Facile one–pot synthesis of some new 2-amino-4*H*-pyran derivatives

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The one-pot reaction of alkylisocyanides **1** and acetylenic esters **2** in the presence of 1, 3-diketones **3** provides an efficient access to 2-amino-4*H*-pyrans **4a–l**. Ketenimines **5** were detected in the early stage of reaction as intermediates. The products **4a–l** are stabilised by an intra molecular N–H…O hydrogen bonding.

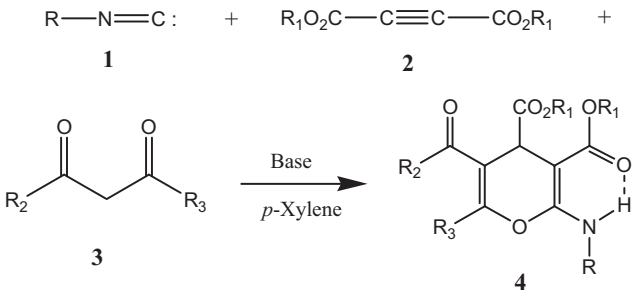
Keywords: one-pot reaction, 2-amino-4*H*-pyran, ketenimine, intramolecular H-bonding

Substituted 2-amino-4*H*-pyrans have been shown to exhibit biological activity as anti-cancer, antihypertensive and coronary dilating agents.[1] They have also served as convenient starting material for synthesis of some condensed heterocycles.[2-9]

These interesting properties of 2-amino-4*H*-pyrans led us to investigate a simple and efficient synthesis with the goal of obtaining more potent pharmacologically active compounds. Various methods are known to give 2-amino-4*H*-pyran derivatives.[10-18] We have already reported the reaction of alkyl isocyanides and dialkyl acetylene dicarboxylates in the presence of 1, 3-diphenyl-1, 3-dione which produced highly functionalised ketenimines[19] and 2-amino-4*H*-pyran derivatives.[20] We now report a one-pot reaction for the synthesis of some new 2-amino-4*H*-pyrans **4a–l** in fairly high yields. (Scheme 1) The results are shown in Table 1.

The addition of equimolar amounts of alkyl isocyanides to acetylenic esters led to 1:1 adducts **6**. Protonation of **6** with 1, 3-diketones **3** gave ketenimines **5**. In the early stage of this reaction, appearance of the C=C=N absorption band (at near 2060 cm^{-1}) is evidence for formation of ketenimine as intermediate. When the intensity of this bond reached to its maximum, (after 100–150 min, the results are shown in Table 1), the base (triethylamine) was added and the reaction mixture was refluxed for 1-2 days. The reaction was completed when the absorption band of C=C=N group, near 2060 cm^{-1}, in the IR spectrum of reaction mixture disappeared. The final products **4a–l** can be isolated and purified in this stage.

A possible mechanism for the formation of intermediates **5a–l** and products **4a–l** is shown in Scheme 2. Addition of alkylisocyanide **1** to the acetylenic ester **2** formed the 1 : 1 adduct **6**, which was followed by protonation by 1, 3-diketone **3**. The ketenimine **5** was formed upon attack of anion of **3** to positively charged adduct of **6**. The ketenimine **5** has an acidic proton which is deprotonated by using the base (triethylamine) and converted into **4**. As the ketenimines **5a–l**, were not stable we could not isolate them in a pure form.



Scheme 1

Structures **4a–l** were assigned to the isolated products based on their elemental analysis, IR, ^1H NMR, ^{13}C NMR and mass spectral data. The mass spectra of **4a–l** displayed molecular ion peaks at appropriate *m/z* values but were not very intense, probably due to ester groups and steric hinderance of functional groups in their structures. Initial fragmentation involved the loss of 4*H*-pyran side chains (CO_2R', HCO_2R', R'OH, CH_3CO, C_6H_5CO, CH_3, C_6H_5) and scission of the rings.

The IR spectral data for compounds **4a–l** showed the N–H absorption (3335–3535 cm^{-1}) which was not exchanged in CCl_4. This a evidence for intramolecular H-bonding. We have recently reported the X-ray structures of 2-amino-4*H*-pyran derivatives including **4c**.[21-22]

In the IR spectrum of **4a–l** there were two sharp carbonyl absorptions (1749–1675 cm^{-1}) and three sharp C–O absorptions (Experimental section).

The ^1H NMR spectrum of **4a** showed seven sharp singlet peaks, readily recognisable as arising from *tert*-butyl (δ = 1.36 ppm), one methyl and one acetyl (2.20, 2.37 ppm), two methoxy (3.67, 3.81 ppm), methyne (4.52 ppm) and a singlet signal at 8.51 ppm for the amine group which appears downfield as a result of the presence of electron withdrawing groups in the rigid 4*H*-pyran ring and intra molecular N–H…O hydrogen bonding. The ^1H NMR spectra of **4b–l**

Table 1 2-Amino-4*H*-pyrans (**4**), time/min: the time for completing the synthesis of intermediate (**5**)

Compd. entry	R	R_1	R_2	R_3	Time/min	Yield/%
4a	*t*-But	Me	Me	Me	120	86
4b	*t*-But	Me	Me	Me	140	68
4c	*t*-But	*t*-But	Me	Me	135	74
4d	Cyclohexyl	Me	Me	Me	115	83
4e	Cyclohexyl	Et	Me	Me	140	70
4f	Cyclohexyl	*t*-But	Me	Me	135	76
4g	Benzyl	Me	Me	Me	100	84
4h	Benzyl	Et	Me	Me	120	72
4i	Cyclohexyl	Me	Me	Ph	150	70
4j	Cyclohexyl	Me	Ph	Me		4i/4 j : 2/3
4k	Cyclohexyl	Et	Me	Ph	155	65
4l	Cyclohexyl	Et	Ph	Me		4k/4 l : 2/3

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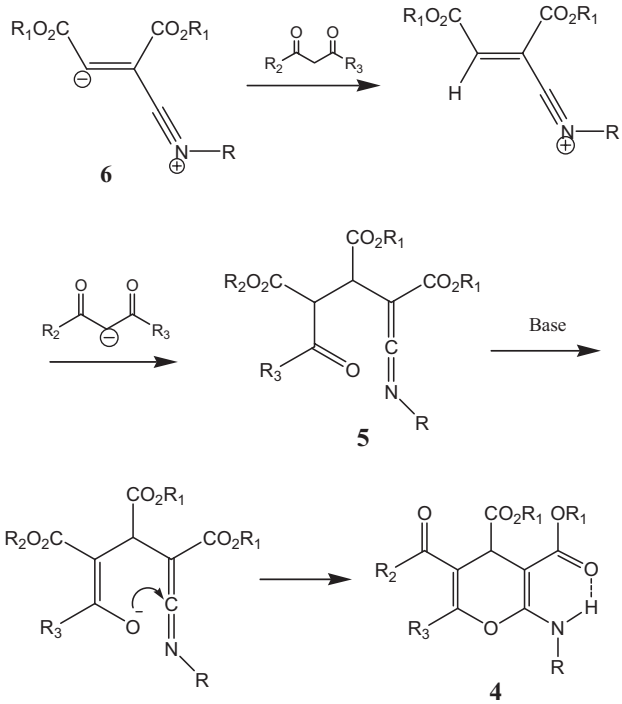

Scheme 2

were similar to that of **4a**, except for the signals of the cyclohexyl, benzyl and ester groups and difference in the N–H groups and their proton- proton coupling.

The ^{13}C NMR spectrum of **4a** displayed resonances in agreement with appropriate structure of **4a**, only resonance of $C_3(C{=}CO_2Me)$ is more shielded than we expected as a result of the electron pairs of the N, O atoms existing in α-position to this carbon in the 4*H*-pyran ring. Partial assignments of these resonances are given in the experimental section. The ^{13}C NMR spectral data for compounds **4b–l**, as shown in the experimental section, were consistent with the proposed structures.

The reaction described here represents a simple and efficient entry to the synthesis of highly functionalised 2-amino-4*H*-pyrans with potential biological activities.

Experimental

Chemicals and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Column chromatography was performed on silica Gel (0.015–0.04 mm, mesh-size) and TLC on precoated plastic sheets (25 $DC_{UV\text{-}254}$) respectively. Melting points were measured on Gallenkamp melting point apparatus and were not corrected. Elemental analysis for C, H and N were performed using a Thermo Finnigan Flash EA1112 instrument. IR spectra were measured on a Shimidazu FT-IR-4300 spectrophotometer as KBr discs. ^1H NMR and ^{13}C NMR spectra were determined in $CDCl_3$ on a Bruker 500 spectrometer and chemical shifts were expressed in ppm downfield from tetramethylsilane. Mass spectra were recorded on a Finnegan-MAT 8430 spectrometer at an ionisation potential of 70ev.

General procedure

To a magnetically stirred solution of alkylisocyanide (5 mmol) and acetylenic ester (5 mmol) in *p*-xylene, (20 ml) a mixture of 1, 3-diketone, 5 mmol in *p*-xylene (10 ml) was added drop wise at –10°C over 20 min. The reaction mixture was allowed to warm up to room temperature and was refluxed in the presence of triethylamine (0.01 g, 1 mmol). The reaction was monitored by TLC. After completing the reaction the solvent was removed under reduced pressure and the residue was purified by column chromatography using ethyl acetate-hexane (1:3) as eluent. The products were obtained as white to yellow crystals. The products was recrystallised by water-acetone as co-solvent.

Dimethyl-2-(N-tert-butylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4a**): M.p. 107–108ºC. IR (KBr) υ_{max}: 3386 (NH), 2954, 2937 (CH), 1747, 1699 (C=O), 1602 (C=C), 1444, 1379 (C–H), 1296, 1197, 1080 (C–O) cm^{-1}; ^1H NMR δ 1.36 (9H, *t*-Bu, s), 2.25 (3H, CH_3, s), 2.37 (3H, CH_3CO, s), 3.67, 3.81(6H, $2CH_3CO$, 2 s), 4.52 (1H, CH, s), 8.51 (1H, NH, brs) ppm; ^{13}C NMR δ 17.46 (CH_3), 28.46 ($^{13}CH_3$–CO), 29.35(CH_3 of *t*-Bu), 33.70 (^{13}C Me_3), 49.87(^{13}CH–CO_2Me), 51.22, 51.35 (CH_3 of $2CO_2Me$), 81.25 (=^{13}C–CO_2Me), 112.78 (=^{13}C–CO Me), 154.98 (=^{13}C–CH_3), 159.53 (=^{13}C–NH), 166.20, 172.11 (2C=O of CO_2Me), 196.01 (C=O) ppm; MS: *m/z* (fragment, %)325 (M^+, 4), 267(M^+–CO_2Me, 100), 210 (M^+–CO_2Me, *t*-Bu, 36), 43 (CH_3CO^+, 25); Anal. Calc. for $C_{16}H_{23}NO_6$: C, 59.23; H, 6.84; N, 4.31; Found: C, 59.20; H, 6.80; N, 4.32%.

Diethyl-2-(N-tert-butylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4b**): M.p. 96–98ºC. IR (KBr) υ_{max}: 3369(NH), 3020, 2967 (CH), 173 3.1701 (C=O), 1600 (C=C), 1446, 1365 (C–H), 1286, 1245, 1201, 1074 (C–O) cm^{-1}; ^1H NMR δ 1.09–1.32 (6H, CH_3 of CO_2Et, 2t), 1.37 (9H, $C(CH_3)_3$, s), 2.39, 2.44 (6H, $2CH_3$, 2 s), 3.94–4.28 (4H, *J* = 6.59 Hz, $2CH_2$ of Et, 2q), 4.45(1H, CH, s), 8.50 (1H, NH, brs) ppm; ^{13}C NMR δ 13.55, 14.76 ($2CH_3$ of $2CO_2Et$), 18.25(CH_3), 29.50 ($^{13}CH_3CO$), 40.46($^{13}CMe_3$), 49.57(^{13}CH–CO_2Et), 59.98, 61.13 ($2CH_2$ of CO_2Et), 82.40 (=^{13}C–CO_2Et), 113.91(=^{13}C–COMe), 155.03 (=^{13}C–CH_3), 159.76 (=^{13}C–NH), 169.59, 172.11(2C=O of CO_2Et), 193.30 (C=O) ppm; MS: *m/z* (fragment, %) 354 (M^+, 5), 280 (M^+–CO_2Et, 85), 255 (M^+–CO_2Et, *t*-Bu, 72), 43(CH_3CO^+, 100); Anal. Calc. for $C_{18}H_{27}NO_6$: C, 61.17; H, 7.70; N, 3.96; Found: C, 61.14; H, 7.68; N, 3.99%.

Ditert-butyl-2-(tert-butylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4c**): M.p. 128–130ºC. IR(KBr) υ_{max}: 3352 (NH), 2998, 2947(CH), 1747, 1687(C=O), 1593 (C=C), 1444, 1371 (C–H), 1291, 1184, 1057(C–O) cm^{-1}; ^1H NMR δ 1.34–1.37, 1.47 (27H, 3*t*-Bu, 3 s), 2.22 (3H, CH_3, s), 2.39 (3H, CH_3, s), 4.29 (1H, CH, s), 8.51 (1H, NH, brs) ppm; ^{13}C NMR δ 18.57 (CH_3), 28.33, 28.99 ($2CH_3$ of $2CO_2t$-Bu), 29.67 (CH_3 of CH_3CO), 30.67(CH_3 of N-*t*-Bu), 40.91 (^{13}C-N-*t*-Bu), 52.45 (^{13}CH-CO_2t-Bu), 79.53, 81.32 ($2^{13}CO_2t$-Bu), 84.10 ($^{13}C{=}CO_2t$-Bu), 114.27 (=^{13}COPh), 155.08 (=^{13}C-CH_3), 160.20 (=^{13}C-NH), 169.04, 172.34 (2C=O of CO_2t-Bu), 199.63 (C=O)ppm; MS: *m/z* (fragment, %) 409(M^+, 6), 309(M^+–CO_2t-Bu, 100), 253 (M^+–CO_2t-Bu, *t*-Bu, 70), 43 (CH_3CO^+, 25); Anal. Calc. for $C_{22}H_{35}NO_6$: C, 64.52; H, 8.61; N, 3.42; Found:C, 64.50; H, 8.58; N, 3.46%.

Dimethyl-2-(N-cyclohexylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4d**): M.p. 104–106ºC. IR (KBr) υ_{max}: 3395(N–H), 2991, 2896 (C–H), 1739, 1703 (C=O), 1569(C=C), 1446, 1359(C–H), 1288, 1247, 1199, 1164 (C–O) cm^{-1}; ^1H NMR δ 1.31–1.45 (10H, CH_2 of cyclohexyl, m), 2.25 (3H, CH_3, s), 2.40 (3H, CH_3CO, s), 2.64 (1H, CH of cyclohexyl, m), 3.64, 3.70 (6H, $2CH_3$ of CO_2Me, 2 s), 4.49(1H, CH, 2 s), 8.29 (1H, *J* = 8.26 Hz, NH, d) ppm; ^{13}C NMR δ 18.98 (CH_3), 24.88, 25.95, 33.92, 34.23, 39.38 (cyclohexyl carbons), 29.99 ($^{13}CH_3CO$), 50.35, 51.30 ($2CH_3$ of CO_2Me), 52.71 (^{13}C-CO_2Me), 81.95 (=^{13}CH-CO_2Me), 114.25(=^{13}C-$COCH_3$), 156.72 (=^{13}C-CH_3), 159.71 (=^{13}C-NH), 169.64, 173.70 (2C=O of CO_2Me), 198.78 (C=O)ppm; MS: *m/z* (fragment, %)351 (M^+, 4), 292 (M^+–CO_2Me, 100), 210 (M^+–CO_2Me, cyclohexyl, 36), 43 (CH_3CO^+, 25); Anal. Calc. for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99; Found: C, 61.50; H, 7.15; N, 4.11%.

Diethyl-2-(N-cyclohexylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4e**): M.p. 110–112ºC. IR (KBr)υ_{max}:3382(N–H), 2988, 2933 (C–H), 1737, 1683 (C=O), 1568 (C=C) 1440, 1369 (C–H), 1298, 1226, 1184, 1159 (C–O) cm^{-1}; ^1H NMR δ 1.12–1.26 (6H, $2CH_3$ of Et, 2t), 1.35–1.73(10H, CH_2 of cyclohexyl, m), 2.16 (3H, CH_3CO, s), 2.25 (1H, CH of cyclohexyl, s), 2.41(3H, CH_3, s), 3.97-4.23 (4H, *J* = 6.498 Hz, CH_2 of Et, 2q), 4.49 (1H, CH, s), 8.46 (1H, *J* = 8.15 Hz, NH, d) ppm; ^{13}C NMR δ 13.11, 13.58 ($2CH_3$ of Et), 17.47 (CH_3), 23.40, 24.48, 32.74 (CH_2 of cyclohexyl), 29.53 (CH_3 of CH_3CO), 38.10 (CH of cyclo- hexyl), 48.82(^{13}CH-CO_2Et), 58.29, 59.99 (2 CH_2 of Et), 88.60 (=^{13}C-CO_2Et), 112.78 (=^{13}CH-$COCH_3$), 154.99 (=^{13}C-CH_3), 158.07 (=^{13}C-NH), 167.85, 171.88 (2C=O of CO_2Et), 197.64 (C=O) ppm; MS: *m/z* (fragment, %)378 (M^+, 6), 307 (M^+–CO_2Et, 84), 225 (M^+–CO_2Et, cyclohexyl, 65), 43 (CH_3CO^+, 100); Anal.Calc. for $C_{20}H_{29}NO_6$: C, 63.31; H, 7.70; N, 3.69; Found:C, 63.30; H, 7.68; N, 3.72%.

Ditert-butyl-2-(N-cyclohexylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4f**): M.p. 132–134°C. IR (KBr) υ_{max}: 3335 (N–H), 2938, 2862 (C–H), 1720, 1676 (C=O), 1614 (C=C), 1492, 1455, 1367 (C–H), 1299, 1255, 1170, 1095 (C–O) $cm^{-1;}$ ^1H NMR δ 1.33–1.40 (18H, 2*t*-Bu, 2 s), 1.88–2.18 (10H, CH_2 of cyclohexyl, m), 2.23 (3H, CH_3, s), 2.33 (3H, CH_3CO, s), 2.71 (1H, CH of cyclohexyl, s), 4.25 (1H, CH, s), 8.12 (1H, *J* = 8.54 Hz, NH, d)ppm; ^{13}C NMR δ 18.50 (CH_3), 25.40, 26.25, 28.65, 37.43, 37.62 (CH_2 of cyclohexyl),

29.24 ($^{13}CH_3CO$), 42.42 (CH of cyclohexyl), 52.71(^{13}CH - CO_2t-Bu), 83.54 (^{13}C =CO_2t-Bu), 80.44, 82.35($^{13}CO_2t$-Bu), 114.16(=^{13}CH-$COCH_3$), 155.41(=^{13}C–CH_3), 159.96 (=^{13}C–NH), 169.44, 173.86 (2C=O of CO_2t-Bu), 199.48 (C=O) ppm; MS: *m/z* (fragment, %) 436(M^+, 15), 335 (M^+– CO_2t-Bu, 58), 278 (M^+–CO_2t-Bu, cyclohexyl, 100), 43 (CH_3CO^+, 50); Anal. Calc. for $C_{24}H_{37}NO_6$: C, 66.18; H, 8.56; N, 3.22; Found: C, 66.24; H, 8.55; N, 3.27%.

Dimethyl-2-(N-benzylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4g**): M.p. 118–120°C. IR(KBr) υ_{max}: 3371(NH), 3089, 2952, 2852(CH), 1738, 1679(C=O), 1603(C=C), 1454, 1384(C–H), 1261, 1159, 1090 (C–O) cm^{-1}; ^1H NMR δ 2.15(3H, CH_3, s), 2.40(3H, CH_3CO, s), 3.69, 3.37 (6H, $2CH_3CO$, 2 s), 3.78 (2H, *J* = 9.6, 3.3 Hz, CH_2, d of d), 4.52 (1H, CH, s), 7.30–7.32, 7.34–7.37 (5H, Ph protons, 2 m), 8.73 (1H, NH, brs) ppm; ^{13}C NMR δ 19.17(CH_3), 27.51($^{13}CH_3$-CO), 47.63 (CH_2 of benzyl), 49.76 (^{13}CH-CO_2Me), 52.94, 53.74 (CH_3 of CO_2Me), 82.09 (=^{13}C-CO_2Me), 113.18 (=^{13}C-COMe), 127.07, 128.39, 128.92, 129.52(Ph carbons), 153.63 (=^{13}C-CH_3), 158.98 (=^{13}C-NH), 167.02, 173.12 (2C=O of CO_2Me), 196.02(C=O) ppm; MS: *m/z* (fragment, %) 359(M^+, 9), 300 (M^+–CO_2Me, 39), 209 (M^+–CO_2Me, benzyl, 70), 91 (Ph-CH_2^+, 100); Anal. Calc. for $C_{19}H_{21}NO_6$: C, 63.48; H, 5.89; N, 3.89: Found: C, 63.45; H, 5.86; N, 3.92%.

Diethyl-2-(N-benzylamino)-5-acetyl-6-methyl-4H-pyran-3, 4-dicarboxylate (**4h**): M.p. 122–124°C. IR (KBr) υ_{max}: 3369(NH), 3092, 2952, 2853(CH), 1736, 1678 (C=O), 1602(C=C), 1453, 1381(C–H), 1259, 1148, 1095 (C–O)cm^{-1}, ^1H NMR δ 1.21-1.35(6H, CH_3 of CO_2Et, 2t), 2.37, 2.45(6H, $2CH_3$, 2 s), 3.92–4.29(4H, *J* = 6.60 Hz, $2CH_3$ of Et, 2q), 3.77 (2H, *J* = 9.7, 3.4 Hz, CH_2, d of d), 4.47 (1H, CH, s), 7.30–7.33, 7.34–7.37(5H, Ph protons, 2 m), 8.59(1H, NH, brs) ppm; ^{13}C NMR δ 13.56–14.69($2CH_3$ of CO_2Et), 20.01 (CH_3), 26.14 ($^{13}CH_3CO$), 47.26(CH_2 of benzyl), 48.93 (^{13}CH-CO_2Me), 58.87, 60.91($2CH_2$ of CO_2Et), 84.54(=^{13}C-CO_2Et), 112.19(=^{13}C-COMe), 127.70, 128.24, 129.73 (Ph carbons), 156.18 (=^{13}C-CH_3), 160.37(=^{13}C-NH), 168.95, 173.00 (2C=O of $2CO_2Et$), 192.91(C=O) ppm; MS: *m/z* (fragment, %) 387 (M^+, 7), 314 (M^+–CO_2Et, 38), 223 (M^+–CO_2Et, benzyl, 69), 91(Ph-CH_2^+, 100); Anal. Calc. for $C_{21}H_{25}NO_6$: C, 68.09; H, 6.51; N, 3.62; Found; C, 68.07; H, 6.50; N, 3.65%.

Dimethyl-2-(N-cyclohexylamino)-5-acetyl-6-phenyl-4H-pyran-3, 4-dicarboxylate (**4i**): M.p. 128–130ºC. IR (KBr) υ_{max}: 3535 (N–H), 3107, 2990, 2921(C–H), 1747, 1677(C=O), 1614 (C=C), 1292, 1201, 1170, 1098(C–O) cm^{-1}; ^1H NMR δ 1.30-1.46 (10H, CH_2 of cyclohexyl, m), 2.29 (3H, CH_3, s), 2.54 (1H, CH of cyclohexyl, m), 3.68, 3.77 (6H, $2CH_3$ of CO_2Me, 2 s), 4.62 (1H, CH, s), 7.14–7.23, 7.32–7.38 (5H, Ph protons, 2 m), 8.30 (1H, *J* = 8.2 Hz, NH, d) ppm; ^{13}C NMR δ 24.19 (CH_3 of acetyl), 24.42, 25.48, 29.79, 33.64 (CH_2 of cyclohexyl), 42.91(CH of cyclohexyl), 49.68, 50.84 ($2CH_3$ of CO_2Me), 50.08 (^{13}CH–CO_2Me), 79.97 (=^{13}C-CO_2Me), 104.81 (=^{13}C-$COCH_3$), 126.18, 127.72, 128.02, 128.65, 130.91(Ph carbons), 156.02 (=^{13}C-Ph), 159.94 (=^{13}C-NH), 169.80, 172.44 (2C=O of CO_2Me), 195.95 (C=O) ppm. MS: *m/z* (fragment, %) 413 (M^+, 9), 354 (M^+, CO_2Me, 67), 271 (M^+, CO_2Me, cyclohexyl, 100), 43 (CH_3CO^+, 56). Anal. Calc. for $C_{23}H_{27}NO_6$: C, 66.76; H, 6.58; N, 3.88 Found: C, 66.76; H, 6.57; N, 3.90%.

Dimethyl-2-(N-cyclohexyl)-5-benzoyl-6-methyl-4H-pyran-3, 4-di carboxylate (**4j**): M.p. 134–136°C. IR (KBr) υ_{max}: 3530(N–H), 3101, 2980, 2933(C–H), 1749, 1675(C=O), 1603 (C=C), 1280, 1191, 1160, 1094 (C–O) cm^{-1}; ^1H NMR δ 1.28-1.49 (10H, CH_2 of cyclohexyl, m), 2.19 (3H, CH_3 of acetyl, s), 2.63(1H, CH of cyclohexyl, m), 4.70(1H, CH, s) 7.18–7.30, 7.43–7.50 (5H, Ph protons, 2 m), 8.34 (1H, *J* = 8.80 Hz, NH, d) ppm; ^{13}C NMR δ 22.91(CH_3), 23.93, 26.02, 28.98, 29.76, 31.33 (CH_2 of cyclohexyl), 44.09 (CH of cyclohexyl), 48.17, 51.84 ($2CH_3$ of CO_2Me), 52.11 (^{13}CH-CO_2Me), 80.02 (=^{13}C-CO_2Me), 105.99 (^{13}C-COPh), 125.99, 128.40, 129.12, 129.98, 130.75, 131.04 (Ph carbons), 155.12 (=^{13}C-CH_3), 160.02 (=^{13}C-NH), 169.90, 173.40 (2C=O of CO_2Me), 196.59 (C=O) ppm; MS, m/z(fragment, %) 413 (M^+, 8), 334 (M^+–CO_2Me, 65), 271(M^+, CO_2Me, cyclohexyl, 78), 105 ($C_6H_5CO^+$, 100).Anal.Calc.for $C_{23}H_{27}NO_6$: C, 66.79; H, 6.58; N, 3.88; Found: C, 66.77; H, 6.56; N, 3.91%.

Diethyl-2-(N-cyclohexylamino)-5-acetyl-6-phenyl-4H-pyran-3, 4-dicarboxylate (**4k**): M.p. 126–128°C. IR(KBr) υ_{max}: 3385(N–H), 3112, 2993, 2920 (C–H) 1744, 1679(C=O), 1605 (C=C), 1294, 1200, 1169, 1099(C–O) cm^{-1}; ^1H NMR δ 1.01–1.19 (6H, $2CH_3$ of Et, 2t), 1.33–1.69(10H, CH_2 of cyclohexyl, m), 2.21 (3H, CH_3CO, s), 2.34 (1H, CH of cyclohexyl, m), 3.86–4.50 (4H, CH_2 of Et, 2q, *J* = 6.60 Hz), 4.62 (1H, CH, s), 7.10–7.21, 7.35–7.46(5H, Ph protons, 2 m), 8.42(1H, *J* = 8.12 Hz, NH, d) ppm; ^{13}C NMR δ 13.42, 13.85($2CH_3$ of Et), 23.51, 24.18, 25.35, 29.69 (CH_2 of cyclohexyl), 30.05 (CH_3 of CH_3CO), 39.98(CH of cyclohexyl), 49.84 (=^{13}C-CO_2Et), 58.88, 60.09 ($2CH_2$ of Et), 86.51 (=^{13}C-CO_2Et), 111.68(=^{13}C-$COCH_3$), 126.91, 127.02, 128.20, 129.67, 130.25 (Ph carbons), 159.86(=^{13}C-Ph), 160.01 (=^{13}C-NH), 168.18, 171.99 (2C=O of CO_2Me), 196.39(C=O) ppm, MS: *m/z* (fragment, %) 441 (M^+, 14), 365 (M^+– CO_2Et, 74), 285 (M^+–CO_2Et, cyclohexyl, 100), 43 (CH_3CO^+, 66); Anal. Calc. for $C_{25}H_{31}NO_6$: C, 67.99; H, 7.08; N, 3.17; Found: C, 67.96; H, 7.05; N, 3.21%.

Diethyl-2-(N-cyclohexylamino)-5-benzoyl-6-methyl-4H-pyran-3, 4- dicarboxylate (**4l**): M.p. 113–115°C. IR (KBr) υ_{max}: 3369(N–H), 3110, 2988, 2915 (C–H), 1749, 1675(C=O), 1602 (C=C), 1293, 1205, 1165, 1089(C–O) cm^{-1}, ^1H NMR δ 1.05–1.22 (6H, CH_3 of Et, 2t), 1.32–1.56(10H, CH_2 of cyclohexyl, m), 2.02 (3H, CH_3, s), 2.39 (1H, CH of cyclohexyl), 3.81–4.52 (4H, *J* = 6.60, CH_2 of Et, 2q), 4.71(1H, CH, s), 7.23–7.36, 7.41–7.53 (5H, Ph protons, 2 m), 8.63 (1H, *J* = 8.64 Hz, NH, d) ppm; ^{13}C NMR δ 14.17, 14.28 ($2CH_3$ of Et), 24.55, 25.16, 29.61, 33.99 (CH_2 of cyclohexyl), 26.83 (CH_3), 40.33 (CH of cyclohexyl), 50.76 (^{13}CH-CO_2Et), 59.06, 60.15 ($2CH_3$ of Et), 82.95 (=^{13}C-CO_2Et) 112.87 (=^{13}C-COPh), 127.17, 128.50, 129.61, 130.03, 130.33(Ph carbons), 158.6 (=^{13}C-CH_3), 156.99(=^{13}C-NH), 167.87, 170.09 (2C=O of CO_2Et), 194.93 (C=O) ppm. MS: *m/z* (fragment, %) 441 (M^+, 9), 368 (M^+–CO_2Et, 68), 285 (M^+–CO_2Et, cyclohexyl, 83), 105 ($PhCO^+$, 100); Anal. Calc. for $C_{25}H_{31}NO_6$: C, 67.99; H, 7.08; N, 3.17; Found: C, 67.96; H, 7.05; N, 3.22%.

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