Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2011, **21**, 108–109
Mendeleev Communications

Ketenimine N-functionalization of thiazolidine-2,4-diones with acetylenes and isocyanides

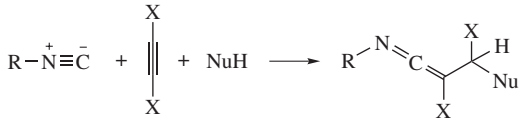
Issa Yavari,* Tayebeh Sanaeishoar, Leila Azad and Maryam Ghazvini

Department of Chemistry, Science and Research Branch, Islamic Azad University, Ponak, Tehran, Iran.
Fax: +98 21 8288 3455; e-mail: yavarisa@modares.ac.ir

DOI: 10.1016/j.mencom.2011.03.018

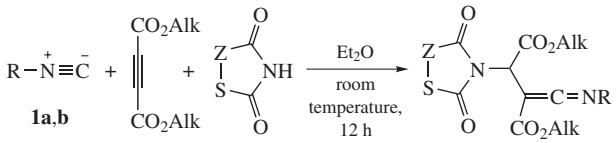
The zwitterionic 1:1 intermediates formed in the reaction between alkyl isocyanides and dialkyl acetylenedicarboxylates are trapped by 2,4-thiazolidine-2,4-diones to afford N-functionalized 2,4-dioxothiazolidines containing a ketenimine moiety.

Reaction between isocyanides, electron-deficient acetylenes and nucleophiles leading to ketenimines, as outlined in Scheme 1, was first documented by Oakes *et al.*[1,2] and applied to dialkyl acetylenedicarboxylates (X = CO_2R) and 1,1,1,4,4,4-hexafluorobut-2-yne (X = CF_3) as acetylenic component and methanol as NuH. Such interesting and promising transformation was nearly forgotten until Yavari *et al.*[3] extended its application to dibenzoylmethane as NuH. Later on, more works on such a reaction were published differing mostly in the nature of NuH used.[4–15]



Scheme 1

Here, we report on the application of such chemistry on highly functionalized thiazolidine-2,4-diones as N-nucleophilic counterpart (Scheme 2, Table 1). Thus, the reaction of isocyanides **1** with acetylenedicarboxylates **2** in the presence of thiazolidine-2,4-dione **3a** or 5-arylidene-2,4-thiazolidinediones **3b–g**, as a proton source/nucleophile, affords the corresponding highly functionalized ketenimines **4** in fairly good yields.[†]



1a,**b** **2a**,**b** **3a–g** **4a–k**

Scheme 2

Table 1 Reaction of isocyanides, acetylenic esters and 2,4-thiazolidinediones.

Isocyanide, R	Acetylenic ester, Alk	Thiazolidinedione, Z	Product	Yield (%)
1a, cyclohexyl	**2a**, Me	**3a**, CH_2	**4a**	91
1a, cyclohexyl	**2b**, Et	**3a**, CH_2	**4b**	88
1b, $Me_3CCH_2CMe_2$	**2a**, Me	**3a**, CH_2	**4c**	90
1b, $Me_3CCH_2CMe_2$	**2b**, Et	**3a**, CH_2	**4d**	88
1a, cyclohexyl	**2a**, Me	**3b**, PhCH=C	**4e**	88
1a, cyclohexyl	**2a**, Me	**3c**, 4-MeC_6H_4CH=C	**4f**	85
1a, cyclohexyl	**2a**, Me	**3d**, 3-MeC_6H_4CH=C	**4g**	87
1a, cyclohexyl	**2a**, Me	**3e**, 4-$O_2NC_6H_4CH$=C	**4h**	75
1a, cyclohexyl	**2a**, Me	**3f**, 4-FC_6H_4CH=C	**4i**	80
1a, cyclohexyl	**2a**, Me	**3g**, 2-thienyl-CH=C	**4j**	85
1b, $Me_3CCH_2CMe_2$	**2a**, Me	**3c**, 4-MeC_6H_4CH=C	**4k**	77

The highly functionalized ketenimines **4** are quite stable; they were recovered unchanged after refluxing in toluene for 3 h. The structures of compounds **4** were deduced from their IR, ^{1}H and ^{13}C NMR spectral data. The ^{1}H NMR spectrum of **4a** showed signals for methoxy (δ 3.70 and 3.77 ppm), methylene (δ 3.99 ppm) and methine (δ 5.99 ppm) protons, together with multiplet for the cyclohexyl (δ 1.20–1.81 and 4.14 ppm) protons. The ^{13}C NMR spectrum of **4a** exhibited 16 resonances in agreement with the proposed structure. ^{1}H and ^{13}C NMR spectra of **4b–k** were similar to those of **4a** except for the side chains, which exhibited characteristic resonances in the appropriate regions of the spectra. The sp^2-hybridized carbon atom of the ketenimine moiety in compounds **4** appears at δ 60.8–65.6 ppm, as a result of strong electron delocalization. IR spectra of compounds **4** show strong absorption bands at 2074–2082 cm^{-1} for the C=C=N moieties.

A plausible mechanism for formation of compounds **4** is represented in Scheme 3 (*cf.* refs. 1–3). It is conceivable that the reaction involves the initial formation of the 1:1 zwitterionic intermediate **5** between isocyanide and the acetylenic ester. The protonation of **5** by the NH-acidic compound and the subsequent attack of the resulting nucleophile on the positively charged species **6** afforded ketenimine **4**.

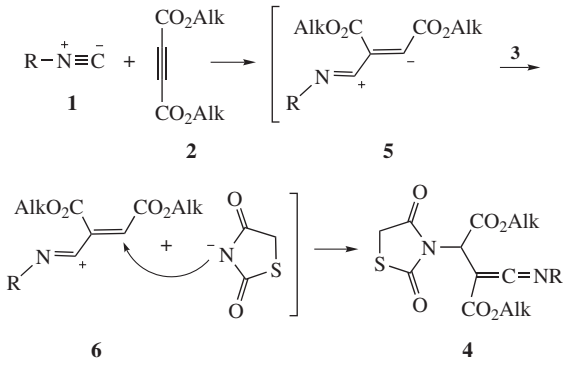
In conclusion, the three-component reaction of alkyl isocyanides with dialkyl acetylenedicarboxylates in the presence of thiazolidinediones provides a simple one-pot synthesis of stable functionalized ketenimines of potential value. This procedure

[†] Chemicals were purchased from Merck and used without further purification. Compounds **3b–g** were prepared from **3a** by the reported method.[16]

Synthesis of compounds **4** *(general procedure).* Alkyl isocyanide **1** (1 mmol) in 2 ml of Et_2O was added dropwise to a stirred solution of thiazolidinedione **3** (1 mmol) and acetylenic ester **2** (1 mmol) in 5 ml of Et_2O at room temperature. After completion of the reaction [12 h; TLC (AcOEt/hexane, 2:1)], the solvent was removed under reduced pressure and the residue was purified by column chromatography [silica gel (230–240 mesh; Merck), hexane/AcOEt, 4:1].

For **4a**: pale yellow oil, yield 0.33 g (91%). IR (ν_{max}/cm^{-1}): 2081 (C=C=N), 1747 and 1700 (C=O). ^{1}H NMR, δ: 1.20–1.81 (m, 10H, $5CH_2$), 3.70 (s, 3H, MeO), 3.77 (s, 3H, MeO), 3.99 (s, 2H, CH_2S), 4.14 (m, 1H, CHN), 5.99 (s, 1H, CH). ^{13}C NMR, δ: 24.2 (CH_2), 25.7 (CH_2), 33.4 (CH_2), 33.5 (CH_2), 34.1 (CH_2), 35.9 (CH_2S), 52.2 (CHN), 53.2 (MeO), 53.7 (MeO), 57.7 (CH), 60.8 (C=C=N), 161.1, 167.4, 170.1, 170.5 and 171.3 (C=C=N and 4C=O). Found (%): C, 52.4; H, 5.3; N, 7.7. Calc. for $C_{16}H_{20}N_2O_6S$ (%): C, 52.16; H, 5.47; N, 7.60.

For characteristics of compounds **4b–k**, see Online Supplementary Materials.



Scheme 3

has the advantages of high yields, mild reaction conditions, and simple experimental and work-up means.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2011.03.018.

References

1 T. R. Oakes, H. G. David and F. J. Nagel, *J. Am. Chem. Soc*., 1969, **91**, 4761.

2 T. R. Oakes and D. J. Donovan, *J. Org. Chem*., 1973, **38**, 1319.

3 I. Yavari, M. Davar-Panah, M. Heydari, K. Najafian and A. Zonouzi, *Monatsh. Chem*., 1996, **127**, 963.

4 A. Shaabani, M. B. Teimouri, P. Mirzaei and H. Bijanzadeh, *J. Chem. Res. (S)*, 2003, 82.

5 I. Yavari, F. Nassiri and H. Djahaniani, *Mol. Divers*., 2004, **8**, 431.

6 A. Shaabani, M. B. Teimouri and S. Arab-Ameri, *Tetrahedron Lett*., 2004, **45**, 8409.

7 I. Yavari, H. Djahaniani and F. Nassiri, *Collect. Czech. Chem. Commun*., 2004, **69**, 1499.

8 I. Yavari, F. Nasiri and H. Djahaniani, *Mol. Divers*., 2004, **8**, 431.

9 I. Yavari, H. Djahaniani and F. Nassiri, *Monatsh. Chem*., 2004, **135**, 543.

10 I. Yavari, L. Moradi, F. Nasiri and H. Djahaniani, *Mendeleev Commun*., 2005, **15**, 156.

11 I. Yavari, F. Nassiri, H. Djahaniani and H. Bijanzadeh, *J. Chem. Res. (S)*, 2005, 537.

12 I. Yavari, H. Zare and B. Mohtat, *Mol. Divers*., 2006, **10**, 247.

13 M. Bayat, H. Imanieh and E. Hosseininejad, *Synth. Commun*., 2008, **15**, 2567.

14 M. Anary-Abbasinejad, H. Anaraki-Ardakani and F. Ghanea, *Monatsh. Chem*., 2009, **140**, 397.

15 M. Anary-Abbasinejad, M. H. Moslemine and H. Anaraki-Ardakani, *J. Fluorine Chem*., 2009, **130**, 368.

16 G. Bruno, L. Costantino, C. Curinga, R. Maccari, F. Monforte, F. Nicolo, R. Ottanand and M. G. Vigorita, *Bioorg. Med. Chem*., 2002, **10**, 1077.

Received: 17th August 2010; Com. 10/3584