SHORT PAPER

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The reaction of isocyanides and dialkyl acetylenedicarboxylates with isatoic anhydride: one-pot synthesis of highly functionalised ketenimines

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The addition of isocyanides to dialkyl acetylenedicarboxylates in the presence of isatoic anhydride leading to highly functionalised ketenimines is reported at room temperature.

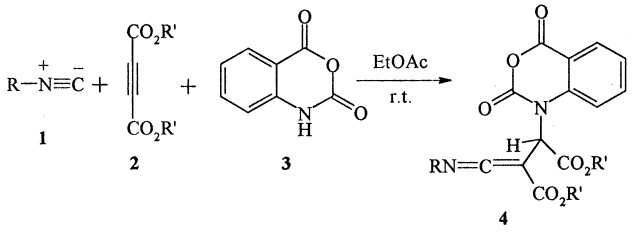
Keywords: isocyanide, dialkyl acetylenedicarboxylate, isatoic anhydride, ketenimine, NH-acid

Ketenimines are heterocumulenes which have recently attracted interest as dehydrating agents for peptide synthesis, as complexing agents for transition metal ions and as co-reagents for oxidations with DMSO.[1,2] They have also found widespread use as reactive starting materials for the formation of four-, five-, and six membered heterocyclic ring systems.[3-7] Recently, methods for the synthesis of ketenimines have been extensively reviewed.[8] Some of these methods are based on the alkylation of isocyanides with activated multiple bonds; the addition of isocyanides to carbenes and the reaction of isocyanides with transition metal organometalic compounds.

In continuation of our interest in the chemistry of isocyanides,[9-13] we now report a simple one-pot preparation of a stable ketenimine using isocyanide **1**, dialkyl acetylenedicarboxylate **2** and a strong N–H acid such as isatoic anhydride **3**.

This three component condensation reaction produces highly functionalised ketenimines **4** in fairly good yields. A mixture of dialkyl acetylenedicarboxylate and isatoic anhydride in dry ethyl acetate at room temperature, when treated with isocyanide affords dialkyl 2-[(alkyl or arylimino)methylene]-3-[2,4-dioxo-2*H*-3,1-benzoxazin-1-(4*H*)-yl]succinates in 60–68 % yields.

The structures of compounds **4a–e** were deduced from their elemental analysis and IR, ^{1}H NMR and ^{13}C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m/z* values.



4	R	R'	Yield/%
a	*tert*-Butyl	Methyl	68
b	Cyclohexyl	Methyl	65
c	2,5-Dimethylphenyl	Methyl	60
d	*tert*-Butyl	Ethyl	64
e	2,5-Dimethylphenyl	Ethyl	60

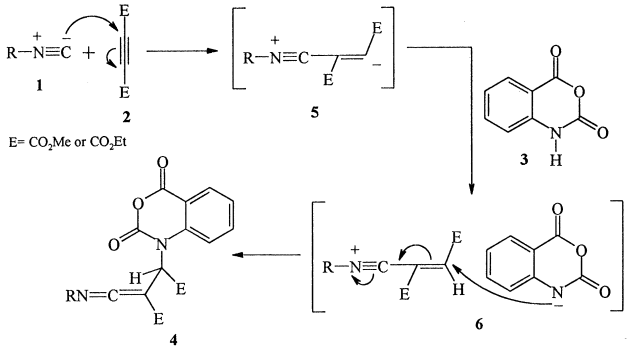
Scheme 1

The ^{1}H NMR spectrum of **4a** exhibited four single sharp lines readily recognised as arising from *tert*-butyl (δ 1.44), methoxy (δ 3.64 and 3.76) and methine (δ 6.22) protons. The aromatic hydrogens give rise to characteristic signals in the aromatic region of the spectrum.

The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed 17 distinct resonances in agreement with the suggested structure. The characteristic signal due to the ketenimine gruop carbons were discernible at δ 59.70 and 147.49. The four carbonyl groups resonated at δ 158.25, 162.07, 167.19 and 170.09. Partial assignment of these resonances is given in the Experimental section.

The ^{1}H and ^{13}C NMR spectra of **4b–e** are similar to those of **4a** and the results are summarised in the Experimental section.

On the basis of well established chemistry of isocyanides it is reasonable to assume that ketenimine **4** results from the initial addition of isocyanide[14-17] to the acetylenic ester and subsequent protonation of the 1:1 adduct **5** by the NH-acid **3**. Then, the positively charged ion **6** might be attacked by the nitrogen atom of the conjugate base of NH-acid, which leads to the ketenimine **4** (Scheme 2).



Scheme 2

In conclusion we have found that the reaction of isocyanides with acetylenic esters in the presence of isatoic anhydride leads to a facile synthesis of N-substituted highly functionalised ketenimines.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a

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FINNIGAN-MAT 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimidazu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-500 AVANCE spectrometer at 500.13 and 125.77 MHz, respectively. NMR spectra were obtained on solutions in acetone-d_6. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) Co.

Typical procedure for preparation of dimethyl 2-[(tert-butylimino)methylene]-3-[2,4-dioxo-2H-3,1-benzoxazin-1-(4H)-yl]succinate (**4a**): To a magnetically stirred solution of isatoic anhydride (0.163 g, 1.0 mmol) and dimethyl acetylenedicarboxylate (0.157 g, 1.1 mmol) in dry ethyl acetate (30 ml) was added *tert*-butyl isocyanide (0.084 g, 1.0 mmol) in ethyl acetate (2 ml) at 0 °C over 10 min. The reaction mixture was allowed to warm up to room temperature and stirred for 3 days. The solvent was removed under reduced pressure and the resultant solid was dissolved in hot diethyl ether (40 ml) and was filtered. The solvent was then evaporated to give product as white crystals (0.268 g, 68 %). m.p. 146–148 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 2080 (N=C=C), 1776, 1730 and 1693 (C=O). ^{1}H NMR (aceton-d_6): δ_H 1.44 (9 H, s, CMe_3), 3.64 and 3.76 (6 H, 2 s, 2 OCH_3), 6.22 (1 H, s, N–CH), 7.29–8.11 (4 H, m, arom.). ^{13}C NMR (Aceton-d_6): δ_C 29.34 (CMe_3), 51.07 and 52.57 (2 OCH_3), 56.26 (N–CH), 59.70 (*C*=C=N), 62.14 (*C*Me$_3$), 111.59, 115.36, 124.18, 130.10, 137.25 and 141.55 (arom.), 147.49 (C=*C*=N), 158.25, 162.07, 167.19 and 170.09 (4 C=O). MS (*m/z*, %) 389 (M$^+$, 10), 332 (68), 266 (98), 163 (96), 146 (47), 119 (100), 92 (51), 57 (72). Anal. Calcd. for $C_{19}H_{20}N_2O_7$ (389.27): C, 58.62; H, 5.17; N, 7.19%. Found: C, 58.73; H, 5.08; N, 7.23%.

Dimethyl 2-[(cyclohexylimino)methylene]-3-[2,4-dioxo-2H-3,1-benzoxazin-1-(4H)-yl]succinate (**4b**): White crystals (0.269 g, 65 %). m.p. 133–134 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 2090 (N=C=C), 1777, 1750 and 1731 (C=O). ^{1}H NMR (Aceton-d_6): δ_H 1.39–2.04 (10 H, m, 5CH_2), 3.63 and 3.72 (6 H, 2 s, 2 OCH_3), 3.96 (1 H, m, =N-CH), 6.25 (1 H, s, N-CH), 7.38–8.11 (4 H, m, arom.). ^{13}C NMR (Aceton-d_6): δ_C 23.57, 25.08, 32.73 and 32.79 (5CH_2), 50.99 and 52.57 (2 OCH_3), 56.42 (N–CH), 58.33 (*C*=C=N), 60.19 (=N–CH), 111.60, 115.42, 124.16, 130.07, 137.23 and 141.59 (arom.), 147.49 (C=*C*=N), 158.29, 161.79, 167.21 and 170.02 (4 C=O). MS (*m/z*, %) 415 (M$^+$, 8), 372 (7), 252 (98), 170 (100), 163 (28), 146 (25), 119 (23), 83 (71). Anal. Calcd. for $C_{21}H_{22}N_2O_7$ (414.46): C, 60.85; H, 5.35; N, 6.75%. Found: C, 60.77; H, 5.42; N, 6.81%.

Dimethyl 2-{[(2,6-dimethylphenyl)imino]methylene}-3-[2,4-dioxo-2H-3,1-benzoxazin-1-(4H)-yl]succinate (**4c**): White crystals (0.262 g, 60 %). m.p. 222–224 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 2100 (N=C=C), 1785, 1756 and 1720 (C=O). ^{1}H NMR (Aceton-d_6): δ_H 2.43 (6 H, s, 2CH_3), 3.62 and 3.74 (6 H, 2 s, 2 OCH_3), 6.42 (1 H, s, N-CH), 6.61-8.12 (7 H, m, arom.). ^{13}C NMR (Aceton-d_6): δ_C 17.62 (2CH_3), 50.97 and 52.68 (2 OCH_3), 54.85 (*C*=C=N), 56.98 (N-CH), 111.63, 115.51, 124.15, 128.40, 130.05, 134.34, 136.92, 137.20, 141.66 and 142.76 (arom.), 147.72 (C=*C*=N), 158.26, 162.80, 167.40 and 169.59 (4 C=O). MS (*m/z*, %) 436 (M$^+$, 10), 377 (7), 333 (21), 274 (100), 214 (31), 163 (18), 146 (43), 119 (98), 92 (75), 77 (81). Anal. Calcd. for $C_{23}H_{20}N_2O_7$ (436.46): C, 63.29; H, 4.61; N, 6.41%. Found: C, 63.12; H, 4.56; N, 6.50%.

Diethyl 2-[(tert-butylimino)methylene]-3-[2,4-dioxo-2H-3,1-benzoxazin-1-(4H)-yl]succinate (**4d**): White crystals (0.267 g, 64 %). m.p. 134–135 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 2100 (N=C=C), 1780, 1725 and 1670 (C=O). ^{1}H NMR (Aceton-d_6): δ_H 1.19 and 1.21 (6 H, 2 t, $^3J_{HH}$=6.48 Hz, 2 CH_3), 1.47 (9 H, s, CMe_3), 4.05 and 4.22 (4 H, m, 2 OCH_2), 6.20 (1 H, s, N–CH), 7.39–8.12 (4 H, m, arom.). ^{13}C NMR (Aceton-d_6): δ_C 13.52 and 13.78 (2 CH_3), 29.37 (CMe_3), 56.25 (N–CH), 60.50 (OCH_2), 60.11 (*C*=C=N), 61.99 (OCH_2), 62.06 (CMe_3), 111.53, 115.41, 124.13, 130.08, 137.24 and 141.64 (arom.), 147.42 (C=*C*=N), 158.29, 162.71, 166.61 and 169.66 (4 C=O). MS (*m/z*, %) 417 (MH$^+$, 22), 360 (100), 331 (15), 287 (53), 254 (42), 163 (79), 119 (52), 57 (98). Anal. Calcd. for $C_{21}H_{24}N_2O_7$ (416.47): C, 60.56; H, 5.80; N, 6.72%. Found: C, 60.68; H, 5.66; N, 6.60%.

Diethyl 2-{[(2,6-dimethylphenyl)imino]methylene}-3-[2,4-dioxo-2H-3,1-benzoxazin-1-(4H)-yl]succinate **4e**: White crystals (0.279 g, 60 %). m.p. 159–160 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 2091 (N=C=C), 1774, 1713 and 1681 (C=O). ^{1}H NMR (Aceton-d_6): δ_H 1.14 and 1.21 (6 H, 2 t, $^3J_{HH}$=6.47 Hz, 2 CH_3), 2.45 (6 H, s, 2 CH_3), 4.15-4.23 (4 H, m, 2 OCH_2), 6.41 (1 H, s, N–CH), 7.20–8.12 (7 H, m, arom.). ^{13}C NMR (Aceton-d_6): δ_C 13.38 and 13.96 (2 CH_3), 17.91 ($Me_2C_6H_4$), 55.33 (*C*=C=N), 57.11 (N–CH), 60.17 and 62.14 (2 OCH_2), 111.57, 115.58, 124.10, 128.27, 128.36, 130.02, 131.71, 133.92, 137.16 and 141.75 (arom.), 147.67 (C=*C*=N), 158.30, 160.13, 166.80 and 169.11 (4 C=O). MS (*m/z*, %) 464 (M$^+$, 17), 347 (29), 302 (100), 273 (19), 146 (32), 105 (23), 77 (40). Anal. Calcd. for $C_{25}H_{24}N_2O_7$ (464.52): C, 64.64; H, 5.20; N, 6.03%. Found: C, 64.80; H, 5.31; N, 5.90%.

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References

1 M.W. Barker and W.E. McHenry, in *The Chemistry of Ketens, Allenes and Related Compounds*, ed. S. Patai, Wiley, Chichester, 1980, p 702.
2 G.R. Krow, *Angew. Chem. Int. Ed. Engl.*, 1971, **10**, 435.
3 R. Aumann, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1456.
4 N.P. Gambarian, *Russ. Chem. Rev.*, 1976, **45**, 630.
5 J.D. Coyle and P.A. Raply, *J. Chem. Soc. Perkin Trans. 1*, 1985, 1957.
6 R. Aumann, B. Jasper, M. Läge and B. Krebs, *Organometallics*, 1994, **13**, 3502.
7 R. Gertzmann, M.H. Möller, U. Rodewald, R. Fröhlich, M. Grehl and E-U. Würthwein, *Tetrahedron*, 1995, **51**, 3767.
8 J.P. Michael and C.B.D. Koning, in *Comprehensive Organic Functional Group Transformations*, ed. A.R. Katritzky, O. Meth-Cohn and C.W. Rees, Elsevier Science Ltd, Cambridge, 1995, p. 555.
9 I. Yavari, A. Shaabani and M.T. Maghsoodlou, *Monatsh. Chem.*, 1997, **128**, 697.
10 I. Yavari, A. Shaabani, S. Asghari, M. Olmsted and N. Safari, *J. Fluorine Chem.*, 1997, **86**, 77.
11 A. Shaabani and F. Farrokhzad, *J. Chem. Res.(S)*, 1997, 344.
12 A. Shaabani, S. Ajabi, F. Farrokhzad and H.M. Bijanzadeh, *J. Chem. Res.(S)*, 1999, 582.
13 A. Shaabani, I. Yavari, M.B. Teimouri, A. Bazgir and H.M. Bijanzadeh, *Tetrahedron*, 2001, **57**, 1375.
14 I. Ugi, *Isonitrile Chemistry*, Academic Press, London, 1971.
15 I. Ugi, Angew. Chem. Int. Ed. Engl., 1982, **21**, 810.
16 A. Dömling and I. Ugi, *Angew. Chem. Int. Ed.*, 2000, **39**, 3168.
17 V. Nair, A.U. Vinod, J. Somarajan, A.R. Sreekanth and Nigam P. Rath, *Tetrahedron Lett.*, 2000, **41**, 6675.

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