Synthesis of polyfunctional ketenimines and 1-azadienes use of *tert*-butyl isocyanide and acetylenic esters in the presence of 3-chloropentane-2, 4-dione

Sakineh Asghari*, Mohammad Qandalee[a] and Hamid Reza Bijan-Zadeh[b]

[a]*Department of Chemistry, University of Mazandaran, P.O. Box. 453, Babolsar, Iran*

[b]*Department of Chemistry, University of Tarbiat Modarres, PO Box 14155-4838, Tehran, Iran*

The 1:1 reactive intermediate generated by the addition of *tert*-butyl isocyanide to dialkyl acetylenedicarboxylates was trapped by 3-chloropentane-2, 4-dione to yield polyfunctionalised ketenimines and 1-azadienes.

Keywords: *tert*-butyl isocyanide, dialkyl acetylenedicarboxylate, ketenimine, 1-aza-dienes

In recent years, ketenimines have attracted interest as dehydrating agents for peptide synthesis, as complexing agents for transition metal ions, and as co-reagents for DMSO oxidation.[1, 2] They have also found widespread use as reactive starting materials for the generation of four-, five-, and six-membered heterocyclic ring systems.[3–6] The addition of nucleophilic carbenes such as isocyanides to dialkyl acetylenedicarboxylates has been investigated in detail by a number of research groups.[7–10]

We here describe a reaction of *tert*-butyl isocyanide **1** with dialkyl acetylenedicarboxylate **2** in the presence of 3-chloropentane-2, 4-dione 3. This three-component condensation reaction produces highly functionalised ketenimines **4** and isomeric 1-azabutadiene **5** in fairly good yields (Scheme 1).

The ^{1}H NMR spectrum of **3** only exhibited a singlet at about 2 ppm for two CH_3 groups and a broad signal at about 15.4 ppm. This result indicates that compound **3** exists as enol tautomer.

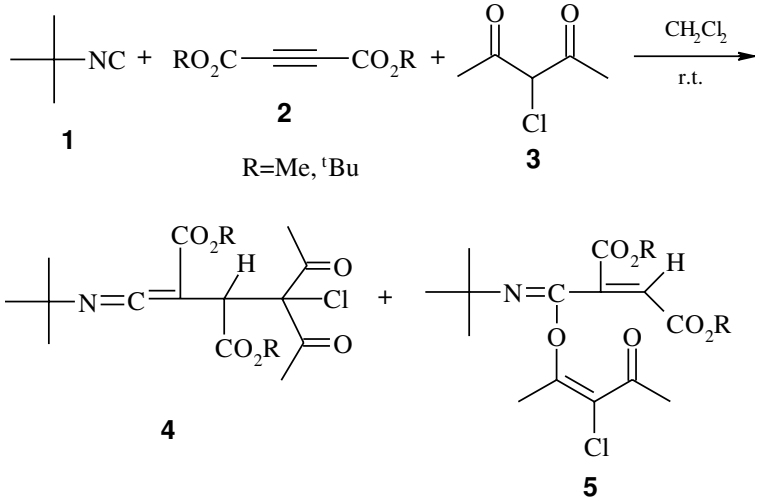
On the basis of the well established chemistry of isocyanide,[11–13] it is reasonable to assume that compounds **4** and **5** result from the initial addition of the *tert*-butylisocyanide to the acetylenic ester and a concomitant protonation of the 1;1 adduct by enol form of compound **3**. Then, the positively charged ion **6** can be attacked at two positions by negative carbon atom (soft site) or negative oxygen atom (hard site) of enolate. Ketenimines **4a–b** were produced by conjugate addition and 1-azadienes **5a–b** were formed by direct addition (Scheme 2).

The structure of **4** and **5** were deduced from their mass spectrometric data and their ^{1}H and ^{13}C NMR and IR spectra. The ^{1}H NMR spectrum of **4a** exhibited a sharp signal for tert-butyl (δ=1.43 ppm), two singlets for two methoxy groups (3.68 and 3.71 ppm), and a singlet for CH group (4.63 ppm). The ^{13}C NMR spectrum of **4a** exhibited 14 sharp lines in agreement with the proposed structure. The ^{1}H and ^{13}C NMR spectra of **4b** are similar to that of **4a**, except for the signals of alkoxy groups. The mass spectrum of **4a** exhibited molecular ion peaks at *m/z* 359(M^+)(3%), and 361 (M^+)(1%). Initial fragmentations involved loss from or complete loss of the side chains of the ketenimine system.

The ^{1}H NMR spectrum of **5a** displayed sharp signals for the *tert*-butyl (δ=1.40 ppm), methyl (2.08 and 2.46 ppm), methoxy (3.80 and 3.89 ppm), and vinyl proton (6.34 ppm). The ^{13}C NMR spectrum of **5a** exhibited fourteen sharp lines in agreement with the proposed structure. This spectrum indicated signals for *tert*-butyl (δ=28.53 ppm), methoxy (52.38 and 52.83 ppm) and CH olefinic carbon (128.86 ppm). Partial assignment of these resonances for **4a–b** and **5a–b** is given in the experimental section.

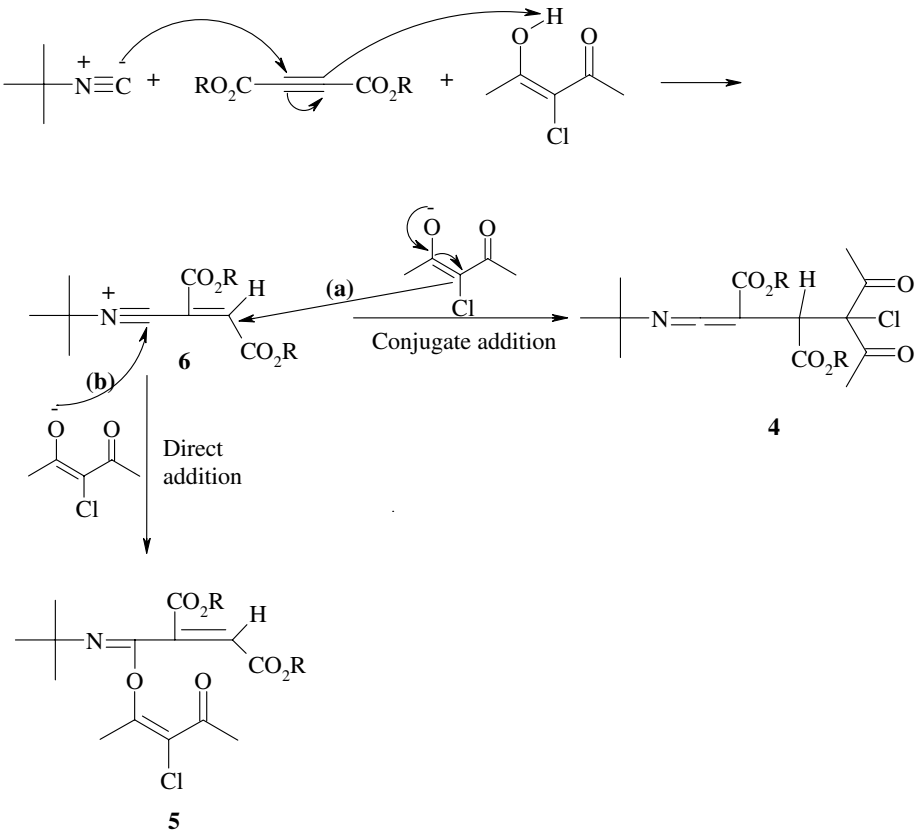
The structural assignments of **4a–b** and **5a–b** were supported by their IR spectra. Of special interest is the strong ketenimine absorption band at about 2050 cm^{-1}.

In conclusion, the reaction of *tert*-butyl isocyanide with acetylenic esters in the presence of 3-chloropentane-2, 4-dione provides a simple one-pot entry into the synthesis of polyfunctionalised ketenimines and 1-azadienes of potential synthetic interest.



Scheme 1

* Correspondent. E-mail: s.asghari@umz.ac.ir



Scheme 2

Experimental

Dialkyl acetylenedicarboxylates, *tert*-butyl isocyanide and 3-chloropentane-2, 4-dione were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured on an Electerothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O Rapid analyser. ^{1}H, ^{13}C NMR spectra were measured with a Bruker DRX-500 Avance spectrometer at 500 and 125.8 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu IR- 470 spectrometer.

Preparation of dimethyl 2-(1-acetyl-1-chloro-2-oxopropyl)-3-[(tert-butylimino)methylene]succinate (**4a**) *and dimethyl (E)-2-[(tert-butylimino){[(E)-2-chloro-1-methyl-3-oxobut-1-enyl]oxy}methyl]but-2-enedioate* (**5a**).

General procedure

To a magnetically stirred solution of 3-chloropentane-2, 4-dione (0.269 g, 2 mmol) and dimethyl acetylenedicarboxylate (0.245 ml, 2 mmol) in CH_2Cl_2(10 ml), dropwise, 0.45 g of *tert*-butyl isocyanide (2 mmol) in CH_2Cl_2 (4 ml) was added at –10°C over 10 min. The mixture was allowed to stand at room temperature for 24 hrs. The solvent was removed under reduced pressure and the residue was purified by silica gel (Merck silica gel, 230–400 mesh) column chromatography using hexane:ethyl acetate (3:2) as eluent. Two products were isolated. The solvent was removed under reduced pressure; ketenimine **4a** and 1-azadiene **5a** were obtained as yellow powders.

Dimethyl 2-(1-acetyl-1-chloro-2-oxopropyl)-3-[(tert-butylimino) methylene]succinate (**4a**): Yellow powder, m.p. 83–85°C, yield 65 %, IR (KBr) (ν_{max}, cm^{-1}): 1695–1730 (C=O) and 2040 (N=C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.43 (9H, s, CMe_3), 2.36 and 2.38 (6H, 2s, $2CH_3CO$), 3.68 and 3.71 (6H, 2s, $2OCH_3$), 4.63 (1H, s, CH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ_c 25.25 and 26.98 ($2CH_3CO$), 29.6 ($NCMe_3$), 48.16 (CH), 51.52 and 52.52 ($2OCH_3$), 58.33 (CMe_3), 62.1 (N=C=C), 83.19 (C-Cl), 164.28 and 169.27 (2C=O, esteric), 170.08 (C=N), 197.34 and 200.03 (2C=O, ketone); MS: *m/z* (%): 359 (M, 4), 361 (M, 1), 273 (M-$2CH_3CO$, 5.4), 275 (M-$2CH_3CO$, 1. 9), 241(M-$2CH_3CO$, 36), 243 (M - $2CO_2CH_3$, 13), 240 (M-(^{t}BuNC+ HCl), 33], 227 [M+1-($CH_3COClCOCH_3$), 100], 197 [M-($CH_3COClCOCH_3$+CH_3O), 11], 184 [M- (MeO_2CCCCO_2Me+$2CH_3$), 45.5], 186 [M – (MeO_2CCCCO_2Me+ $2CH_3$), 13.8]. Anal. Calcd. For $C_{16}H_{22}ClNO_6$ (359.81): C, 53.41, H, 6.16, N, 3.89 %. Found: C, 53.62, H, 6.18, N, 3.9 %.

Di-tert-butyl 2-(1-acetyl-1-chloro-2-oxopropyl)-3-[(tert-butylimino) methylene]succinate (**4b**): Yellow powder, m.p. 93–95°C, yield 60 %; IR (KBr) (ν_{max}, cm^{-1}): 1700–1725 (C=O), 2060 (N=C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.43 (9H, s, $NCMe_3$), 1.43 and 1.43 (18H, 2s, $OCMe_3$), 2.38 and 2.38 (6H, 2s, $2CH_3CO$), 4.45 (1H, s, CH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ_c 25.20 and 27.33 (2 CH_3CO), 27.48 ($NCMe_3$), 28.14 and 29.84, ($2OCMe_3$), 48.92 (CH), 60.78 ($NCMe_3$), 61.63 (N=C=C), 79.94 and 82.59 ($2OCMe_3$), 83.09 (CCl), 167.20 and 169.47 (2C=O, esteric), 172.47 (C=N), 198.27 and 200.25 (2C=O, ketones); MS: *m/z* (%); 443 (M, 24.5), 445 (M, 9), 408 (M- Cl, 10.5), 3/1 [M+1- (CH_3COCCl CO CH_3), 59], 277 [M- (OC_4H_9+ C_4H_9+ HCl), 23], 255 [M+1- ($CH_3COCClCOCH_3$+C_4H_8+H), 66], 189 [M- (^{t}BuNCCCO$_2$^{t}Bu+ C_4H_9+H), 100], 191 [M-(^{t}BuNC-$CCO_2{}^t$Bu+C_4H_9+H), 35]; Anal. Calcd. For $C_{22}H_{34}ClNO_6$ (443.97): C, 59.52, H, 7.72, N, 3.15 %. Found: C, 59.75, H, 7.74, N, 3.16 %.

Dimethyl (E)-2-[(tert-butylimino){[(E)-2-chloro-1-methyl-3-oxobut-1-enyl] oxy}methyl]but-2-enedioate **(5a):** Yellow powder, m.p. 112–114°C, yield 30 %; IR (KBr) (ν_{max}, cm^{-1}): broad bond at about 1720 (C=O), 1670 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.40 (9H, s, $NCMe_3$), 2.08 and 2.46 (6H, 2s, $2CH_3$), 3.80 and 3.80 (6H, 2s, 20Me), 6.34 (1H, s, CH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ_c 24.26 and 28.04 ($2CH_3$), 28.53 ($NCMe_3$), 52.38 and 52.82, (2OMe), 60.87 ($NCMe_3$), 128.86 (CH), 128.86 (CH), 134.58, 135.05 and 143.93 (olefinic carbons), 164.42 and 165.92 (2C=O, esteric), 170.85 (C=N), 193.24 (C=O, ketone); MS: *m/z* (%); 360 (M +1, 7.5), 362 (M+3, 2), 315 (M+1-CH_3CO, 15), 317 (M+3-CH_3CO, 5.7), 287 (M-CH CO_2Me, 27), 289 (M+2-$CHCO_2Me$, 8), 237 [M+1-(CH_3COCCl +CH_3O), 44], 226 (M-$CH_3COCClCOCH_3$, 8); 203 [M+1-(MeO_2CCCCO_2Me+CH_3), 100], 205 (M+3-(MeO_2CCC CO_2Me +CH_3), 35]; Anal. Calcd. For $C_{16}H_{22}ClNO_6$ (359.81): C, 53.41, H, 6.16, N, 3.89 %. Found: C, 53.20, H, 6.14, N, 3.88 %.

Di tert-butyl (E)-2-[(tert-butylimino){[(E)-2-chloro-1-methyl-3-oxobut-1-enyl]oxy}methyl]but-2-enedioate **(5b):** Yellow powder, m.p. 142–144 °C, yield 35 %; IR (KBr) (ν_{max}, cm^{-1}): broad bond at about 1725 (C=O), 1675 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.41 (9H, s, $NCMe_3$), 1.52 and 1.55 (18H, 2s, $OCMe_3$), 2.09 and 2.43

(6H, 2s, $2CH_3$), 6.22 (1H, s, CH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ_c 24.56 (CH_3CO), 27.64 ($NCMe_3$), 28.10 and 28.70, ($2OCMe_3$), 28.26 (CH_3-C=C), 61.07 ($NCMe_3$), 82.59 and 83.66 ($2OC\ Me_3$), 132.17 (CH), 133.66, 136.42 and 141.93 (olefinic carbons), 163.44 and 163.63 (2C=O, esteric), 171.14 (C=N), 193.37 (C=O, ketone); MS: *m/z* (%); 444 (M+1, 39.1), 446 (M+3, 14.5), 277 [M-(OC_4H_9+ C_4H_9+ HCl), 21.3], 255 [M+1-($CH_3COCClCOCH_3$+ C_4H_8), 8], 189 (M+1-(^{t}BuNC CO_2Me+ C_4H_9+ H), 100], 191 (M+3-(^{t}BuNC CO_2Me + C_4H_9+H), 35]; $C_{22}H_{34}ClNO_6$ (443.97): C, 59.52, H, 7.72, N, 3.15 %. Found: C, 59.28, H, 7.71, N, 3.14 %.

Received 10 March 2005; accepted 3 November 2005
Paper 05/3151

References

1 M.W. Barker and W.E. McHenry, *The Chemistry of Ketenes, Allenes and Related Compounds*, S. Patai (ed.), Wiley, Chichester, 1980, pp. 702-720.
2 G.R. Krow, *Angew. Chem. Int. Ed. Engl*., 1971, **10**, 435.
3 N.P. Gambarian, *Russ. Chem. Rev.*, 1976, **45**, 1251.
4 I. Yavari, A. Shaabani, S.Asghari, M.M. Olmstead and N. Safari, *J. Fluor. Chem.,* 1997, **86**, 77-80.
5 I. Yavari, A.A. Esmaili, S. Asghari and H.R. Bijan-Zadeh, *J. Chem. Res*., 1999, 368-369.
6 R. Aumann, B. Jasper, M. Lage and B. Krebs, *Organometallics,* 1994, **13**, 3502.
7 Y. Suzuki and N.T. Takizawa, *Tetrahedron Lett.*, 1970, **11**, 2667.
8 Y. Suzuki and Y. Litaka, *Bull. Chem. Soc. Jpn*., 1971, **44**, 56.
9 T.R. Oakes and T.J. Donovan, *J. Org. Chem.*, 1973, **38**, 1319.
10 H. Junjappa, M.K. Saxena, D. Ramaiah, B.B. Loharay, N.P. Rath and M.V. George, *J. Org. Chem.*, 1998, **63**, 9801.
11 S. Marcaccini and T. Torroba, *Org. Prep. Proc. Intl.*, 1993, **25**, 141.
12 D. Moderhack, *Synthesis,* 1985, 1083.
13 H.M. Walborsky and M.P. Persiasamy, *The Chemistry of Functional Groups,* S. Patai and Z. Rappoport (eds), Suppl C, chap 20, Wiley, New York, 1983, p 835.