Mol Divers (2007) 11:101–105
DOI 10.1007/s11030-007-9064-6

FULL LENGTH PAPER

Chemo- and stereoselective reaction between alkyl isocyanides and dimethyl 1,3-acetonedicarbocxylate in the presence of acetylenic esters

Farogh Nasiri · Fatemeh Nazem · Kourosh Pourdavaie

Received: 18 March 2007 / Accepted: 23 May 2007 / Published online: 29 June 2007

Abstract The reaction of alkyl isocyanides with dimethyl 1,3-acetonedicarboxylate in the presence of dialkyl acetylenedicarboxylates in CH_2Cl_2 at ambient temperature leads to highly functionalized 2-amino-4*H*-pyrans and 1,2-dialkyl 4,6-dimethyl-(1*E*, 3*E*)-3 (alkylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylates.

Keywords 2-Amino-4*H*-pyrans · Enaminones · Alkyl isocyanides · Acetylenic esters · CH acids

Introduction

The design of multicomponent reactions (MCR) is an important field of research in combinatorial chemistry [1]. Because they are one-pot reactions, generally MCRs afford good yields and ready operations and are fundamentally different from two-component reactions in several aspects [2]. Therefore, great efforts have been and still are being made to fined and develop new multicomponent reactions [3,4]. The great potential of isocyanides for the development of multicomponent reactions lies in the diversity of bond forming processes available, their functional group tolerance, and the high levels of chemo-, regio-, and stereoselectivity often observed [4]. The chemistry of poly functionalized 4*H*-pyrans is an ongoing area of interest because of their wide range of applications [5,6]. These 4*H*-pyrans are isosters of 1,4-dihydropyridine [7,8] with potential pharmacological interest and active synthons that have been extensively used in heterocyclic synthesis [6]. The 4*H*-pyrans are synthesized mainly by a three-component coupling reaction of aromatic aldehydes, malononitrile, and β-ketones/β-diketones [9] catalyzed by bases like triethylamine [10], piperidine [11], etc. However, this method does not always succeed [12]. We previously reported the reaction between alkyl isocyanides and cyclic 1,3-diketones in the presence of acetylenic esters [13]. In the current work, we wish to report that a one-pot chemo- and stereoselective reaction between alkyl isocyanides **1** and dialkyl acetylenedicarboxylates **2** in the presence of dimethyl 1,3-acetonedicarboxylate **3** can produce the desired highly functionalized 2-amino-4*H*-pyran derivatives **4a–4f** and enaminocarbonyl compounds **5a–5f**.

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Materials and methods

Acetylenic esters, alkyl isocyanides, and dimethyl 1,3-acetonedicarboxylate were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured with an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O-Rapid analyzer. These results agreed favorably with the calculated values. IR spectra were measured with a Shimadzu IR-460 spectrometer. NMR spectra were recorded with a Bruker DRX-250 AVANCE instrument (250.1 MHz for ^{1}H and 62.9 MHz for ^{13}C) with $CDCl_3$ as solvent. Chemical shifts are given in ppm (δ) relative to internal TMS, and coupling constant (J) are reported in Hertz (Hz). Mass spectra were recorded with a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV.

The general procedure for preparation of **4a–4f** and **5a–5f** is as follows (exemplified by **4a** and **5a**):

To stirred solution of 0.35 g dimethyl 1,3-acetonedicarboxylate (2 mmol) and 0.28 g dimethyl acetylenedicarboxylate (2 mmol) in 10 mL CH_2Cl_2, was added, dropwise at 0 °C

over 10 min 0.17 g *tert*-butyl isocyanide (2 mmol) in 2 mL CH_2Cl_2. The reaction mixture was then allowed to warm up to room temperature and stand for 24 h. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography (Merck 230–400 mesh) using *n*-hexane-EtOAc mixture as eluent.

0.1 Trimethyl 2-(*tert*-butylamino)-6-(2-methoxy-2-oxoethyl)-4*H*-pyran-3,4,5-tricarboxylate (**4a**)

Pale yellow oil, yield 0.50 g (63%).

IR (KBr) (υ_{max}/cm^{-1}): 3,456 (NH), 1,744, 1,737, 1,721, and 1,683 (C=O).

^{1}H NMR: δ 8.57 (1 H, s, NH), 4.55 (1 H, s, CH), 3.85 (2 H, AX, $J_{AX} = 16$ Hz, $\delta_A = 4.20$ and $\delta_X = 3.58$, CH_2), 3.75, 3.70, 3.69, and 3.64 (12 H, 4 s, 4 OCH_3), 1.34 (9 H, s, CMe_3).

^{13}C NMR: δ 173.2, 169.4, 168.6, and 165.9 (4 CO), 160.2 (N–*C*=C), 154.5 (O–*C*=C), 108.4, (O–C=*C*), 72.3 (N–C=*C*), 52.6 (OCH_3), 52.4 (N–*C*Me$_3$), 52.3, 52.2, and 51.0 (3 OCH_3), 37.7 (CH_2), 37.6 (CH), 30.3 (C*Me*$_3$).

MS, *m*/*z* (%): 399 (M^+, 6), 340 (63), 284 (100), 57 (90).

Anal. calcd. for $C_{18}H_{25}NO_9$ (399.4): C, 54.13; H, 6.31; N, 3.51; Found: C, 54.1; H, 6.3; N, 3.5.

0.2 3,4-diethyl 5-methyl 2-(*tert*-butylamino)-6-(2-methoxy-2-oxoethyl)-4*H*-pyran-3,4,5-tricarboxylate (**4b**)

Yellow oil, yield 0.56 g (66%).

IR (KBr) (υ_{max}/cm^{-1}): 3,455 (NH), 1,744, 1,738, 1,734, and 1,684 (C=O).

^{1}H NMR: δ 8.62 (1 H, s, NH), 4.56 (1 H, s, CH), 4.25–4.08 (4 H, m, 2 OCH_2), 3.98 (2 H, AX, $J_{AX} = 16$ Hz, $\delta_A = 4.22$ and $\delta_X = 3.62$, CH_2), 3.80 and 3.74 (6 H, 2 s, 2 OCH_3), 1.38 (9 H, s, CMe_3), 1.31 and 1.24 (6 H, 2 t, $^3J_{HH} = 7$ Hz, 2 OCH_2CH_3).

^{13}C NMR: δ 172.1, 169.6, 168.0, and 166.9 (4 CO), 160.1 (N–*C*=C), 154.2 (O–*C*=C), 108.5 (O–C=*C*), 72.5 (N–C=*C*), 60.5 and 59.8 (2 OCH_2), 52.4 (N–*C*Me$_3$), 52.3 and 52.0 (2 OCH_3), 37.9 (CH_2), 37.7 (CH), 30.3 (C*Me*$_3$), 14.6 and 14.1 (2 OCH_2CH_3).

MS, *m*/*z* (%): 428 (M^+, 8), 354 (100), 322 (80), 57 (85).

Anal. calcd. for $C_{20}H_{29}NO_9$ (427.5): C, 56.20; H, 6.84; N, 3.28; Found: C, 56.2; H, 6.8; N, 3.3.

0.3 3,4-Di (*tert*-butyl) 5-methyl 2-(*tert*-butylamino)-6-(2-methoxy-2-oxoethyl)-4*H*-pyran-3,4,5-tricarboxylate (**4c**)

Colorless crystals, yield 0.66 g (68%), mp 103–105 °C.

IR (KBr) (υ_{max}/cm^{-1}): 3,456 (NH), 1,754, 1,730, 1,728, and 1,682 (C=O).

^{1}H NMR: δ 8.55 (1 H, s, NH), 4.38 (1 H, s, CH), 3.89 (2 H, AX, $J_{AX} = 16$ Hz, $\delta_A = 4.17$, $\delta_X = 3.61$, CH_2), 3.81 and 3.76 (6 H, 2 s, 2 OCH_3), 1.53, 1.43, and 1.40 (27 H, 3 s, 3 CMe_3).

^{13}C NMR: δ 172.2, 168.8, 166.8, and 166.5 (4 CO), 159.7 (N–*C*=C), 153.5 (O–*C*=C), 108.8 (O–C=*C*), 80.5 and 79.3 (2 O*C*Me$_3$), 73.9 (N–C=*C*), 52.3 (N*C*Me$_3$), 52.2 and 51.9 (2 OCH_3), 39.5 (CH_2), 37.7 (CH), 30.5, 28.5, and 28.0 (3 C*Me*$_3$).

MS, *m*/*z* (%): 484 (M^+, 9), 382 (70), 326 (100), 57 (95).

Anal. calcd. for $C_{24}H_{37}NO_9$ (483.6): C, 59.61; H, 7.71; N, 2.90; Found: C, 59.6; H, 7.7; N, 2.9.

0.4 Trimethyl 2-(cyclohexylamino)-6-(2-methoxy-2-oxoethyl)-4*H*-pyran-3,4,5–tricarboxylate (**4d**)

White powder, yield 0.58 g (68%), mp 116–118 °C.

IR (KBr) (υ_{max}/cm^{-1}): 3,504 (NH), 1,744, 1,730, 1,724, and 1,686 (C=O).

^{1}H NMR: δ 8.39 (1 H, d, $^3J_{HH} = 8$ Hz, NH), 4.54 (1 H, s, CH), 4.17 (1 H, m, N–CH), 3.94 (2 H, AX, $J_{AX} = 17$ Hz, $\delta_A = 4.30$, $\delta_X = 3.58$, $CH_2CO_2CH_3$), 3.80, 3.75, and 3.66 (12 H, 3 s, 3 OCH_3), 1.28–2.37 (10 H, m, 5 CH_2).

^{13}C NMR: δ 173.2, 169.2, 168.6, and 156.9 (4 CO), 159.1 (N–*C*=C), 154.8 (O–*C*=C), 108.5 (O–C=*C*), 71.7 (N–C=*C*), 52.3, 52.1, 50.9, and 50.0 (4 OCH_3), 48.6 (N–CH), 37.9 ($CH_2CO_2CH_3$), 37.5 (CH), 33.7, 33.3, 29.7, 25.4, and 24.4 (5 CH_2).

MS, *m*/*z* (%): 425 (M^+, 5), 366 (100), 335 (65).

Anal. calcd. for $C_{20}H_{27}NO_9$ (425.4): C, 56.47; H, 6.40; N, 3.29; Found: C, 56.5; H, 6.4; N, 3.3.

0.5 3,4-Diethyl 5-methyl 2-(cyclohexylamino)-6-(2-methoxy-2-oxoethyl)-4*H*-pyran-3, 4,5-tricarboxylate (**4e**)

Pale yellow powder, yield 0.58 g (65%), mp 79–80 °C.

IR (KBr) (υ_{max}/cm^{-1}): 3,456 (NH), 1,744, 1,740, 1,735, and 1,689 (C=O).

^{1}H NMR: δ 8.42 (1 H, d, $^3J_{HH} = 8$ Hz, NH), 4.55 (1 H, s, CH), 4.31–4.03 (5 H, m, 2 O*C*H_2CH$_3$, and N–CH), 3.90 (2 H, AX, $J_{AX} = 16$ Hz, $\delta_A = 4.27$, $\delta_X = 3.57$, $CH_2CO_2CH_3$), 3.79 and 3.74 (6 H, 2 s, 2 OMe), 1.94–1.59 (10 H, m, 5 CH_2), 1.30 and 1.24 (6 H, 2 t, $^3J_{HH} = 7$ Hz, OCH_2CH_3).

^{13}C NMR: δ 173.0, 169.0, 168.7, and 166.1 (4 CO), 158.9 (N–*C*=C), 154.5 (O–*C*=C), 108.5 (O–C=*C*), 71.7 (N–C=*C*), 60.9 and 59.4 (2 OCH_2), 52.3 and 52.1 (2 OCH_3), 49.9 (N–CH), 37.9 ($CH_2CO_2CH_3$), 37.5 (CH), 33.7, 33.3, 22.4, 24.3, and 24.3 (5 CH_2) 14.6 and 14.1 (2 OCH_2CH_3).

MS, *m*/*z* (%): 454 (M^+, 13), 380 (100), 340 (87).

Anal. calcd. for $C_{22}H_{31}NO_9$ (453.5): C, 58.27; H, 6.89; N, 3.09; Found: C, 58.3; H, 6.9; N, 3.1.

0.6 3,4- Di (*tert*-butyl) 5-methyl 2-(cyclohexylamino)-6-(2-methoxy -2-oxoethyl)-4*H*-pyran-3,4,5-tricarboxylate (**4f**)

Yellow oil, yield 0.66 g (65%).

IR (KBr) (υ_{max}/cm^{-1}): 3,488 (NH), 1,747, 1,740, 1,728, and 1,686 (C=O).

^{1}H NMR: δ 8.27 (1 H, d, $^3J_{HH}$ = 8 Hz, NH), 4.35 (1 H, s, CH), 4.10 (1 H, m, N–CH), 3.86 (2 H, AX, J_{AX} = 16 Hz, δ_A = 4.20, δ_X = 3.51, $CH_2CO_2CH_3$), 3.77 and 3.72 (6 H, 2 s, 2 OCH_3), 1.50 and 1.42 (18 H, 2 s, 2 CMe_3), 1.93–1.25 (10 H, m, 5 CH_2).

^{13}C NMR: δ 172.4, 168.8, 168.6, and 166.4 (4 CO), 158.5 (N–*C*=C), 153.7 (O–*C*=C), 108.8 (O–C=*C*), 80.5 and 79.2 (2 O*C*Me$_3$), 73.2 (N–C=*C*), 52.3 and 51.9 (2 OCH_3), 50.0 (N–CH), 39.5 ($CH_2CO_2CH_3$), 37.5 (CH), 33.9 and 33.5 (2 CH_2), 28.5 and 28.0 (2 C*Me*$_3$), 25.4, 24.7, and 24.6 (3 CH_2).

MS, m/z (%): 510 (M^+, 7), 408 (100), 352 (70).

Anal. calcd. for $C_{26}H_{39}NO_9$ (509.6): C, 61.28; H, 7.71; N, 2.75; Found: C, 61.3; H, 7.7; N, 2.7.

0.7 Tetramethyl (1*E*, 3*E*)-3-(*tert*-butylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylate (**5a**)

Yellow oil, yield 0.26 g (32%).

IR (KBr) (υ_{max}/cm^{-1}): 3,459 (NH), 1,734, 1,702, 1,689, and 1,680 (C=O).

^{1}H NMR: δ 13.30 (1 H, s, NH), 6.89 (1 H, s, CH), 3.81, 3.69, 3.68, and 3.66 (12 H, 4 s, 4 OCH_3), 3.52 (2 H, s, CH_2), 1.27 (9 H, s, CMe_3).

^{13}C NMR: δ 191.0 (CO), 169.9, 168.1, 164.4, and 164.0 (4 CO, ester), 163.9 (N–*C*=C), 140.5 (*C*=CH), 127.8 (C=*C*H), 101.3 (N–C=*C*), 55.9 (*C*Me$_3$), 53.0, 52.3, 51.9, and 50.7 (4 OCH_3), 49.4 (CH_2), 30.4 (C*Me*$_3$).

MS, m/z (%): 399 (M^+, 3), 368 (10), 340 (100).

Anal. calcd. for $C_{18}H_{25}NO_9$ (399.4): C, 54.13; H, 6.31; N, 3.51; Found: C, 54.1; H, 6.3; N, 3.5.

0.8 1,2-diethyl 4,6-dimethyl-(1*E*, 3*E*)-3-(*tert*-butylamino)-5-oxo-1,3-hexadiene1,2,4,6-tetracarboxylate (**5b**)

Yellow oil, yield 0.24 g (28%).

IR (KBr) (υ_{max}/cm^{-1}): 3,456 (NH), 1,730, 1,728, 1,696, and 1,695 (C=O).

^{1}H NMR: δ 13.30 (1 H, s, NH), 6.90 (1 H, s, CH), 4.36–4.06 (4 H, m, 2O*C*H_2CH$_3$), 3.75 and 3.70 (6 H, 2 s, 2 OCH_3), 3.54 (2 H, s, $CH_2CO_2CH_3$), 1.31 (9 H, s, CMe_3), 1.27 and 1.23 (6 H, 2 t, $^3J_{HH}$ = 7 Hz, 2 OCH_2CH_3).

^{13}C NMR: δ 190.9 (CO), 169.6, 168.1, 164.6, and 163.7 (4 CO, ester), 163.4 (N–*C*=C), 140.4 (*C*=CH), 128.3 (C=*C*H), 101.5 (N–C=*C*), 62.3 and 61.5 (2 O*C*H_2CH$_3$), 56.0 (*C*Me$_3$), 52.1 and 50.7 (2 OCH_3), 49.4 ($CH_2CO_2CH_3$), 30.5 (C*Me*$_3$), 14.0 and 13.8 (2 OCH_2*CH3*).

MS, m/z (%): 428 (M^+, 2), 397 (8), 354 (100).

Anal. calcd. for $C_{20}H_{29}NO_9$ (427.5): C, 56.20; H, 6.84; N, 3.28; Found: C, 56.2; H, 6.8; N, 3.3.

0.9 1,2-di(*tert*-butyl) 4,6-dimethyl-(1*E*, 3*E*)-3-(*tert*-butylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylate (**5c**)

Yellow oil, yield 0.27 g (28%).

IR (KBr) (υ_{max}/cm^{-1}): 3,456 (NH), 1,753, 1,742, 1,702, and 1,680 (C=O).

^{1}H NMR: δ 13.30 (1 H, s, NH), 6.80 (1 H, s, CH), 3.78 (2 H, s, CH_2COCH_3), 3.75 and 3.59 (6 H, 2 s, 2 OCH_3), 1.53, 1.45, and 1.39 (27 H, 3 s, 3 CMe_3).

^{13}C NMR: δ 190.5 (CO), 169.5, 168.2, 165.0, and 163.0 (4 CO, ester), 162.4 (N–*C*=C), 140.1 (*C*=C*H*), 129.9 (C=*C*H), 101.7 (N–C=*C*), 83.1 and 82.8 (2 O*C*Me$_3$), 55.9 (N*C*Me$_3$), 51.9 and 50.6 (2 OCH_3), 49.1 ($CH_2CO_2CH_3$), 30.6, 27.7, and 27.6 (3 C*Me*$_3$).

MS, m/z (%): 484 (M^+, 4), 453 (8), 382 (100).

Anal. calcd. for $C_{24}H_{37}NO_9$ (483.6): C, 59.61; H, 7.71; N, 2.90; Found: C, 59.6; H, 7.7; N, 2.9.

0.10 Tetramethyl (1*E*, 3*E*)-3-(cyclohexylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylate (**5d**)

Yellow oil, yield 0.24 g (28%).

IR (KBr) (υ_{max}/cm^{-1}): 3,472 (NH), 1,742, 1,737, 1,702, and 1,673 (C=O).

^{1}H NMR: δ 13.35 (1 H, d, $^3J_{HH}$ = 8 Hz, NH), 6.90 (1 H, s, CH), 3.82 (1 H, m, N–CH), 3.88, 3.74, 3.73, and 3.66 (12 H, 4 s, 4 OCH_3), 3.58 (2 H, s, $CH_2CO_2CH_3$), 1.76–1.57 (10 H, m, 5 CH_2).

^{13}C NMR: δ 191.5 (CO), 169.6, 167.9, 163.9, and 163.6 (4 CO, ester), 163.6 (N–*C*=C), 139.4 (*C*=CH), 129.7 (C=*C*H), 99.9 (N–C=*C*), 54.8 (N–CH), 53.0, 52.3, 51.9, and 50.7 (4 OCH_3), 49.4 ($CH_2CO_2CH_3$), 33.1, 32.9, 25.0, 24.1, and 24.0 (5 CH_2).

MS, m/z (%): 425 (M^+, 5), 394 (10), 366 (100).

Anal. calcd. for $C_{20}H_{27}NO_9$ (425.4): C, 56.47; H, 6.40; N, 3.29; Found: C, 56.5; H, 6.4; N, 3.3.

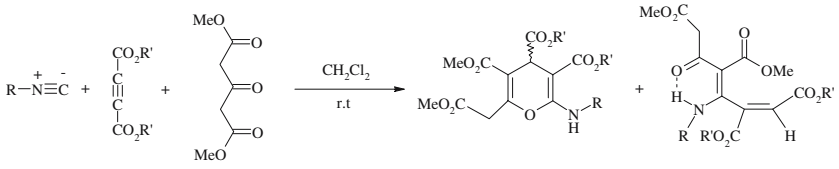
0.11 1,2-diethyl 4,6-dimethyl (1*E*, 3*E*)-3-(cyclohexylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylate (**5e**)

Yellow oil, yield 0.27 g (30%).

IR (KBr) (υ_{max}/cm^{-1}): 3,459 (NH), 1,744, 1,731, 1,730, and 1,695 (C=O).

^{1}H NMR: δ 12.92 (1 H, d, $^3J_{HH}$ = 9 Hz, NH), 6.89 (1 H, s, CH), 4.39–4.14 (4 H, m, 2 O*C*H_2CH$_3$), 3.83 (1 H, m, N–CH), 3.75 (3 H, s, OCH_3), 3.64 (2 H, s, $CH_2CO_2CH_3$),

Scheme 1

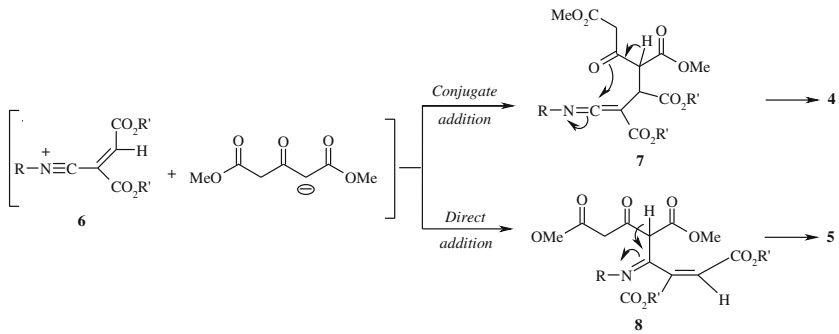


1	R
a	*t*-But
b	*c*-Hexyl

2	R'
a	Me
b	Et
c	*t*-But

4, 5	R	R'	Yield (%) of 4	Yield (%) of 5
a	*t*-But	Me	63	32
b	*t*-But	Et	66	28
c	*t*-But	*t*-But	68	28
d	*c*-Hexyl	Me	68	28
e	*c*-Hexyl	Et	65	30
f	*c*-Hexyl	*t*-But	65	29

Scheme 2



3.60 (3 H, s, OCH_3), 1.81–1.53 (10 H, m, 5 CH_2), 1.34 and 1.25 (6 H, 2 t, $^3J_{HH}$ = 7 Hz, 2 OCH_2CH_3).

^{13}C NMR: δ 191.4 (CO), 169.6, 167.9, 163.8, and 163.5 (4 CO, ester), 163.1 (N–*C*=C), 139.3 (*C*=CH), 127.2 (C=*CH*), 100.1 (N–C=*C*), 62.4 and 61.6 (2 O*C*H_2CH$_3$), 54.8 (N–CH), 51.9 and 50.7 (2 OCH_3), 49.3 (*C*$H_2CO_2CH_3$), 33.1, 32.9, 25.0, 24.1, and 24.0 (5 CH_2), 14.1 and 13.7 (2 OCH_2CH_3).

MS, *m*/*z* (%): 454 (M^+, 5), 423 (8), 380 (100).

Anal. calcd. for $C_{22}H_{31}NO_9$ (453.5): C, 58.27; H, 6.89; N, 3.09; Found: C, 58.3; H, 6.9; N, 3.1.

0.12 1,2-di(*tert*-butyl) 4,6-dimethyl (1*E*, 3*E*)-3-(cyclohexylamino)-5-oxo-1,3-hexadiene-1,2,4,6-tetracarboxylate (**5f**)

Yellow oil, yield 0.30 g (29%).

IR (KBr) (υ_{max}/cm^{-1}): 3,472 (NH), 1,741, 1,736, 1,724, and 1,686 (C=O).

^{1}H NMR: δ 12.82 (1 H, d, $^3J_{HH}$ = 7 Hz), 6.75 (1 H, s, CH), 3.81 (1 H, m, N–CH), 3.75 (2 H, s, *C*$H_2CO_2CH_3$), 3.73 and 3.58 (6 H, 2 s, 2 OCH_3), 1.84–1.58 (10 H, m, 5 CH_2), 1.50 and 1.41 (18 H, 2 s, 2 CMe_3).

^{13}C NMR: δ 191.1 (CO), 169.6, 167.6, 164.3, and 162.9 (4 CO, ester), 162.1 (N–*C*=C), 139.0 (*C*=CH), 128.8 (C=*CH*), 100.4 (N–C=*C*), 83.1 and 82.9 (2 *C*Me_3), 51.9 (N–CH), 51.8 and 50.6 (2 OCH_3), 49.0 (*C*$H_2CO_2CH_3$), 33.0, 32.9, 25.0, 24.1, and 24.0 (5 CH_2).

MS, *m*/*z* (%): 510 (M^+, 3), 437 (12), 408 (100).

Anal. calcd. for $C_{26}H_{39}NO_9$ (509.6): C, 61.28; H, 7.71; N, 2.75; Found: C, 61.3; H, 7.7; N, 2.8.

Results and discussion

The reaction of alkylisocyanides **1** with electron-deficient actylenic esters **2** in the presence of dimethyl acetone-1,3-dicarboxylate **3** affords highly functionalized 2-amino-4*H*-pyrans **4** and enaminoncarbonyl compounds **5** (Scheme 1).

The structures of **4a–4f** and **5a–5f** were deduced from their IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m*/*z* values. The ^{1}H NMR spectrum of **4a** exhibits seven sharp singlets, readily recognizable as arising from the *tert*-butyl (δ = 1.34 ppm), methoxy (δ = 3.64, 3.69, 3.70, and 3.75 ppm), methine (δ = 4.55 ppm), and NH (δ = 8.57 ppm) protons. The methylene protons of **4a** are diasterotopic and exhibit an AX (J_{AX} = 16 Hz, δ_A = 4.20, δ_X = 3.58 ppm). The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed 16 distinct resonances in agreement with the proposed structure. The ^{1}H NMR spectrum of **5a** showed signals for *tert*-butyl (δ = 1.27 ppm), methylene (δ = 3.52 ppm), methoxy (δ = 3.66, 3.68, 3.69, and 3.81 ppm), olefinic (δ = 6.89 ppm), and NH (δ = 13.30 ppm) protons. The ^{13}C NMR spectrum of **5a** showed 16 distinct resonances in agreement

with the proposed structure. The (*E*) configurations of the two carbon–carbon double bounds in **5** are based on the chemical shift of the olefinic [14] and NH protons [15].

Although we have not yet established the mechanism of the reaction between alkyl isocyanides and acetylenic esters in the presence of dimethyl 1,3-acetonedicarboxylate in an experimental manner, a possible explanation is proposed in Scheme 2. On the basis of the well-established chemistry of isocyanides [4,16,17] it is reasonable to assume that **4** and **5** result from an initial addition of the alkyl isocyanide to the acetylenic ester and subsequent protonation of the 1:1 adduct by the CH-acid. Then the positively charged ion might be attacked from two positions by the enolate anion of the CH-acid; conjugate addition leads to ketenimine **7**. Such an addition product may isomerize, under the reaction conditions employed, to produce the 2-amino-4*H*-pyran system **4**. Direct addition produces the immine **8**. This addition product undergoes a stereoselective imine-to-enamine tautomerism to generate the enaminone system **5**.

In conclusion, the chemo- and stereoselective three component reactions of alkyl isocyanides with electron deficient acetylenic esters in the presence of dimethyl 1,3-acetonedicarboxylate provides a simple one-pot entry in to the synthesis of highly poly functional 4*H*-pyran derivatives and enaminocarbonyl compounds of potential synthetic interest. The present method carries the advantage that not only is the reaction performed under natural condition but also the starting material and reagents can be mixed without any activation or modification.

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