SHORT PAPER

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The reaction of alkyl isocyanides and dialkylacetylene dicarboxylates with phthalic anhydride derivatives: a novel synthesis of γ-spiroiminolactones[†]

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The addition of alkyl isocyanides to dialkyl acetylenedicarboxylates in the presence of phthalic anhydride derivatives leading to highly functionalised γ-spiroiminolactones is reported.

Keywords: phthalic anhydride, acetylenic ester, alkyl isocyanide, γ-spiroiminolactone

The nucleophilic addition of alkyl isocyanide (**1**) to acetylenic esters (**2**) such as dimethyl acetylenedicarboxylate (DMAD) is well documented.[1-4] The highly reactive zwitterionic intermediate produced in the reaction between alkyl isocyanide and electron deficient acetylenic esters undergoes further reaction with acetylenic ester and alkyl isocyanide in different molar proportions, ultimately leading to a variety of complex heterocyclic systems.[5-10]

Recently, this highly reactive zwitterionic intermediate has been trapped with aldehydes,[11] *o*- and *p*-quinones,[12] 1,3-diphenylpropane-1,3-dione[13] and 2-bromomalonates[14] producing 2-aminofuranes, iminolactones, ketenimines and 2*H*-pyran-2-one derivatives, respectively.

In continuation of our interest in the chemistry of alkyl isocyanides[15-19] and electron deficient acetylenic esters,[20-23] we examined the reaction of alkyl isocyanides (**1**) with acetylenic esters (**2**) in the presence of phthalic anhydride derivatives (**3**) as trapping agents for the reactive zwitterionic intermediate with the purpose of preparing highly functionalised ketenimines (**4**) (Scheme 1, Pathway A). However, we have found that this reaction did not afford the corresponding ketenimines, but that, as an unusual behaviour of phthalic anhydride derivatives (**3**), γ-spiroiminolactones (**5**) were obtained in high yields (Scheme 1, Pathway B).

The structures of compounds **5a–d** 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.

The ^{1}H NMR spectrum of **5a** consisted of a multiplet of signals for the cyclohexyl ring (δ 1.16–1.80) and two single sharp lines for methoxy groups (δ 3.62 and 3.97). A multiplet resonance is observed for the N-CH group (δ 3.65) and the aromatic hydrogens give rise to characteristic signals in the aromatic region of the spectrum.

The ^{1}H decoupled ^{13}C NMR spectrum of **5a** showed 21 distinct resonances in agreement with the suggested structure. The characteristic signal due to the spiro carbon was discernible at δ 109.1 and the three carbonyl groups resonated at δ 159.3, 161.2 and 166.4. Partial assignment of these resonances is given in the experimental section.

The ^{1}H and ^{13}C NMR spectra of **5b–d** are similar to those of **5a** and the results are summarised in the experimental section.

In conclusion we have found that the reaction of alkyl isocyanides with acetylenic esters in the presence of phthalic anhydride derivatives leads to a facile synthesis of highly functionalised γ-spiroiminolactones.

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 FINNIGAN-MAT 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu 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 $CDCl_3$ using TMS as internal standard. The chemicals used in this work were purchased from the Fluka (Buchs, Switzerland) chemical company.

Typical procedure for preparation of (**5a**): To a magnetically stirred solution of phthalic anhydride (0.149 g, 1 mmol) and dimethyl acetylenedicarboxylate (0.157 g, 1.1 mmol) in dry benzene (30 ml) was added cyclohexyl isocyanide (0.110 g, 1 mmol) via a syringe and refluxing was continued for 3h. The solvent was removed under vacuum and the residue was washed with diethyl ether and was recrystallised from ethanol to give a white crystals (0.336 g, 84 %). m.p. 196–198 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 3115, 1785, 1722, 1700, 1398. ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.16–1.80 (10 H, m, 5 CH_2), 3.62 and 3.97 (6 H, 2 s, 2 OCH_3), 3.65 (1 H, m, N-CH), 7.47–7.98 (4 H, m, arom.). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 24.44, 24.48, 25.54, 33.08 and 33.18 (5 CH_2), 52.92 and 53.39 (2 OCH_3), 57.47 (N–CH), 109.10 (Spiro Carbon), 122.41, 125.82, 126.88, 131.70, 135.08, 136.63, 139.74, 143.57 and 150.66 (C=C, N=C and arom.), 159.39, 161.29 and 166.40 (3 C=O). MS (*m*/*z*, %) 400 (M^+, 31), 367 (28), 302 (100), 243 (23), 163 (74), 97 (38). Anal. Calcd. for $C_{21}H_{21}NO_7$ (399.44): C, 61.14; H, 5.29; N, 3.50%. Found: C, 60.93; H, 5.18; N, 3.46%.

Preparation of (*5b*): Similar reaction conditions as above were employed but using *tert*-butyl isocyanide and diethyl acethylenedicarboxylate instead of cyclohexyl isocyanide and dimethyl acethylenedicarboxylate yielded white crystals (0.306 g, 76 %). m.p. 101–103 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 3115, 1785, 1732, 1722, 1696, 1401. ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.02 (3 H, t, $^3J_{HH}$=7.1 Hz, CH_3), 1.29 (9 H, s, CMe_3), 1.39 (3 H, t, $^3J_{HH}$=7.1 Hz, CH_3), 4.04 and 4.43 (4 H, 2 q, $^3J_{HH}$=7.1 Hz, 2 OCH_2), 7.45–7.97 (4 H, m, arom.). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 13.51 and 14.06 (2 CH_3), 29.59 (C*Me*$_3$), 55.92 (*C*Me$_3$), 61.97 and 62.59 (2 OCH_2), 109.49 (Spiro Carbon), 122.28, 125.66, 127.14, 131.51, 134.97, 136.04, 141.11, 143.97 and 148.41 (C=C, N=C and arom.), 158.92, 161.13 and 166.60 (3 C=O). MS (*m*/*z*, %) 402 (M^+, 22), 386 (100), 340 (48), 227 (14), 149 (33), 104 (55), 76 (60), 57 (97). Anal. Calcd. for $C_{21}H_{23}NO_7$ (401.46): C, 62.82; H, 5.77; N, 3.48%. Found: C, 62.97; H, 5.90; N, 3.34%.

Preparation of (**5c**): Similar reaction conditions as for **5a** but using tetrachlorophthalic anhydride instead of phthalic anhydride yielded white crystals (0.398 g, 74 %). m.p. 189–191 °C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 3013, 1803, 1745, 1730, 1698, 1400. ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.16–1.80 (10 H, m, 5 CH_2), 3.64 (1 H, m, N–CH), 3.73

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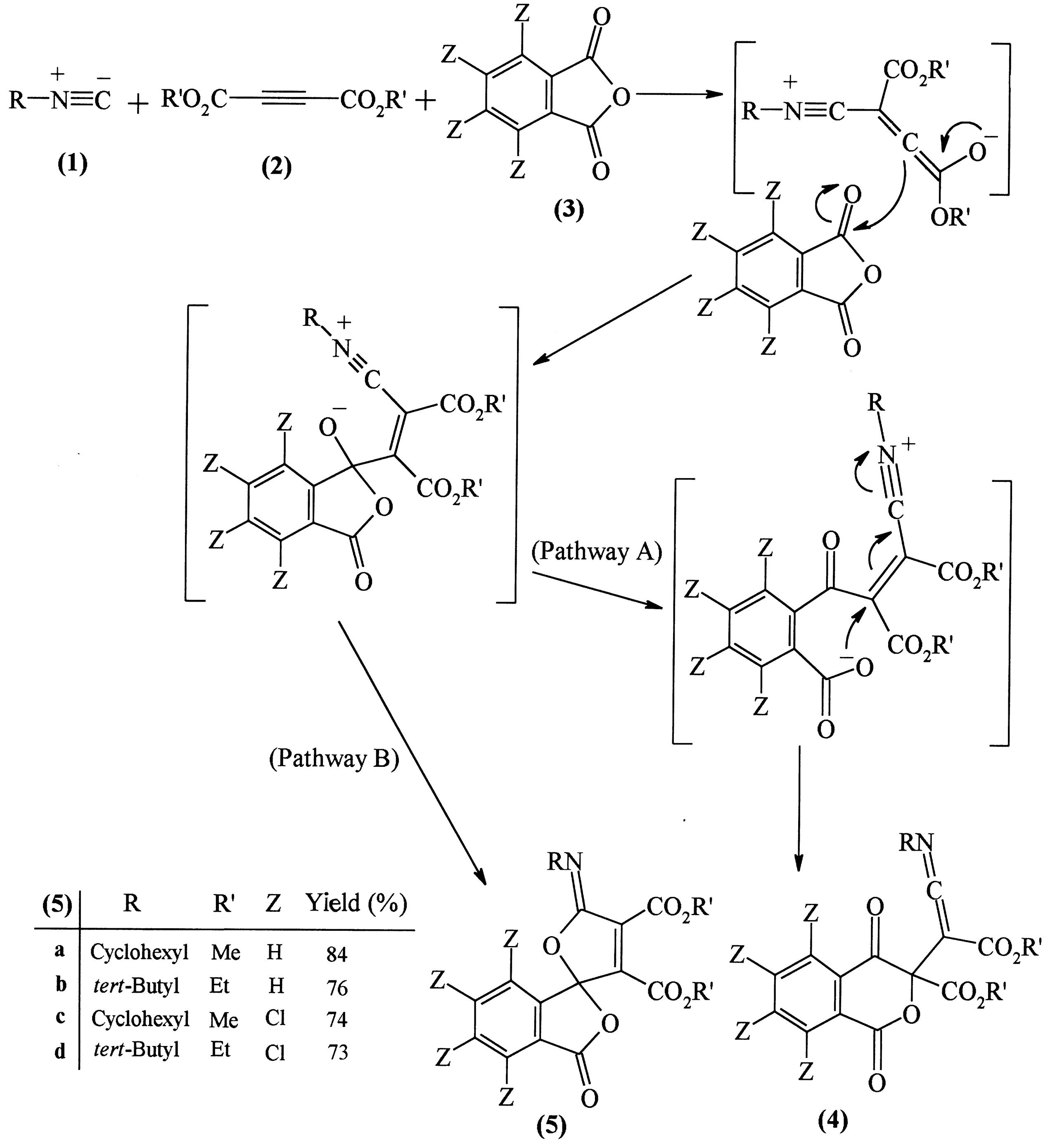
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.



(5)	R	R'	Z	Yield (%)
a	Cyclohexyl	Me	H	84
b	*tert*-Butyl	Et	H	76
c	Cyclohexyl	Me	Cl	74
d	*tert*-Butyl	Et	Cl	73

Scheme 1

and 3.97 (6 H, 2 s, 2 OCH_3). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 24.38, 24.50, 25.52, 33.11 and 33.27 (5 CH_2), 53.32 and 53.46 (2 OCH_3), 57.83 (N–CH), 106.93 (Spiro Carbon), 124.05, 127.98, 131.56, 134.43, 138.12, 140.43, 140.48, 140.68 and 150.06 (C=C, N=C and arom.), 159.38, 160.75 and 160.96 (3 C=O). MS (*m*/*z*, %) 538 (M^+, 38), 505 (77), 440 (69), 403 (23), 301 (31), 97 (100). Anal. Calcd. for $C_{21}H_{17}NO_7Cl_4$ (537.22): C, 46.95; H, 3.18; N, 2.60%. Found: C, 46.73; H, 3.12; N, 2.49%.

Preparation of (**5d**): Similar reaction conditions as for **5a** but using *tert*-butyl isocyanide, diethyl acethylenedicarboxylate and tetrachlorophthalic anhydride instead of cyclohexyl isocyanide, dimethyl acethylenedicarboxylate and phthalic anhydride yielded white crystals (0.394 g, 73 %). m.p. 141–142 °C. IR (KBr) (ν_{max}, cm^{-1}): 3120, 1800, 1733, 1692, 1400. ^1H NMR ($CDCl_3$, Me_4Si): δ_H 1.16 (3 H, t, $^3J_{HH}$=7.1 Hz, CH_3), 1.30 (9 H, s, CMe_3), 1.39 (3 H, t, $^3J_{HH}$=7.1 Hz, CH_3), 4.14 and 4.42 (4 H, 2 q, $^3J_{HH}$=7.1 Hz, 2 OCH_2). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 13.63 and 14.07 (2 CH_3), 29.64 ($C\mathit{Me}_3$), 56.30 (CMe_3), 62.46 and 62.68 (2 OCH_2), 106.85 (Spiro Carbon), 124.29, 127.89, 131.38, 133.29, 137.92, 140.36, 140.64, 141.99 and 147.62 (C=C, N=C and arom.), 158.86, 160.54 and 161.11 (3 C=O). MS (*m*/*z*, %) 540 (M^+, 5), 524 (64), 450 (24), 286 (35), 242 (97), 214 (65), 179 (26), 142 (65), 107 (71), 84 (43), 57 (100). Anal. Calcd. for $C_{21}H_{19}NO_7Cl_4$ (539.23): C, 46.77; H, 3.55; N, 2.59%. Found: C, 46.29; H, 3.71; N, 2.70%.

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