Pergamon

Tetrahedron, Vol. 52, No. 45, pp. 14273-14280, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00879-4

A Synthetic Entry into Fused Pyran Derivatives Through Carbon Transfer Reactions of 1,3-Oxazinanes and Oxazolidines With Carbon Nucleophiles.

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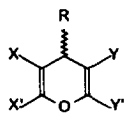
Abstract : Acid catalysed condensations of various 2 substituted 1,3-oxazinanes **3** and 1,3- oxazolidines **4** with cyclic carbon nucleophiles viz. 5,5-dimethyl-1,3-cyclohexanedione and 1,3-cyclohexanedione furnish xanthene derivatives, whereas a Knoevenagel reaction proceeds with acyclic nucleophiles. In case of **4b** and **4c**, a unique synthesis of functionalised α-tetralones has emerged. Reactions of mixtures of cyclic and acyclic carbon nucleophiles with **3** provide some functionalised and partially reduced benzopyran derivatives.

INTRODUCTION

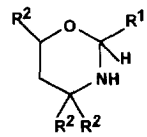
Polyfunctionalised benzo-4*H*-pyrans **1** and xanthenediones **2** constitute a structural unit of a number of natural products[1] and because of the inherent reactivity of the inbuilt pyran ring are versatile synthons[2]. Their conventional synthesis involves acid as well as base catalysed condensation of appropriate active methylene carbonyl compounds with aldehydes and are plagued by the limitation of prolonged reaction times, poor yields, side reactions of aldehydes and above all lack of convincing structural proofs[3]. We envisaged, that like ethyl-β-aminocrotonate[4] or enaminones, appropriate active methylene compounds, where enolic isomers predominate[5], could undergo analogous, 2 : 1 stoichiometric, acid catalysed reactions with oxazinanes **3** / oxazolidines **4** to form oxygen isosteres of dihydropyridine derivatives.

RESULTS AND DISCUSSION

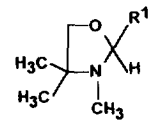
5,5-Dimethyl-1,3-cyclohexanedione (dimedone), a mono carbon nucleophile with enhanced enolic character, reacts with 2-phenyloxazinane **3a** in refluxing acetonitrile : acetic acid (10:1) to furnish 2,2'-(phenylmethylene)-bis [5,5-dimethyl-1-hydroxycyclohex-1-en-3-one] **7a** (95%). When the reaction is performed in refluxing acetic acid, the cyclodehydrated product 1,8-dioxo-3,3,6,6-tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene, **8a** is formed (92%). Other 2-substituted oxazinanes react with dimedone



1 X,X'=Cyclic; Y,Y'=Substituents
2 X,X'=Y,Y'= Cyclic

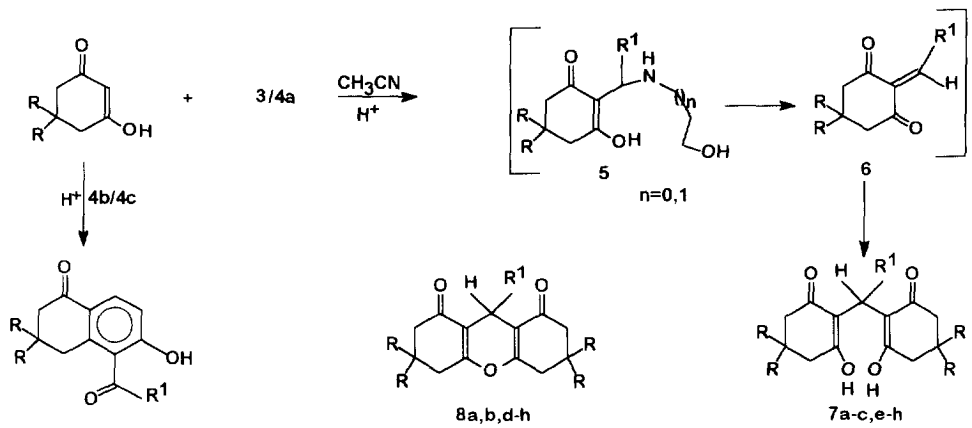


3a R^1= C_6H_5, R^2= Me
3b R^1= R^2 = Me
3c R^1= R^2 = H
3d R^1= CH_2CO_2Et, R^2 = Me



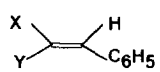
4a R^1=$CH_2COC_6H_5$
4b R^1=$CH_2COCH_2CO_2Et$
4c R^1 =$CH_2COCH_2COCH_3$

to provide further examples of 7 and/or **8** in a synthetically useful manner. However, in the reaction of **3c** with dimedone only **7c** is formed and **8c** was not isolated. Reaction of **3d** with dimedone in refluxing acetonitrile : trifluoroacetic acid (10 : 0.1) resulted in straightforward formation of **8d**. Similarly **4a** reacts

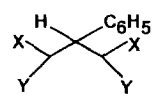


9a R^1 = OEt, R = Me
9b R^1 = OEt, R = H
9c R^1 = CH_3, R = CH_3

a R^1=C_6H_5, R=CH_3; b R^1=R=CH_3
c R^1=H, R=CH_3; d R^1=CH_2CO_2Et, R=CH_3
e R^1 = C_6H_5, R = H; f R^1 = CH_3, R = H
g R^1=$CH_2COC_6H_5$, R=CH_3; h R^1=$CH_2COC_6H_5$, R=H



10a X = CN, Y = CO_2Et; 10b X = Y = CN
10c X = NO_2, Y = H; 10d X = Y = COC_6H_5
10e X = Y = CO_2Et



11

with dimedone in refluxing acetonitrile : acetic acid (10 : 1) to furnish corresponding **8g,** without the isolation of 7**g**. 1,3-Cyclohexanedione similarly reacts with 1,3-oxazinanes **3a** and **3b** to provide corresponding 7 in refluxing CH_3CN : CH_3COOH and **8** in refluxing acetic acid. Reaction of 1,3-cyclohexanedione with **4a**[6] furnished **8h**. Contrarily, **4b** reacts with dimedone and 1,3-cyclohexanedione under acid catalysed conditions

(acetonitrile : acetic acid ::10 : 1) to furnish different products -funtionalised α-tetralones **9a** and **9b** respectively and **4c** gives with dimedone **9c**.

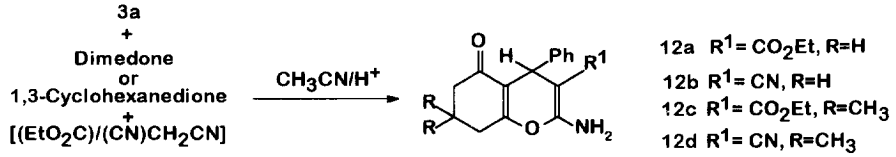
For utilising this approach for procuring polyfunctionalised 4*H*-pyrans, we performed the reactions of acyclic carbon nucleophiles with **3a**, but the reactions with 2,4-pentanedione and ethyl acetoacetate did not take place[5]. However, we found that ethyl cyanoacetate and **3a** react in 1 : 1 stoichiometric ratio in anhydrous acetonitrile: acetic acid (10:1) to form β-cyano-β-carbethoxy styrene **10a** in quantitative yield. Other carbon nucleophiles such as malononitrile, nitromethane, dibenzoyl methane and diethyl malonate also react with **3a** in an analogous manner to furnish corresponding styrene derivatives **10 b-e**. The expected 2:1 stoichiometeric products **11** were not formed probably because under acid catalysed conditions the acyclic active methylene compounds are either not sufficiently enolic or reactive to react with **10** to form **11** which in turn could undergo cyclisation[7]. Thus, in contrast to the corresponding base catalysed reactions of aldehydes with active methylene compounds resulting in the formation of pyran ring[8], acid catalysed condensations with **3** result in the formation of olefinic products, but the yields of **10** obtained here, are better or comparable with the conventional base catalysed Knoevenagel[9] reactions. Additionally, this methodology has the inbuilt advantage of the possibility of varied functionalisation of the product and operational facility due to the absence of elimination of water, which is formed in the conventional synthesis.

These reactions represent an overall transfer of C-2 unit of **3** and **4a** at aldehyde group oxidation level in between two molecules of dimedone/1,3-cyclohexanedione and could be visualized to proceed through an initial intermediate **6** followed by formation of **7** and cyclodehydration. In the case of the reactions of **4b** and **4c** with these nucleophiles, intramolecular cyclisation of **6** [R=$CH_2COCH_2CO(OEt)/(CH_3)$] prevails over the intermolecular addition of the nucleophiles and 1:1 stoichiometric products **9** are formed. These results demonstrate a broad based synthetically useful incorporation of functionalised substituents at C-9 of **8** emanating from appropriately substiuted C-2 unit of **3** or **4**, and thus, circumvent inherent limitations of non-availability and side reactions of corresponding functionalised aldehydes. With the possibility of presence of varied C-2 substituents in **4b** and **4c**, a convenient and unprecedented synthesis of functionalized α-tetralones has been achieved. In the case of acyclic nucleophiles, the reaction stops at thermodynamically more stable **10**, analogs of **6**.

Evidently, the alkylidene 1,3-diketone **6**, undergoes Michael addition with cyclic carbon nucleophiles to furnish **8**, whereas, the acyclic carbon nucleophiles could not undergo similar additions on analogous alkylidene compounds **10**. We envisaged that if the nature of product formation **8** vs **10** is being guided by reactivity difference of cyclic and acyclic carbon nucleophiles, then **10** might undergo Michael addition with more reactive cyclic carbon nucleophiles. More so, 1:1 stoichiometric mixture of cyclic and acyclic carbon nucleophiles should react with **3** to furnish benzo-4*H*-pyran derivatives **1**.

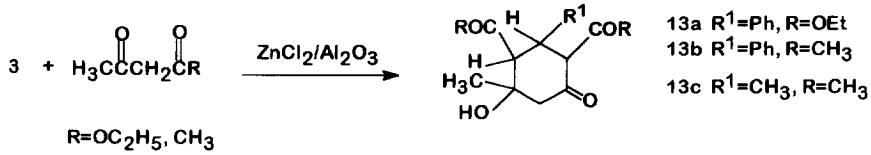
In accordance with this argument, the reaction of β-cyano-β-carbethoxy styrene **10a** with 1,3-cyclohexanedione in refluxing acetonitrile : acetic acid (10:1) solution after 30 min. revealed the formation of 4*H*-benzopyran derivative **12a** in 92% yield. Also the reaction of 1,3-cyclohexanedione and ethyl cyanoacetate (1:1 stoichiometric mixture) with **3a** furnished **12a** in 78% yield.

Other cyclic/acyclic carbon nucleophile mixtures such as 1,3-cyclohexanedione/malononitrile, dimedone/ethyl cyanoacetate, and dimedone/ malononitrile reacted with **3a** to furnish corresponding differently substituted and highly functionalised benzo-4*H*-pyran derivatives **12b-d** respectively in excellent yields. The present acid catalysed approach to these substituted partially reduced benzo-4*H*- pyrans constitutes a unique method, since these compounds are extremely sensitive to base[8], however the presence of at least one nitrile group in



the active methylene compound seems to be necessary for the formation of **12**. Thus, in view of facile functionalisation of **3** and **4**, the present approach could be implemented to obtain other derivatives of **8**, **10**, or **12**.

Michael additions have been advantageously performed by using surface mediated solid phase reactions employing anhydrous zinc chloride impregnated alumina (Al_2O_3)[10]. We envisaged that acyclic nucleophiles, ethyl acetoacetate or 2,4-pentanedione might react with oxazinanes **3** under these conditions to furnish 4*H*-pyran systems and a combination of a cyclic and an acyclic carbon nucleophile might react with **3** to yield benzo-4*H*-pyran derivatives . However, such reactions of ethyl acetoacetate with **3a** and acetylacetone with



3a and **3b** in the presence of $ZnCl_2$ impregnated on Al_2O_3 furnished **13a, 13b** and **13c** respectively. The formation of the pyran ring system during reactions of aldehydes with 2,4-pentanedione or ethyl acetoacetate in presence of $ZnCl_2$ as reported by Wolinsky[11] was not observed in our hands. The reaction of **3a** with a combination of ethyl cyanoacetate and 1,3-cyclohexanedione gave **12a**.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on PYE UNICAM SP 3-300 spectrophotometer. ^1H and ^{13}C NMR spectra were run on Bruker AC 200 instrument using TMS as the internal standard. Mass (70 ev) spectra and elemental analysis were performed on Shimadzu QP 2000A spectrometer and Perkin Elmer 2400 CHN elemental analyser, respectively. TLC was performed on

microplates coated with silica gel -G and the spots were developed in iodine chamber. Column chromatography was performed on silica gel (60-120 mesh). CH_3CN and THF were dried over P_2O_5 and sodium/benzophenone ketyl respectively. 1,3-oxazinanes **3** and 1,3-oxazolidines **4** were synthesised by reported methods[6,12].

Reactions of 1,3-oxazinanes (3) / 1,3-oxazolidines (4) with carbon-nucleophiles.
Method A

A solution of **3** (0.01 mol) or **4** (0.01 mol) and carbon nucleophiles, (0.02 mol) (.01 mol each in case of combination) in anhydrous acetonitrile (30-40 ml) containing an acid (10:1) was stirred or refluxed till the reaction was completed (TLC). The reaction mixture was basified with cold aqueous sodium carbonate solution and extracted with chloroform (3x50ml). The extract was washed with cold water (2x50ml) and dried (anhydrous sodium sulphate). Solvent was removed and the residue was chromatographed using hexane, chloroform, ethylacetate and their mixtures as eluents.

Method B

Chromatographic grade alumina (1g), activated by heating at 200°C for 5 hrs in vacuo and subsequent cooling (under purified nitrogen atmosphere), was mixed, at 0°C, with a solution of anhydrous zinc chloride (1 mmol) in THF (6 ml) and the mixture stirred for 10 minutes. Excess THF was removed under reduced pressure and the $ZnCl_2/Al_2O_3$ catalyst was used for subsequent reactions of **3** and carbon nucleophiles (1mmol) in solid phase. The reaction mixture was stirred or shaken at ambient temperature under N_2 atmosphere till the reaction was completed (TLC). The mixture was extracted with anhydrous dichloromethane and the residue after distillation of the solvent was column chromatographed.

*Using **method A**, the following compounds were obtained.*

2,2'-(Phenylmethylene) bis-(5,5-dimethyl-1-hydroxycyclohex-1-en-3-one) (7a) : Yield 95%; Reaction time 5 hrs.; Solid, m. p. 196°C (lit.[13] 195°C); IR (KBr) ν : 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.10 (s, 6H, 2xCH_3), 1.24 (s, 6H, 2xCH_3), 2.43-2.25 (m, 8H, 4xCH_2), 5.54 (s, 1H, CH), 7.07-7.30 (m, 5H, ArH), 11.91 (brs, exchanges with D_2O, 2H, OH); ^{13}C NMR ($CDCl_3$) δ: 27.42, 29.62, 31.41, 32.76, 46.47, 47.06, 115.59, 125.78, 126.78, 128.21, 138.06, 189.36, 190.42.

2,2'-(Methylmethylene) bis-(5,5-dimethyl-1-hydroxycyclohex-1-en-3-one) (7b) : Yield 95%; Reaction time 8 hrs; Solid, m. p. 138°C (lit.[13] 141°C); IR (KBr) ν : 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.05 (s, 12H, 4xCH_3), 1.24 (d, J = 7.54 Hz, 3H, CH_3), 2.72 (s, 8H, 4xCH_2), 4.14 (q, J = 7.46 Hz, 1H, CH), 12.52 (brs, exchanges with D_2O, 2H, OH); ^{13}C NMR ($CDCl_3$) δ: 16.04, 18.94, 21.27, 24.02, 27.12, 32.72, 33.38, 37.07, 117.96, 118.97, 164.61, 191.19, 197.51.

2,2'- Methylene bis- (5,5-dimethyl-1-hydroxycyclohex-1-en-3-one) (7c) : Yield 25%; Reaction time 2 hrs. , Solid, m. p. 189°C (lit.[13] 189°C); IR (KBr) ν : 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.06 (s, 12H, 4xCH_3), 2.30 (s, 8H, 4xCH_2,) 3.17 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ: 15.90, 27.12, 29.40, 31.73, 45.96, 113.41, 189.50.

2,2'- (Phenylmethylene) bis-(1-hydroxycyclohex-1-en-3-one) (7e) : Yield 80%; Reaction time 4 hrs.; Solid, m. p. 208°C (lit.[14] 208°C); IR (KBr) ν : 1620 cm^{-1} ; ^1H NMR ($CDCl_3$) δ: 2.00-2.60 (m, 12H, 6xCH_2), 5.47 (s, ,1H, CH), 7.08-7.30 (m, 5H, ArH), 12.35 (brs, exchanges with D_2O, 2H, OH); ^{13}C NMR ($CDCl_3$) δ: 20.13, 32.87, 32.97, 33.49, 116.47, 125.85, 126.50, 128.17, 137.88, 190.87, 192.08.

2,2'- (Methylene) bis-(1-hydroxycyclohex-1-en-3-one) (7f) : Yield 93 %; Reaction time 5 hrs.; Solid, m. p. 146°C (lit.[14] 148-50°C); IR (KBr) ν : 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.48 (d, J = 7.54 Hz, 3H, CH_3), 1.80-2.60 (m, 12H, 6xCH_2), 4.11 (q, J = 7.46 Hz, 1H, CH), 12.91 (brs, exchanges with D_2O, 2H, OH); ^{13}C NMR ($CDCl_3$) δ: 16.04, 18.94, 19.95, 20.51, 20.96, 22.21, 32.72, 33.37, 37.07, 117.96, 118.97, 164.61, 191.19, 197.51.

1,8-Dioxo-3,3,6,6-tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene (8a) : Yield 92%; Reaction time 4 hrs.; Solid, m. p. 205°C (lit.[15] 205°C); IR (KBr) ν : 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.99 (s, 6H, 2xCH_3), 1.10 (s, 6H, 2xCH_3), 2.19 (s, 2H, CH_2), 2.20 (s, 2H, CH_2), 2.47 (s, 4H, 2xCH_2), 4.75 (s, 1H, CH), 7.09-7.31 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ: 27.43, 29.38, 32.31, 40.98, 50.85, 115.78, 126.47, 128.15, 128.49, 144.21, 162.36, 196.48.

1,8-Dioxo-3,3,6,6,9-pentamethyl-1,2,3,4,5,6,7,8-octahydroxanthene (8b) : Yield 94%; Reaction time 14 hrs.; Solid, m. p. 172°C (lit.[15] 176- 177°C); IR (KBr) ν : 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.09 (s, 12H, 4xCH_3), 1.70 (d, J = 6.5 Hz, 3H, CH_3), 2.26 (s, 4H, 2xCH_2), 2.35 (s, 4H, 2xCH_2), 3.63 (q, J = 6.46 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ: 21.52, 27.08, 29.09, 31.94, 40.71, 50.81, 116.63, 182.54, 196.92.

1,8-Dioxo-9-carbethoxymethyl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (8d) : Yield 44%; Reaction time 38 hrs.; Solid, m. p. 118°C (lit.[16] 121°C); IR (KBr) ν : 1720, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.13 (s, 12H, 4xCH_3), 1.18 (t, J = 7.11 Hz, 3H, CH_3), 2.31 (s, 4H, 2xCH_2), 2.41 (s, 4H, 2xCH_2), 2.74 (d, J = 4.11, 2H, CH_2), 3.91 (t, J = 4.21 Hz, 1H, CH), 4.04 (q, J = 7.13 Hz, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ: 14.25, 23.80, 27.09, 29.47, 31.19, 32.04, 36.50, 40.93, 50.88, 60.02, 113.20, 164.61, 172.13, 197.10.

1,8-Dioxo-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene (8e) : Yield 92%; Reaction time 4 hrs.; Solid, m. p. 255°C (lit.[17] 256°C); IR (KBr) ν : 1655 cm^{-1} ; ^1H NMR ($CDCl_3$) δ: 1.94-2.65 (m, 12H, 6xCH_2), 4.61 (s, 1H, CH), 7.10-7.32 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ: 20.32, 27.17, 31.65, 38.97, 116.95, 126.41, 128.11, 128.39, 144.39, 163.87, 196.45.

1,8-Dioxo-9-methyl-1,2,3,4,5,6,7,8-octahydroxanthene (8f) : Yield 90%; Reaction time 6 hrs.; Solid, m. p. 98°C (lit.[18] 103°C); IR (KBr) ν : 1650 cm^{-1} ; ^1H NMR ($CDCl_3$) δ: 1.07 (d, J = 6.13 Hz, 3H, C_9-CH_3), 1.91-2.61 (m, 12H, 6xCH_2), 3.66 (q, J=6.49 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ : 20.40, 20.86, 22.11, 27.02, 36.99, 117.92, 164.25, 197.18.

1,8-Dioxo-9-benzoylmethyl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (8g) : Yield 77%; Reaction time 6 hrs.; Solid m. p. 131°C; IR (KBr) ν : 1690, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.99 (s, 6H, 2x CH_3), 1.05 (s, 6H, 2x CH_3), 2.26 (s, 4H, 2x CH_2), 2.29 (s, 4H, 2x CH_2), 3.75 (d, J = 7.07 Hz, 2H, CH_2), 4.79 (t, J = 7.09 Hz, 1H, CH), 7.39- 7.56 (m, 3H, ArH), 7.91- 7.96 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$) δ: 24.34, 26.35, 29.79, 31.08, 38.60, 46.15, 46.88, 116.42, 127.99, 128.51, 132.98, 136.90, 189.27, 190.28; MS *m/z* : 392 (M^+).

1,8-Dioxo-9-benzoylmethyl-1,2,3,4,5,6,7,8-octahydroxanthene (8h) : Yield 66%; Reaction time 6 hrs.; Solid m. p. 155°C; IR (KBr) ν : 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.80-2.49 (m, 12H, 6xCH_2), 3.70 (d, J = 6.5 Hz, 2H, CH_2), 4.77 (t, J = 6.88 Hz, 1H, CH), 7.40-7.95 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ: 19.75, 24.66, 32.58, 33.23, 38.90, 117.55, 127.89, 128.42, 132.88, 136.80, 190.80, 191.74, 197.76; MS *m/z* : 336 (M^+).

3,3-Dimethyl-5-ethoxycarbonyl-6-hydroxy-3,4-dihydro-1,2(2H)-napthalenone (9a) : Yield 63%; Reaction time 5 hrs.; Solid m. p. 117°C; IR (KBr) ν : 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.06 (s, 6H, 2x CH_3), 1.47 (t, J = 7.12 Hz, 3H, CH_3), 2.44 (s, 2H, CH_2), 3.13 (s, 2H, CH_2), 4.50 (q, J = 7.16 Hz, 2H, CH_2), 6.93 (d, J = 8.84 Hz, 1H, CH), 8.18 (d, J = 8.8 Hz, 1H, CH); 11.59 (brs, 1H, exchanges with D_2O, OH), ^{13}C NMR ($CDCl_3$) δ: 28.47, 32.92, 43.51, 50.84, 62.15, 112.03, 116.68, 125.29, 133.63, 146.23, 166.59, 170.92, 196.22; MS *m/z* : 262 (M^+); (Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.70; H, 6.87. Found: C, 68.21; H, 6.66).

5-Ethoxycarbonyl-6-hydroxy-3,4-dihydro-1,2(2H)-napthalenone (9b) : Yield 61 %; Reaction time 5 hrs.; Solid, m. p. 115°C; IR (KBr) ν : 1670, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 1.47 (t, 3H, J = 7.1 Hz, CH_3), 2.08 (quintet, J = 6.02 Hz, 2H, CH_2), 2.58 (t, J = 6.02 Hz, 2H, CH_2), 3.26 (t, J = 6.1 Hz, 2H, CH_2), 4.48 (q, J = 7.12 Hz, 2H, CH_2), 6.93 (d, J = 8.84 Hz, 1H, CH), 8.20 (d, J = 8.88 Hz, 1H, CH), 11.68 (s, 1H, exchanges with D_2O, OH); ^{13}C NMR ($CDCl_3$) δ: 14.12, 22.79, 29.54, 37.66, 82.08, 111.41, 116.63, 125.97, 133.95, 148.22, 166.26, 170.91, 196.15; MS *m/z* : 234 (M^+); (Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 64.43; H, 5.63).

5-Acetyl-3,3-dimethyl-5-ethoxycarbonyl-6-hydroxy-3,4-dihydro-1,2(2H)-napthalenone (9c) : Yield 39%, Reaction time 10 hrs, Solid, m.p. 128°C, IR (KBr) ν : 3430, 1685, 1655 cm^{-1}, ^1H NMR ($CDCl_3$+ DMSO-d_6) δ : 1.05 (s, 6H, 2xCH_3), 2.38 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.64 (s, 2H, CH_2), 6.87 (d, 1H, J = 8.45, CH), 7.83 (d, J = 8.57 Hz, 1H, CH) 10.78 (brs, exchanges with D_2O, 1H, OH); ^{13}C NMR ($CDCl_3$+DMSO-d_6) δ : 27.83, 31.50, 32.87, 51.21, 114.22, 123.75, 128.53, 129.09, 140.54, 158.92, 195.45, 203.73 ; MS *m/z* : 232 (M^+).

Benzylidine ethylcyanoacetate (10a) : Yield 70%; Reaction time 5 hrs.; Solid, m. p. 49°C (lit.[19] m. p. 44-47°C); IR (KBr) ν : 2220, 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 1.35 (t, J = 6 Hz, 3H, CH_3), 4.3 (q, J = 6 Hz, 2H, CH_2), 7.8-7.9 (m, 5H, ArH), 8.1 (s, 1H, CH).

Benzylidinemalononitrile (10b) : Yield 90%; Reaction time 2 hrs.; Solid, m. p. 87°C (lit.[20] m. p. 83.5 - 84°C); IR (KBr) ν : 2260 cm^{-1} , ^1H NMR ($CDCl_3$) δ : 7.50-8.30 (m, 6H, ArH and CH).

β-Nitrostyrene (10c) : Yield 90 %; Reaction time 5 hrs.; Solid, m. p. 58°C (lit.[21] m. p. 58°C); IR (KBr) ν : 1550, 1370 cm^{-1} ; ^1H NMR ($CDCl_3$) δ : 7.30-7.90 (m, 7H, ArH).

Benzylidinedibenzoylmethane (10d) : Yield 72%; Reaction time 40 hrs.; Solid, m. p. 87°C (lit.[8] m. p. 87-88°C); IR (KBr) ν : 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 6.7-7.9 (m, 16H, ArH and CH).

Benzylidine diethylmalonate (10e) : Yield 55%; Reaction time 8 hrs.; liquid (lit.[20] liquid); IR (KBr) ν : 1745 cm^{-1}. ; ^1H NMR ($CDCl_3$) δ : 1.35 (t, J = 6 Hz, 6H, 2xCH_3), 4.2 (q, J = 6 Hz, 4H, 2xCH_2), 7.1-7.65 (m, 5H, ArH), 7.7 (s, 1H, CH).

2-Amino-5,6,7,8-tetrahydro-5-oxo-4-phenyl-4*H*-benzo-[b]-pyran-3-ethylcarboxylate (12a) (also obtained by method B) : Yield 78%, Reaction time 1 hr.; Solid m. p. 180-81°C; IR (KBr) ν : 3400, 3300, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 1.14 (t, J = 7.06 Hz, 3H, CH_3), 1.97-2.56 (m, 6H, 3x CH_2), 4.02 (q, J = 7.09 Hz, 2H, OCH_2), 4.68 (s, 1H, CH), **6.16** (brs, exchanges with D_2O, 2H, NH_2), 7.14–7.25 (m, 5H, ArH), ^{13}C NMR ($CDCl_3$) δ : 14.19, 20.20, 26.94, 33.76, 36.62, 59.63, 80.74, 118.15, 126.03, 127.79, 128.24, 146.02, 158.37, 162.98, 169.10, 196.50; MS *m/z* : 313 (M^+); (Anal. Calcd. for C_{18} H_{19} NO_4 : C, 69.01; H, 6.07; N, 4.47. Found: C, 69.27; H, 5.89; N, 4.60).

2-Amino-5,6,7,8-tetrahydro-5-oxo-4-phenyl-4*H*-benzo-[b]-pyran-3-carbonitrile (12b): Yield 86%; Reaction time 2 hrs.; Solid, m. p. 227°C; IR (KBr) ν : 3400, 3300, 2193cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6) δ : 1.99-2.62 (m, 6H, 3x CH_2), 4.26 (s, 1H, CH), **6.49** (brs, exchanges with D_2O, 2H, NH_2), 7.17 - 7.29 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ : 18.33, 25.11, 33.87, 34.93, 57.22, 112.55, 118.31, 125.10, 125.62, 126.79, 142.97, 157.06, 163.03, 194.84; MS *m/z* : 266 (M^+); (Anal. Calcd. for C_{16} H_{14} N_2O_2 : C, 72.11; H, 5.26; N, 10.52. Found: C, 72.47; H, 4.98; N, 10.71).

2-Amino-5,6,7,8-tetrahydro-5-oxo-4-phenyl-7,7-dimethyl-4*H*-benzo-[b]-pyran-3-ethylcarboxylate (12c) : Yield 73 %, Reaction time 1 hr.; Solid, m. p. 138°C; IR (KBr) ν : 3400, 3300, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 0.97 (s, 3H, CH_3); 1.09 (s, 3H, CH_3), 1.16 (t, J = 7.06 Hz, 3H, CH_2), 2.18 (m, 2H, CH_2), 2.43 (s, 2H, CH_2), 4.02 (q, J = 7.06 Hz, 2H, CH_2), 4.70 (s, 1H, CH), **6.16** (brs, exchanges with D_2O, 2H, NH_2), 7.26 - 7.16 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ : 14.20, 27.33, 29.07, 32.17, 33.65, 40.59, 50.68, 59.59, 116.75, 126.01, 127.74, 128.22, 145.89, 158.50, 161.47, 169.08, 196.44; MS *m/z* : 341 (M^+); (Anal. Calcd. for C_{20} H_{23} NO_4 : C, 70.38; H, 6.74; N, 4.10. Found: C,70.62; H, 6.34; N, 4.28).

2-Amino-5,6,7,8-tetrahydro-5-oxo-4-phenyl-7,7-dimethyl-4*H*-benzo-[b]-pyran-3-carbonitrile (12d) : Yield 81%; Reaction time 2 hrs.; Solid, m. p. 218°C; IR (KBr) ν : 3350, 2201 cm^{-1}; ^1H NMR ($CDCl_3$+ DMSO- d_6) δ : 1.01 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.18 (m, 2H, CH_2), 2.50 (s, 2H, CH_2), 4.42 (s, 1H, CH), 6.67 (brs, exchanges with D_2O, 2H, NH_2), 7.17 - 7.26 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ : 25.46, 26.97, 30.24, 33.99, 48.62, 57.17, 111.42, 118.18, 125.04, 125.60, 126.70, 142.92, 157.00, 160.94, 194.37; MS *m/z* : 294 (M^+); (Anal. Calcd. for C_{18} H_{18} N_2O_2 : C, 73.46; H, 6.12; N, 9.52. Found: C, 73.73; H, 5.89; N, 9.77).

*Using **method B**, the following compounds were obtained.*

Diethyl-3-methyl-3-hydroxy-5-phenyl cyclohexanone-4, 6-dicarboxylate (13a) : Yield 29%, Reaction time 96 hrs.; Solid m. p. 155 °C; IR (KBr) ν: 1730, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.8 (t, J = 7.14 Hz, 3H, CH_3), 1.0 (t, J = 7.14 Hz, 3H, CH_3), 1.35 (s, 3H, CH_3), 2.61 (distorted AB q , J = 14.28 Hz, 2H, CH_2), 3.05 (d, J = 12.06 Hz, 1H, CH), 3.68 (d, J = 12.06 Hz, 1H, CH), 3.73 (dd, J = 2.68 Hz, and , 1.0 Hz, 1H, CHPh), 3.85 (two q , J = 6.5 Hz, 2H, CH_2), 4.0 (m, 3H, CH_2 and OH); 7.27 - 7.33 (m, 5H, ArH), ^{13}C NMR ($CDCl_3$) δ : 13.41, 13.97, 28.70, 45.29, 52.79, 57.10, 61.02, 62.57, 73.04, 96.19, 127.25, 128.13, 128.65, 138.24, 167.60, 173.84, 201.09; MS *m/z* : 331(M^+-H_2O); (Anal. Calcd. for C_{19} H_{24} O_6 : C, 65.51; H, 6.89. Found: C, 64.93; H, 6.28).

4,6-Diacetyl-3-methyl-3-hydroxy-5-phenyl cyclohexanone (13b) : Yield 54 %; Reaction time 68 hrs.; Solid, m. p. 156 °C; IR (KBr) ν: 3430, 1720, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 1.16 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.38 - 2.64 (distorted AB q , J = 14.20 Hz and J = 2.02 Hz, 2H, CH_2, converted into a q after D_2O exchange, J = 14.26 Hz, 2H), 3.71 (d, J = 12.33 Hz, 1H, CH), 3.20 (d, J = 11.58 Hz, 1H, CH),

3.92 (dd, J = 3.97 Hz and J = 5.15 Hz, 2H, CHPh and OH converted into a t, J = 12.06 Hz after D_2O exchange), 7.14 - 7.34 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ : 26.40, 30.11, 34.33, 45,50, 53.51, 61.64, 67.92, 96.24, 127.62, 128.13, 129.34, 203.18, 210.12, 215.53; MS *m/z* : 270 (M^+-H_2O); (Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.83; H, 6.94. Found: C,70.23; H, 6.72).

4,6-Diacetyl-3-hydroxy-3,5-dimethyl-cyclohexanone (13c) : Yield 27%, Reaction time 120 hrs.; Solid m. p. 103°C; IR (KBr) ν: 1720, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 0.96 (d, J = 5.55 Hz, 3H, CH_3), 1.28 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.26- 2.59 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.83 (d, J = 11.03 Hz, 1H, CH), 2.92 (q, J = 4.94 Hz, 1H, CH), 3.02 (d, J = 10.18 Hz, 1H, CH), 3.48 (brs, 1H, OH, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) δ : 18.43, 29.64, 30.04, 33.92, 34.48, 53.52, 61.79, 69.00, 73.38, 204.65, 205.29, 214.97; MS *m/z* : 226 (M^+-H_2O); (Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.71; H, 7.96. Found: C, 63.62; H, 7.82).

Acknowledgements The authors thank CSIR, New Delhi for financial assistance.

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(*Received in UK* 8 *May* 1996; *revised* 23 *September* 1996; *accepted* 26 *September* 1996)