 11 (s) IR ν_{max} (film) 3330 (broad), 1575, 1545, 1475, 1415, 1315, 735, 680 cm^{-1} MS m/z (%) 289 (M^+,7), 204 (11), 186 (28), 160 (100), 133 (47), 77 (13)

6-Phenyl-6-hydroxy-2-(N-Phenylamino)-hex-2-en-4-one (**4ad**) Mp 95-97 °C (CH_2Cl_2/hexane), (Found C, 76 79, H, 6 73, N, 4 82 $C_{18}H_{19}NO_2$ requires C, 76 84, H, 6 81, N, 4 98 %), ^{1}H-NMR δ 1 99 (s, 3H, CH_3), 2 73 (d, J=6 3, 2H, CH_2), 4 73 (bs, 1H, OH), 5 18 (s, 1H, CH), 5 19 (t, J=6 3, 1H, C<u>H</u>OH), 7 10-7 50 (m, 10H, 2Ph), 12 55 (bs, 1H, NH) ^{13}C-NMR δ 19 51 (q), 49 17 (t), 71 00 (d), 97 20 (d), 124 31 (d), 125 37 (d), 125 60 (d), 126 85 (d), 127 93 (d), 128 80 (d), 137 70 (s), 143 47 (s), 161 27 (s), 196 73 (s) IR ν_{max} (nujol) 3280 (broad), 1580, 1550, 1520, 710, 665 cm^{-1} MS m/z (%) 263 (M^+-18,13), 186 (100), 77 (23), 51 (8)

8-Phenyl-6-Hydroxy-2-(N-Phenylamino)-octa-2,7-dien-4-one (**4ae**) Mp 92-94 °C (CH_2Cl_2/hexane), (Found C, 78 26, H, 6 77, N, 4 71 $C_{20}H_{21}NO_2$ requires C, 78 15, H, 6 89, N, 4 56 %), ^{1}H-NMR δ 1 98 (s, 3H, CH_3), 2 61 (dd, J=15 4, 8 4, 1H, α'-CH_2,Ha), 2 69 (dd, J=15 3, 3 9, 1H, α'-CH_2, Hb), 4 60 (bs, 1H, OH), 4 76-4 85 (m, 1H, <u>CH</u>OH), 5 20 (s, 1H, CH), 6 29 (dd, J=15 9, 6 0, 1H, γ'-CH), 6 69 (d, J=15 9, 1H, δ'-CH), 7 08-7 43 (m, 10H, 2Ph), 12 50 (bs, 1H, NH) ^{13}C-NMR δ 19 67 (q), 47 25 (t), 69 81 (d), 97 48 (d), 124 52 (d), 125 73 (d), 126 25 (d), 127 17 (d), 128 25 (d), 128 93 (d), 129 38 (d), 131 27 (d), 136 72 (s), 137 98 (s), 161 62 (s), 196 61 (s) IR ν_{max} (nujol) 3230 (broad), 1580, 1550, 1520, 715, 665 cm^{-1} MS m/z (%) 289 (M^+-18, 35), 261 (17), 170 (26), 144 (38), 77 (69)

6-Methyl-6-hydroxy-2-(N-Phenylamino)-hept-2-en-4-one (**4af**) Oil (Found C, 72 18, H, 8 09, N, 5 84 $C_{14}H_{19}NO_2$ requires C, 72 07, H, 8 21, N, 6 00 %), ^{1}H-NMR δ 1 18 (s, 6H, $2CH_3$), 1 91 (s, 3H, γ-CH_3), 2 38 (s, 2H, CH_2), 5 06 (s, 1H, CH), 5 11 (bs, 1H, OH), 6 95-7 28 (m, 5H, Ph), 12 52 (bs, 1H, NH) ^{13}C-NMR δ 19 41 (q), 29 13 (q), 51 39 (t), 69 79 (s), 98 14 (d), 124 17 (d), 125 50 (d), 128 70 (d), 137 70 (s), 161 34 (s), 193 72 (s) IR ν_{max} (film) 3405 (broad), 1570, 1335, 1250, 750, 695 cm^{-1} MS m/z (%) 233 (M^+,30), 200 (9); 175 (30), 160 (100), 132 (32), 77 (15)

6-Phenyl-6hydroxy-2-(N-Phenylamino)-hept-2-en-4-one (**4ag**) Mp 104-106 °C (CH_2Cl_2/hexane) (Found C, 77 39, H, 7 29, N, 4 57 $C_{19}H_{21}NO_2$ requires C, 77 26, H, 7 17, N, 4 74 %), ^{1}H-NMR δ 1 54 (s, 3H, CH_3), 1 96 (s, 3H, γ-CH_3), 2 68 (d, J=15 4, 1H, CH_2,Ha), 2 94 (d, J=15 4, 1H, CH_2,Hb), 5 06 (s, 1H, CH), 5 96 (s, 1H, OH), 7 05-7 55 (m, 10H, 2Ph), 12 40 (bs, 1H, NH) ^{13}C-NMR δ 19 89 (q), 30 90 (q),

51 56 (t), 73 90 (s); 98 26 (d), 124 67 (d), 124 83 (d), 126 07 (d), 126 29 (d), 128 02 (d); 129 12 (d); 136 24 (s), 148 31 (s), 161 74 (s), 197 42 (s) IR ν_{max} (nujol) 3360 (broad); 1580, 1555, 735 cm^{-1} MS[9].

8-Phenyl-6-methyl-6-hydroxy-2-(N-Phenylamino)-oct-2-en-4-one (**4ah**) Oil (Found C, 77 81; H, 7 91, N, 4 21 $C_{21}H_{25}NO_2$ requires C, 77 99, H, 7 79, N, 4 33 %), ^{1}H-NMR δ 1 40 (s, 3H, CH_3), 1 80-1 95 (m, 2H, CH_2), 2 00 (s, 3H, γ-CH_3), 2 51 (d, J=14 8, 1H, α'-CH_2,Ha), 2 61 (d, J=14 8, 1H, α'-CH_2,Hb), 2 70-2 90 (m, 2H, CH_2), 5 20 (s, 1H, CH), 5 40 (bs, 1H, OH), 7 10-7 40 (m, 10H, 2Ph), 12 70 (bs, 1H, NH) ^{13}C-NMR δ 19 52 (q), 26 78 (t), 30 14 (q), 43 99 (t), 49 94 (t), 71 82 (s), 98 34 (d), 124 34 (d), 125 24 (d), 125 68 (d), 127 96 (d), 128 05 (d), 128 81 (d), 137 72 (s), 142 49 (s), 161 65 (s), 197 75 (s) IR ν_{max} (film) 3400 (broad), 1580, 1340, 1250, 740, 690 cm-1 MS m/z (%) 305 (M^+-18, 19), 304 (20), 200 (20), 160 (35), 131 (39), 91 (100); 77 (31)

6,6-Diphenyl-6-hydroxy-2-(N-Phenylamino)-hex-2-en-4-one (**4ai**) Mp 168-169 °C (CH_2Cl_2/hexane) (Found C, 80 77, H, 6 57, N, 4 07 $C_{24}H_{23}NO_2$ requires C, 80 64, H, 6 49, N, 3 92 %), ^{1}H-NMR δ 1 98 (s, 3H, CH_3), 3 29 (s, 2H, CH_2), 5 20 (s, 1H, CH), 6 70 (s, 1H, OH), 7 05-7 50 (m, 15H, 3Ph), 12 30 (bs, 1H, NH) ^{13}C-NMR δ 19 96 (q), 50 28 (t), 77 71 (s); 98 15 (d), 124 85 (d), 125 94 (d), 126 58 (d), 128 05 (d), 128 29 (d), 129 12 (d), 136 24 (s), 147 32 (s), 161 90 (s), 197 04 (s) IR ν_{max} (nujol) 3320 (broad), 1585, 1555, 685 cm^{-1} MS[9]

8-Phenyl-6-methyl-6-hydroxy-2-(N-Phenylamino)-octa-2,7-dien-4-one (**4al**) Oil (Found C, 78 32; H, 7 42, N, 4 44 $C_{21}H_{23}NO_2$ requires C, 78 47, H, 7.21, N, 4 36 %), ^{1}H-NMR δ 1 44 (s, 3H, CH_3), 1 95 (s, 3H, γ-CH_3), 2 62 (d, J=15 0, 1H), 2 68 (d, J=15 0, 1H), 5 18 (s,1H, α'-CH), 5 75 (bs, 1H, OH), 6 36 (d, J=15 9, 1H, γ'-CH), 6 72 (d, J=15 9, 1H, δ'-CH), 7 00-7 50 (m, 10H, 2Ph); 12 55 (bs, 1H, NH) ^{13}C-NMR δ 19 18 (q), 28 12 (q), 50 05 (t), 71 95 (s), 97 76 (d), 123 97 (d), 125 33 (d), 125 79 (d), 126 36 (d), 126,47 (d), 127 77 (d), 128 46 (d), 135 81 (d), 136 60 (s), 137 33 (s), 161 43 (s), 196 54 (s) IR ν_{max} (film) 3340 (broad), 1575, 1545, 1325, 1240, 735, 680 cm^{-1} MS m/z (%) 321 (M^+,57), 278 (43), 264 (43), 160 (93), 133 (100), 77 (64)

6,8-Diphenyl-6-hydroxy-2-(N-Phenylamino)-octa-2,7-dien-4-one (**4am**) Mp 116-118 °C (CH_2Cl_2/hexane) (Found C, 81 57, H, 6 69, N, 3 46 $C_{26}H_{25}NO_2$ requires C, 81 43, H, 6 57, N, 3 65 %), ^{1}H-NMR δ 1 96 (s, 3H, CH_3), 3 01 (d, J=15 4, 1H), 3 09 (d, J=15 4, 1H), 5 19 (s,1H), 6 49 (d, J=15 9, 1H, γ'-CH), 6 51 (bs, 1H, OH), 6 71 (d, J=15 9, 1H, δ'-CH), 7 00-7 70 (m, 15H, 3Ph), 12 40 (bs, 1H, NH) ^{13}C-NMR δ 19 92 (q), 50 04 (t), 76 27 (s), 98 23 (d), 124 89 (d), 125 41 (d), 126 17 (d), 126 62 (d), 126 72 (d), 127 30 (d), 127 74 (d), 128 21 (d), 128 43 (d), 129 13 (d), 135 50 (d), 137 14 (s), 137 87 (s), 145 99 (s), 162 08 (s), 196 70 (s) IR ν_{max} (nujol) 3260 (broad), 1570, 1540, 730, 680 cm^{-1} MS m/z (%) 383 (M^+,5), 264 (25), 160 (100), 133 (29), 105 (19), 77 (31)

Synthesis of δ-hydroxy-β-enamino ketones* 5ba-bl *and β'-hydroxy-β-enamino ketones* 4ba-bl *from reaction of aldehydes or ketones with the α'-dianion* (2b) *and γ-dianion* (3b) *generated from 4-methylamino-pent-3-en-2-one* (1b) *by treatment with MeLi/TMEDA. A solution of MeLi (5 mmol in THF, 6ml) was dropped into a stirred solution of **1b** (2 mmol in THF, 6ml) and TMEDA (5 mmol) at 0 °C under nitrogen The temperature was allowed to rise to 20 °C and the mixture stirred at this temperature for 1 hour The mixture was cooled at -70 °C then a solution of the appropriate carbonyl compound (6 mmol in THF, 3ml) was slowly added (30 min) The temperature was allowed to rise to 20 °C and the mixture stirred at this temperature for 1 hour further Then the solution was poured into saturated aqueous ammonium chloride (5 ml) and extracted with diethyl ether, the organic layer was dried, evaporated

under reduced pressure and submitted to a chromatographic separation on a silica gel column (hexane ethyl acetate from 5 1 to 1.1 as eluent) Yields of isolated pure δ-hydroxy-β-enamino ketones **5ba-bl** and β'-hydroxy-β-enamino ketones **4ba-bl** are reported in Table 2 Physical data follows·

6-Hydroxy-4-(N-methylamino)-non-3-en-2-one (**5ba**) Oil (Found C, 64 68, H, 10.51, N, 7 74 $C_{10}H_{19}NO_2$ requires C, 64 83 H, 10.34, N, 7.56 %), ^{1}H-NMR δ 0 72-0 93 (m, 3H, $(CH_2)_2C\underline{H}_3$), 1 21-1 49 (m, 4H, $(C\underline{H}_2)_2CH_3$), 1 85 (s, 3H, CH_3), 2 20 (dd, J=15 9, 4.8, 1H, γ-CH_2,Ha), 2 25 (dd, J=15 9, 2 7, 1H, γ-CH_2,Hb); 2 85 (d, J=5 3, 3H, N-CH_3), 3 67-3 77 (m, 1H, C$\underline{H}$OH), 3 86 (bs, 1H, OH); 4 87 (s, 1H, CH), 10 72 (bs, 1H, NH) ^{13}C-NMR δ 13 75 (q), 18 40 (t), 28 28 (q), 29 47 (q), 39 27 (t), 39 35 (t), 69 44 (d), 94 99 (d), 165.62 (s), 194 12 (s) IR ν_{max} (film) 3325 (broad), 1685, 1635, 1580, 1245, 725 cm^{-1} MS m/z (%) 185 (M^+,34), 170 (11), 142 (38), 124 (24), 113 (79), 98 (100), 71 (62), 56 (40)

6-Hydroxy-2-(N-methylamino)-non-2-en-4-one (**4ba**) Oil (Found C, 64 73; H, 10 49, N, 7 49 $C_{10}H_{19}NO_2$ requires C, 64 83 H, 10 34, N, 7 56 %), ^{1}H-NMR δ 0 86-0 97 (m, 3H, $(CH_2)_2C\underline{H}_3$), 1 25-1 55 (m, 4H, $(C\underline{H}_2)_2CH_3$), 1 89 (s, 3H, γ-CH_3), 2 21 (dd, J=15 1, 9 0, 1H, α'-CH_2,Ha); 2 36 (dd, J=15 1, 2 9, 1H, α'-CH_2,Hb), 2 90 (d, J=5 5, 3H, N-CH_3), 3 86-3 97 (m, 1H, C$\underline{H}$OH), 4 03 (bs, 1H, OH), 4 93 (s, 1H, CH), 10 74 (bs, 1H, NH) ^{13}C-NMR δ 14 02 (q), 18 69 (q), 29 54 (q), 39 07 (t), 39 13 (t), 45 74 (t), 69 31 (d), 95 32 (d), 165 44 (s), 196 56 (s) IR ν_{max} (film) 3325, 1690, 1640, 1590; 1550, 725 cm^{-1} MS m/z (%) 185 (M^+,23), 142 (11), 114 (36), 98 (100), 71 (54), 56 (32)

7,7-Dimethyl-6-Hydroxy-4-(N-methylamino)-oct-3-en-2-one (**5bb**) Oil (Found· C, 66 41, H, 10 51, N, 7 14 $C_{11}H_{21}NO_2$ requires· C, 66 29 H, 10 62, N, 7 03 %), ^{1}H-NMR δ 0 80 (s, 9H, $C(CH_3)_3$), 1 80 (s, 3H, CH_3), 2 05 (dd, J=13 6, 10 5, 1H, CH_2,Ha), 2 23 (dd, J=13 6, 2 0, 1H, CH_3,Hb), 2 81 (d, J=5 2, 3H, N-CH_3), 3 30 (dd, J=10 5, 2 0, 1H, C$\underline{H}$OH), 3.53 (bs, 1H, OH), 4 86 (s, 1H, CH), 10 69 (bs, 1H, NH) ^{13}C-NMR δ 25 11 (q), 27 98(q), 29 05 (q), 33.53 (t), 34 79 (s), 77.23 (d), 94 64 (d), 166.85 (s), 193 54 (s) IR ν_{max} (film) 3280 (broad), 1590, 1550, 1345, 1300, 1060; 725 cm^{-1} MS m/z (%) 199 (M^+,28), 184 (15), 142 (100), 114 (37), 98 (95)

6-Hydroxy-4-(N-methylamino)-dodec-3-en-2-one (**5bc**) Mp 150-152 °C (CH_2Cl_2/Hexane) (Found C, 68 51, H, 10 93, N, 6 32 $C_{13}H_{25}NO_2$ requires C, 68 68 H, 11 08, N, 6 16 %), ^{1}H-NMR δ 0 76-0.90 (m, 3H, $(CH_2)_5C\underline{H}_3$), 1 14-1 53 (m, 10H, $(C\underline{H}_2)_5CH_3$), 1 92 (s, 3H, α'-CH_3), 2 25 (dd, J=13 9, 7 6, 1H, γ-CH_2,Ha), 2.30 (dd, J=13 9, 5 1, 1H, α'-CH_2,Hb), 2 91 (d, J=5 1, 3H, N-CH_3), 3 14 (bs, 1H, OH), 3 68-3 82 (m, 1H, C$\underline{H}$OH), 4 92 (s, 1H, CH), 10 76 (bs, 1H, NH) ^{13}C-NMR δ 14 01 (q), 22 54 (t), 25 55 (t), 28 83 (q), 29 17 (t), 29 58 (q), 31 74 (t), 37 34 (t), 39 46 (t), 70.02 (d); 95 17 (d), 164 78 (s), 194 91 (s) IR ν_{max} (nujol) 3240, 1595, 1540, 1300, 1280, 790, 740, 710 cm^{-1} MS m/z (%) 227 (M^+,11), 142 (60), 124 (31), 114 (27), 113 (100), 98 (68), 71 (49), 56 (31)

6-Hydroxy-2-(N-methylamino)-dodec-2-en-4-one (**4bc**) Oil (Found C, 68 61, H, 11 12, N, 6 23 $C_{13}H_{25}NO_2$ requires C, 68 68 H, 11 08, N, 6 16 %), ^{1}H-NMR δ 0.60-0 80 (m, 3H, $(CH_2)_5C\underline{H}_3$), 1 07-1 51 (m, 10H, $(C\underline{H}_2)_5CH_3$), 1 82 (s, 3H, γ-CH_3), 2 10 (dd, J=14 6, 9 2, 1H, α'-CH_2,Ha), 2 25 (dd, J=14 6, 3 0, 1H, α'-CH_2,Hb), 2 77 (d, J=5 2, 3H, N-CH_3), 3 71-3 82 (m, 1H, C$\underline{H}$OH), 4 00 (bs, 1H, OH), 4 79 (s, 1H, CH), 10,53 (bs, 1H, NH) ^{13}C-NMR δ 13 62 (q), 18 25 (q), 22 17 (t), 25 09 (t), 28 12 (t), 28 95 (t), 29 10 (q), 36 67 (t), 46 36 (t), 69 13 (d), 94 65 (d), 13 82 (s), 194 03 (s) IR ν_{max}(film) 3240 (broad), 1595, 1540, 1300, 1280, 790, 740, 710 cm^{-1} MS m/z (%) 227 (M^+,17), 142 (24), 114 (55), 113 (44), 98 (100), 71 (73), 56 (30)

6-Phenyl-6-hydroxy-4-(N-methylamino)-hex-3-en-2-one (**5bd**) Oil (Found C, 71 38, H, 7 93, N, 6 34 $C_{13}H_{17}NO_2$ requires C, 71 21 H, 7 81, N, 6 39 %), ^{1}H-NMR δ 2 04 (s, 3H, CH_3), 2 49 (bs, 1H, OH), 2 59 (dd, J=13.7, 5 4, 1H, CH_2, Ha), 2 64 (dd, J=13 7, 7 8, 1H, CH_2, Hb), 2 89 (d, J=5 4, 3H, N-CH_3), 4 93 (dd, J=7 8, 5 4, 1H, C<u>H</u>OH), 5 19 (s, 1H, CH), 7 25-7 40 (m, 5H, Ph), 10 85 (bs, 1H, NH) ^{13}C-NMR δ 28 93 (q), 29 53 (q), 41 41 (t), 72 76 (d), 95 35 (d), 125 54 (d), 128 09 (d); 128 67 (d); 143 13 (s), 163 83 (s), 195 00 (s) IR ν_{max} (film) 3200(broad), 1580, 1530, 730, 680 cm^{-1} MS m/z (%) 201 (M^+-18, 67), 200 (34), 184 (19), 124 (100), 110 (22), 98 (30), 56 (28)

6-Phenyl-6-hydroxy-2-(N-methylamino)-hex-2-en-4-one (**4bd**) Oil (Found C, 71 36, H, 7 85, N, 6 45 $C_{13}H_{17}NO_2$ requires C, 71 21 H, 7 81, N, 6 39 %), ^{1}H-NMR δ 1 29 (bs, 1H, OH), 1 94 (s, 3H, CH_3), 2 58 (dd, J=15 0, 7 9, 1H, CH_2, Ha), 2 64 (dd, J=15 0, 4 3, 1H, CH_2, Hb), 2 96 (d, J=5 2, 3H, N-CH_3), 4 96 (s, 1H, CH), 5 07 (dd, J=7 9, 4 3, 1H, C<u>H</u>OH), 7 25-7 40 (m, 5H, Ph), 10 85 (bs, 1H, NH) ^{13}C-NMR δ 18 79 (q), 29 69 (q), 48 74 (t), 71 90 (d) 95 28 (d), 125 75 (d), 127 16 (d), 128 28 (d), 144 00 (s), 165 84 (s), 197 70 (s), IR ν_{max} (film) 3360 (broad), 1720, 1600, 1550, 1425, 695 cm^{-1} MS m/z (%) 201 (M^+-18, 64), 200 (30), 184 (32), 170 (23), 141 (24), 124 (100), 110 (25), 103 (41), 94 (32), 56 (52)

8-Phenyl-6-hydroxy-4-(N-methylamino)-octa-3,7-dien-2-one (**5be**) Oil (Found C, 73 56, H, 7 96, N, 5 74 $C_{15}H_{19}NO_2$ requires C, 73 44 H, 7 81, N, 5 71 %), ^{1}H-NMR δ 2 03 (s, 3H, CH_3), 2 31 (bs, 1H, OH), 2 53 (d, J=6 7, 2H, CH_2), 2 99 (d, J=5 5, 3H, N-CH_3), 4 51-4 59 (m, 1H, C<u>H</u>OH), 5 08 (s, 1H, α-CH), 6 25 (dd, J=15 9, 6 4, 1H, γ-CH), 6 65 (dd, J=15 9, 1 1, 1H, δ-CH), 7 25-7 49 (m, 5H, Ph), 10 85 (bs, 1H, NH) ^{13}C-NMR δ 28 90 (q), 29 71 (q), 39 46 (t), 71 06 (d), 95 49 (d), 126 51 (d), 127 93 (d), 128 70 (d), 130 52 (d), 130 82 (d), 136 23 (s), 163 74 (s), 195 05 (s) IR ν_{max} (film) 3290 (broad), 1685, 1635, 1595, 1345, 1235, 735, 680 cm^{-1} MS m/z (%) 227 (M^+-18, 20), 184 (100), 169 (29), 150 (16), 94 (20), 77 (19)

8-Phenyl-6-hydroxy-2-(N-methylamino)-octa-2,7-dien-4-one (**4be**) Oil (Found C, 73 49, H, 7 75, N, 5 83 $C_{15}H_{19}NO_2$ requires C, 73 44 H, 7 81, N, 5 71 %), ^{1}H-NMR δ 1 96 (s, 3H, CH_3), 2 42 (dd, J=13 7, 5 5, 1H, CH_2,Ha), 2 53 (dd, J=13 7, 8 1, 1H, CH_2,Hb), 2 89 (d, J=5 2, 3H, N-CH_3), 3 80 (bs, 1H, OH), 4 47-4 55 (m, 1H, C<u>H</u>OH), 5 03 (s, 1H, α-CH), 6 22 (dd, J=15 9, 6 7, 1H, γ'-CH), 6 60 (d, J=15 9, 1H, δ'-CH), 7 14-7 44 (m, 5H, Ph), 10 80 (bs, 1H, NH) ^{13}C-NMR δ 18 73 (q), 29 61 (q), 46 54 (t), 70 38 (d), 95 34 (d), 126 42 (d), 127 30 (d), 128 41 (d), 129 48 (d), 131 54 (d), 137 01 (s), 165 68 (s), 195 59 (s) IR ν_{max}(film) 3320 (broad), 1590, 1340, 1270, 980, 730, 675 cm^{-1} MS m/z (%) 227 (M^+-18, 16), 212 (62), 184 (100), 169 (30), 123 (24), 91 (27), 77 (23)

6-Methyl-6-hydroxy-4-(N-methylamino)-hept-3-en-2-one (**5bf**) Oil (Found C, 63 06, H, 9 83, N, 7 99 $C_9H_{17}NO_2$ requires C, 63 13 H, 10 01, N, 8 18 %), ^{1}H-NMR δ 1 18 (s, 6H, 2CH_3), 1 83 (s, 3H, α'-CH_3), 2 25 (s, 2H, CH_2), 2 84 (d, J=5 3, 3H, N-CH_3), 3 34 (bs, 1H, OH), 4 80 (s, 1H, CH), 10 80 (bs, 1H, NH) ^{13}C-NMR δ 28 30 (q), 29 70 (q), 29 87 (q), 43 52 (t), 70 15 (s), 96 37 (d), 164 63 (s), 193 39 (s) IR ν_{max} (film) 3240 (broad), 1605, 1520, 740 cm^{-1} MS m/z (%) 171 (M^+, 27), 138 (20), 113 (33), 98 (100)

6-Methyl-6-hydroxy-2-(N-methylamino)-hept-2-en-4-one (**4bf**) Oil (Found C, 63 19, H, 9 92, N, 8 24 $C_9H_{17}NO_2$ requires C, 63 13 H, 10 01, N, 8 18 %), ^{1}H-NMR δ 1 10 (s, 6H, 2CH_3), 1 83 (s, 3H, γ-CH_3), 2 65 (d, J=5 3, 3H, N-CH_3), 2 81 (s, 2H, CH_2), 3 30 (bs, 1H, OH), 4 98 (s, 1H, α-CH), 10 85 (broad s, 1H, NH) ^{13}C-NMR δ 29 52 (q), 29 70 (q), 30 41 (q), 44 02 (t), 70 83 (s), 94 07 (d), 162 56 (s), 193 39 (s) IR ν_{max} (film) 3300 (broad), 1605, 1520, 1350, 945 cm^{-1} MS m/z (%) 171 (M^+, 30), 156 (7), 138 (19), 113 (31), 98 (100)

6-Phenyl-6-hydroxy-4-(N-methylamino)-hept-3-en-2-one (**5bg**) Oil (Found C, 72 19, H, 8 34, N, 5 89 $C_{14}H_{19}NO_2$ requires C, 72 07 H, 8 21, N, 6 00 %), ^{1}H-NMR δ 1 48 (s, 3H, CH_3), 1.85 (s, 3H, α'-CH_3), 2 65 (d, J=15 1, 1H, CH_2, Ha), 2 80 (d, J=15 1, 1H, CH_2, Hb), 2 84 (d, J=5 2, 3H, N-CH_3), 4 90 (s, 1H, CH), 6 15 (bs, 1H, OH), 7 10-7 50 (m, 5H, Ph), 10 70 (bs, 1H, NH) ^{13}C-NMR δ 18 60 (q), 29 45 (q), 30 79 (q), 50 83 (t), 73 80 (s), 96 02 (d), 124 51 (d), 125 98 (d), 127 78 (d), 148 41 (s), 165.71 (s), 195 55 (s) IR ν_{max} (film) 3360 (broad), 1620, 1550, 730 cm^{-1} MS m/z (%) 233 (M^+,18), 147 (8), 113 (26), 98 (100)

8-Phenyl-6-Methyl-6-hydroxy-4-(N-methylamino)-oct-3-en-2-one (**5bh**) Oil (Found C, 73 42, H, 8 81, N, 5 44 $C_{16}H_{23}NO_2$ requires C, 73 53 H, 8 87, N, 5 36 %), ^{1}H-NMR δ 1 31 (s, 3H, CH_3), 1 74-1 92 (m, 2H, CH_2), 1 96 (s, 3H, α'-CH_3), 2 30 (d, J=13 3, 1H, γ-CH_2, Ha), 2 45 (d, J=13 3, 1H, γ-CH_2, Hb), 2 66-2 75 (m, 2H, CH_2), 2 90 (d, J=5 3, 3H, N-CH_3), 3 20 (bs, 1H, OH), 5 00 (s, 1H, CH), 7 10-7 30 (m, 5H, Ph), 11 00 (broad m, 1H, NH) ^{13}C-NMR δ 26 48 (q), 28.42 (q), 29 61 (q), 29 91 (t), 42.31 (t), 44 45 (t), 71 94 (s), 96 56 (d), 125 46 (d), 128 01 (d), 128 07 (d), 141 84 (s), 164 40 (s), 193 46 (s) IR ν_{max} (film) 3250 (broad), 1585, 1550, 730, 685 cm^{-1} MS m/z (%) 243 (M^+-18, 7), 228 (15), 186 (18), 152 (30), 138 (100), 91 (30)

8-Phenyl-6-Methyl-6-hydroxy-2-(N-methylamino)-oct-2-en-4-one (**4bh**) Oil (Found C, 73 49, H, 8 99, N, 5 47 $C_{16}H_{23}NO_2$ requires C, 73 53 H, 8 87, N, 5 36 %), ^{1}H-NMR δ 1 22 (s, 3H, CH_3), 1 74-1 92 (m, 2H), 2 06 (s, 3H, γ-CH_3), 2 69 (d, J=13 3, 1H, α'-CH_2, Ha), 2 72 (d, J=4 9, 3H, N-CH_3), 2 68-2 76 (m, 2H), 3 26 (d, J=13 3, 1H, α'-CH_2, Hb), 3 30 (bs, 1H, OH), 5 10 (s, 1H, α-CH), 7 08-7 28 (m, 5H, Ph), 11 05 (broad s, 1H, NH) ^{13}C-NMR δ 26 45 (q), 28 43 (q), 29 94 (q), 30 53 (t), 42 74 (t), 45 44 (t), 72 67 (s), 94 42 (d), 125 20 (d), 127 95 (d), 128 03 (d), 142 43 (s), 162 32 (s), 193 46 (s) IR ν_{max} (film) 3270 (broad), 1590, 1505, 1270, 730, 685 cm^{-1} MS m/z (%) 243 (M^+-18, 7), 228 (11), 186 (18), 152 (33), 138 (100), 91 (26)

6,6-Diphenyl-6-hydroxy-4-(N-methylamino)-hex-3-en-2-one (**5bi**) Mp 170-172 (CH_2Cl_2/Hexane) (Found C, 77 38, H, 7 02, N, 4 95 $C_{19}H_{21}NO_2$ requires C, 77 26 H, 7 17, N, 4 74 %), ^{1}H-NMR δ 2 15 (s, 3H, a'-CH_3), 2 49 (d, J=5 3, 3H, N-CH_3), 3 20 (s, 2H, CH_2), 3 90 (bs, 1H, OH), 4 72 (s, 1H, CH), 7 20-7 80 (m, 10H, 2Ph), 10 85 (bs, 1H, NH) ^{13}C-NMR δ 18 83 (q), 29 65 (q), 42 61 (t), 77 75 (s), 96 97 (d), 125 92 (d), 127 95 (d), 136 23 (d), 146 17 (s), 162 43 (s), 195 44 (s) IR ν_{max} (nujol) 3220 (broad), 1575, 1525, 1300, 680 cm^{-1} MS[9]

6,6-Diphenyl-6-hydroxy-2-(N-methylamino)-hex-2-en-4-one (**4bi**) Mp 158-160 (CH_2Cl_2/Hexane) (Found C, 77 32, H, 7 08, N, 4 91 $C_{19}H_{21}NO_2$ requires C, 77 26 H, 7 17, N, 4 74 %), ^{1}H-NMR δ 1 87 (s, 3H, CH_3), 2 42 (d, J=5 1, 3H, N-CH_3), 3 70 (s, 2H, CH_2), 5 15 (s, 1H, CH), 6 60 (bs, 1H, OH), 7 20-7 80 (m, 10H, 2Ph), 10 70 (bs, 1H, NH) ^{13}C-NMR δ 28.90 (q), 30 77 (q), 44 80 (t), 77 48 (s), 96 13 (d), 126 90 (d), 127 37 (d), 128 24 (d), 147 53 (s), 161 35 (s),197 20 (s) IR ν_{max} (nujol) 3230 (broad), 1560, 1530, 1320, 720 cm^{-1} MS[9]

8-Phenyl-6-Methyl-6-hydroxy-4-(N-methylamino)-octa-3,7-dien-2-one (**5bl**) Oil (Found C, 74 26, H, 8 24, N, 5.34 $C_{16}H_{21}NO_2$ requires C, 74 10 H, 8 16, N, 5 40 %), ^{1}H-NMR δ 1 45 (s, 3H, CH_3), 1 96 (s, 3H, α'-CH_3), 2 47 (d, J=13 4, 1H, CH_2, Ha), 2 52 (d, J=13 4, 1H, CH_2,Hb), 2 86 (d, J=5 5, 3H, N-CH_3), 3 36 (bs, 1H, OH), 5 00 (s, 1H, CH), 6 26 (d, J=16 2, 1H, γ'-CH), 6 59 (d, J=16 2, 1H, δ'-CH), 7 10-7 35 (m, 5H, Ph), 10.94 (bs, 1H, NH) ^{13}C-NMR δ 28 20 (q), 28 71 (q), 29 93 (q), 43 50 (t), 72 34 (s), 96 79 (d), 126 18 (d), 127 23 (d), 127 34 (d), 128 36 (d), 135 31 (d), 136 47 (s), 163 53 (s), 193 93 (s) IR ν_{max}

(film) 3235 (broad), 1590; 1505, 1405; 1340, 735, 680 cm^{-1} MS m/z (%) 259 (M^+, 17), 241 (22), 216 (67), 202 (56), 113 (100), 98 (63), 71 (39), 56 (31)

8-Phenyl-6-Methyl-6-Hydroxy-2-(N-methylamino)-octa-2,7-dien-4-one (**4bl**) Oil (Found C, 74 18, H, 8 29, N, 5 46 $C_{16}H_{21}NO_2$ requires C, 74 10 H, 8 16, N, 5.40 %), ^{1}H-NMR δ 1.35 (s, 3H, CH_3), 1 91 (s, 3H, γ-CH_3), 2 49 (d, J=15 0, 1H); 2 51 (d, J=15 0, 1H), 2 91 (d, J=5 5, 3H, N-CH_3), 4 93 (s,1H, α-CH), 5 96 (bs, 1H, OH), 6 27 (d, J=16 2, 1H, γ'-CH), 6 63 (d, J=16 2, 1H, δ'-CH), 7 08-7 40 (m, 5H, Ph), 10 83 (bs, 1H, NH) ^{13}C-NMR δ 18 49 (q), 28 45 (q), 29 37 (q), 49 78 (t), 72 31 (s), 95 85 (d), 126 17 (d), 126 73 (d), 126 77 (d), 128 10 (d), 136 31 (d), 137 17 (s), 165 61 (s), 195 46 (s) IR ν_{max} (film) 3300 (broad), 1685, 1585, 1530, 1415, 1325, 730, 680 cm^{-1} MS m/z (%) 241 (M^+-18, 8), 226 (7), 146 (65), 131 (100), 113 (52), 103 (88)

Synthesis of δ-hydroxy-β-enamino ketones* 5cd-co *from reaction of aldehydes or ketones with the γ-dianion* (3c) *generated from 1-phenyl-3-methylamino-but-2-en-1-one* (1c) *by treatment with MeLi/TMEDA. The reaction was carried out as above reported for **5ba-bl** and **4ba-bl** Yields of isolated pure δ-hydroxy-β-enamino ketones **5cd-co** are reported in Table 3 Physical data follows

1,5-Diphenyl-5-hydroxy-3-(N-methylamino)-pent-2-en-1-one (**5cd**) Mp 112-114 (CH_2Cl_2/Hexane) (Found C, 76 77, H, 6 74, N, 5 15 $C_{18}H_{19}NO_2$ requires C, 76 84 H, 6 81, N, 4 98 %), ^{1}H-NMR δ 1 70 (bs, 1H), 2 71 (dd, J=13 8, 4 9, 1H), 2 79 (dd, J=13 8, 8 3, 1H), 2 94 (d, J=5 4, 3H, N-CH_3), 4 96-5 01 (m, 1H, C<u>H</u>OH), 5 72 (s, 1H, CH), 7 25-7 85 (m, 10H, 2Ph), 11 45 (broad s, 1H, NH) ^{13}C-NMR δ 29 74 (q), 41 81 (t), 72 97 (d), 92 33 (d), 125 61 (d), 126 93 (d), 128 11 (d), 128 18 (d), 128 71 (d), 130 55 (d), 139 70 (s), 143 10 (s), 165 60 (s), 187 40 (s) IR ν_{max} (nujol) 3300(broad), 1600, 1560, 1350, 770 cm^{-1} MS m/z (%) 263 (M^+-18, 8), 186 (17), 158 (100), 143 (33), 128 (13), 105 (16), 77 (22)

1-Phenyl-5-hydroxy-3-(N-methylamino)-hept-2-en-1-one (**5cm**) Oil (Found C, 72 21, H, 8 33, N, 5 84 $C_{14}H_{19}NO_2$ requires C, 72 07 H, 8 21, N, 6 00 %), ^{1}H-NMR δ 0 92 (t, J=7 4, 3H, $CH_2C\underline{H}_3$), 1 40-1 60 (m, 2H, $C\underline{H}_2CH_3$), 2 32 (dd, J=13 2, 4 9, 1H), 2 37 (dd, J=13 2, 7 6, 1H), 2 86 (d, J=5 5, 3H, N-CH_3), 3 60-3 70 (m, 1H, C<u>H</u>OH), 3 90 (bs, 1H, OH), 5 60 (s, 1H, CH), 7 20-7 80 (m, 5H, Ph), 11 35 (bs, 1H, NH) ^{13}C-NMR δ 10 10 (q), 29 76 (q), 30 36 (t), 39 74 (t), 71 47 (d), 92 32 (d), 126 87 (d), 128 12 (d), 130 41 (d), 140 40 (s), 167 83 (s), 187 26 (s) IR ν_{max} (film) 3370 (broad), 1600, 1545, 1340, 750 cm^{-1} MS m/z (%) 233 (M^+,12), 186 (38), 175 (42), 174 (34), 105 (100), 77 (43)

1-Phenyl-5-hydroxy-3-(N-methylamino)-5-cycloexyl-pent-2-en-1-one (**5cn**) Oil (Found C, 75 35, H, 8 89, N, 4 74 $C_{18}H_{25}NO_2$ requires C, 75 22 H, 8 77, N, 4 87 %), ^{1}H-NMR δ 0 87-1 33 (m, 6H), 1 52-1 81 (m, 5H), 2 22 (dd, J=13 6, 9 1, 1H), 2 29 (dd, J=13 6, 3 6,1H), 2 76 (d, J=5 2, 3H, N-CH_3), 3 45-3 37 (m, 1H, C<u>H</u>OH), 3 87 (bs, 1H, OH), 5 55 (s, 1H, CH), 7 20-7 80 (m, 5H, Ph), 11 30 (broad q, 1H, NH) ^{13}C-NMR δ 26 08 (t), 26 19 (t), 26 41 (t), 27 91 (t), 29 06 (t), 29 58 (d), 36 94 (q), 44 09 (t), 74 14 (d), 92 19 (d), 126 83 (d), 127 97 (d), 130 20 (d), 140 38 (s), 168 78 (s), 186 74 (s) IR ν_{max} (film) 3370 (broad), 1740, 1600, 1550, 1330 cm^{-1} MS m/z (%) 269 (M^+-18, 19), 186 (100), 105 (55), 77 (36)

1-Phenyl-5-hydroxy-3-(N-methylamino)-5-methyl-hex-2-en-1-one (**5cf**) Mp 100-102 (CH_2Cl_2/Hexane) (Found C, 72 19, H, 8 28, N, 5 88 $C_{14}H_{19}NO_2$ requires C, 72 07 H, 8 21, N, 6 00 %), ^{1}H-NMR δ 1 37 (s, 6H, CH_3), 1 71 (bs, 1H, OH), 2 56 (s, 2H, CH_2), 3 09 (d, J=5 4, 3H, N-CH_3), 5 70 (s, 1H, CH), 7 35-7 90 (m, 5H, Ph), 11 65 (broad s, 1H, NH) ^{13}C-NMR δ 30 00 (q), 30 47 (q), 44 24 (t), 70 86 (s), 93 55 (d), 126 88 (d), 128 19 (d), 130 49 (d), 140 44 (s), 166 09 (s), 187 20 (s) IR ν_{max} (nujol) 3300 (broad), 1610,

1545, 740 cm^{-1} MS m/z (%) 233 (M^+,25), 218 (7); 200 (32), 175 (46), 174 (100); 158 (41), 105 (79), 77 (54)

1,5-Diphenyl-5-hydroxy-3-(N-methylamino)-hex-2-en-1-one (**5cg**) Mp 134-135 (CH_2Cl_2/Hexane) (Found C, 77 13, H, 7 09, N, 4 83 $C_{19}H_{21}NO_2$ requires C, 77 26 H, 7 17, N, 4 74 %), ^{1}H-NMR δ 1.74 (s, 3H, CH_3), 2 51 (bs, 1H, OH), 2 75-2 85 (m, 5H), 5 52 (s, 1H, CH), 7 20-7 75 (m, 10H, 2Ph), 11 50 (broad s, 1H, NH) ^{13}C-NMR δ 29.90 (q), 30 03 (q), 45 42 (t), 74 26 (s), 93 70 (d), 124 75 (d), 126.88 (d), 127 21 (d), 128 13 (d), 128 43 (d), 130 47 (d), 140 36 (s), 147 00 (s), 164 78 (s), 187 25 (s) IR ν_{max} (nujol) 3275(broad), 1615, 1550, 710 cm^{-1} MS [9]

1-Phenyl-5-hydroxy-3-(N-methylamino)-5-ethyl-hept-2-en-1-one (**5co**) Oil (Found C, 73 42, H, 8 79, N, 5 41 $C_{16}H_{23}NO_2$ requires C, 73 53 H, 8 87, N, 5 36 %), ^{1}H-NMR δ 0 84 (t, J=7 5, 6H, $CH_2\underline{CH_3}$); 1 51 (q, J=7 5, 4H, $C\underline{H_2}CH_3$), 2.37 (s, 2H, γ-CH_2), 2 50 (bs, 1H, OH), 2.94 (d, J=5 2, 3H, N-CH_3), 5.60 (s, 1H, CH), 7 25-7 82 (m, 5H, Ph), 11 65 (broad s, 1H, NH) ^{13}C-NMR δ 8 02 (q), 30 39 (q); 31 06 (t), 40 18 (t), 75 08 (s), 93 61 (d), 126 83 (d), 128 08 (d), 130 28 (d), 140 60 (s), 166 82 (s); 186 47 (s) IR ν_{max} (film) 3360 (broad), 1600, 1525, 1330, 1220 cm^{-1} MS m/z (%) 243 (M^+-18, 11), 228 (8); 214 (100), 105 (71), 77 (29)

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9 Termal decomposition occur in the ionization chamber