



SYNTHESIS OF (*E*)-2-CYANO-5-PHENYLPENT-2-EN-4-YNOIC ACID ESTERS AND *N*-SUBSTITUTED AMIDES

Cite this: *INEOS OPEN*,
2022, 5 (5), 130–132
DOI: 10.32931/fo2223a

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Received 27 March 2023,
Accepted 19 May 2023

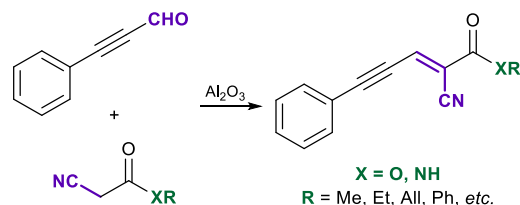
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Abstract

(*E*)-2-Cyano-5-phenylpent-2-en-4-ynoic acid esters and *N*-substituted amides were synthesized by the Knoevenagel condensation of 3-phenylpropionaldehyde with the corresponding cyanoacetates or cyanoacetamides in the presence of basic alumina used as a catalyst. The IR and Raman spectra of the resulting compounds show strong absorption bands in the range of 1565–1580 cm⁻¹ which are attributed to the vibrations of the C=C bond in the enyl moiety.

Key words: phenylpropionaldehyde, (*E*)-2-cyano-5-phenylpent-2-en-4-ynoic acid esters and *N*-substituted amides, basic alumina, Knoevenagel condensation.



Introduction

The derivatives of 2-cyanoacrylic acid are of particular interest owing to their potential biological activity and great synthetic opportunities, especially in the field of heterocyclic and polymer chemistry [1–3].

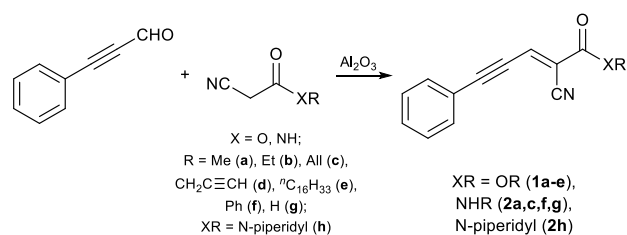
A large variety of cyanoacrylic acid derivatives have been synthesized to date. For example, the Knoevenagel condensation was used to obtain the derivatives of cyanoacrylic acid bearing carbazole units, which, owing to the formation of hydrogen bonds, exhibit variable fluorescence properties in solvents, water, and alcohols, as well as in the presence of metal ions and can be used as fluorescent labels in chemosensors [4].

However, fluorescent 3-ethynylphenyl derivatives of 2-cyanoacrylic acid have not been described, except for the 3-ethynylphenyl derivative of 2-cyanoacrylic acid *N*-phenylamide, which, according to the results of XRD analysis, features planar arrangement of the acetylene and vinylene groups in the central conjugated moiety [5, 6].

Results and discussion

A series of (*E*)-2-cyano-5-phenylpent-2-en-4-ynoic acid esters (**1**) and *N*-substituted amides (**2**) were obtained by the Knoevenagel condensation of phenylpropionaldehyde with the corresponding cyanoacetates or cyanoacetamides in the presence of Al₂O₃ used as a catalyst (Scheme 1) [7–9].

The use of a heterogeneous catalyst, namely, basic alumina [10] allows for reducing the contribution of side processes. The structures and compositions of compounds **1** and **2** were unambiguously confirmed by elemental analysis, IR, Raman, and NMR spectroscopy. The yields and selected physicochemical characteristics of the resulting products are presented in Table 1.



Scheme 1

Table 1. Yields and selected physicochemical characteristics of compounds **1** and **2**

Comp.	Yield, %	Mp, °C	Elemental analyses (found/calcd)			Formula
			C	H	N	
1a	76	69–70	73.85	4.34	6.58	C ₁₃ H ₉ NO ₂
			73.92	4.29	6.63	
1b	78	73–74	74.62	4.90	6.24	C ₁₄ H ₁₁ NO ₂
			74.65	4.92	6.22	
1c	80	47–48	75.86	4.61	5.87	C ₁₅ H ₁₁ NO ₂
			75.93	4.67	5.90	
1d	82	86–87	76.78	3.78	5.81	C ₁₅ H ₉ NO ₂
			76.59	3.85	5.95	
1e	75	68–69	79.95	9.36	3.28	C ₂₈ H ₃₉ NO ₂
			79.76	9.32	3.32	
2a	67	108–110	74.22	4.78	13.25	C ₁₃ H ₁₀ N ₂ O
			74.27	4.79	13.33	
2c	64	104–105	76.10	5.02	11.67	C ₁₅ H ₁₂ N ₂ O
			76.22	5.11	11.85	
2f	65	179–180	79.41	4.31	10.10	C ₁₈ H ₁₂ N ₂ O
			79.31	4.44	10.29	
2g	72	132–134	73.37	4.13	14.32	C ₁₂ H ₈ N ₂ O
			73.46	4.11	14.28	
2h	68	65–66	77.13	5.98	10.54	C ₁₇ H ₁₆ N ₂ O
			77.25	6.10	10.60	

Similar IR and Raman spectra of α,β -unsaturated esters **1** and amides **2** (Table 2) show the expected characteristic intensive absorption bands (IR) and weak lines (Raman) of C=O stretches ($1735\text{--}1720\text{ cm}^{-1}$) for esters **1** as well as amide I ($1675\text{--}1660\text{ cm}^{-1}$) and amide II ($1540\text{--}1530\text{ cm}^{-1}$) bands for amides **2**. Of special interest is the assignment of absorption bands of C=C and C=N stretches [11] and a strong band in the range of $1565\text{--}1580\text{ cm}^{-1}$, which is not observed in the IR spectra of 2-cyanocinnamates [12], the derivatives of phenylacetylene [13] and methyl (*E*)-5-phenylpent-2-en-4-ynoate [14].

The optimal geometry, vibration frequencies, and IR intensities for *E*- and *Z*-isomers of Ph–C≡C–CH=C(CN)–COOMe (**1a**) were calculated by the DFT-B3LYP functional method with the standard 6-31G(d,p) basis using the Gaussian-98 software package [15]. According to the results obtained, the *E*-isomer appeared to be more stable than its *Z*-counterpart by ~ 3.5 kcal/mol. Thus, Ph–C≡C–CH=C(CN) moiety in **1a** is planar.

Table 2. IR/Raman spectroscopic data for compounds **1** and **2**

Comp.	IR bands/Raman lines, ν/cm^{-1}					
	Ph	C=O	C=N	C≡C	C=C	Other peaks
1a	1597	1734	2230	2193	1575	–
1b	1599	1731	2230	2188/ 2189	1579/ 1571	–
1c	1598	1727	2220	2185/ 2189	1576/ 1574	1647 (=CH ₂)
1d	1600	1736	2227	2189/ 2193	1576/ 1570	3293 (\equiv CH)
1e	1599	1721	2235	2195	1575	–
2a	1600	1662	2222	2187/ 2185	1565/ 1565	3305, 3380 (NH)
				1583/ 1581		1538 Amide II
2c	1600	1666	2222	2190	1569/ 1566	1641 (=CH ₂), 3279 (NH) 1534 Amide II
2f	1596	1661	2224	2192/ 2194	1569/ 1566	3251 (NH) 1527 Amide II
2g	1600	1674	2220	2187	1569	3451, 3458 (NH)
						1613 Amide II
2h	1600	1664	2219	2192	1568	–

Of note is satisfactory agreement between the calculated and experimental values both in terms of the band frequencies ($\Delta\nu < 30\text{ cm}^{-1}$) and intensities (qualitatively).

A weak band at $2225 \pm 10\text{ cm}^{-1}$ in the IR and Raman spectra of compounds **1** and **2** was attributed to vibrations of the C=N bond and falls into the region of $\nu(\text{CN})$ of α,β -unsaturated alkyl nitriles. The absorption bands of C=C bond vibrations in the IR and Raman spectra had high intensity and low frequency and appeared at $2190 \pm 5\text{ cm}^{-1}$. The intense absorption band at $1565\text{--}1580\text{ cm}^{-1}$ is mainly associated with vibrations of the C7=C8 bond, which kinematically interacts with the phenyl core when the C=C bond is completely neutral.

Two absorption bands of $\nu(\text{C}=\text{C})$ and $\nu(\text{NH})$ in the IR and Raman spectra of compound **2a** are likely to correspond to two conformers that differ in the twist angle between the phenyl ring and the central moiety of the molecule [16].

The carbon signals in the ^{13}C NMR spectra were assigned based on the closely related results of HMBC experiments for **1a** and **2a**. The NMR spectrum of **1a** showed intense correlation peaks between the =CH proton signal and the carbon resonances at 111.3 ppm and 113.7 ppm as well as its weak cross-peak with the ^{13}C signal at 114.2 ppm, which weakly interacts with the methyl protons. Therefore, the mentioned signals refer to C5, C9, and C8 carbon nuclei. The signal of C6 carbon nucleus was observed at 85.2 ppm. Similar assignments were made for compound **2a**.

Hence, the Knoevenagel condensation of phenylpropionaldehyde on the surface of basic alumina can readily afford (*E*)-5-phenyl-2-cyanopent-2-en-4-ynoic acid esters and amides.

Experimental section

General remarks

The IR spectra of solid samples were recorded on a Perkin-Elmer 1725-FTIR spectrometer equipped with a Perkin-Elmer Diffuse Reflectance (PEDR) accessory and a modified sample holder. The FT-Raman spectra were measured on a Perkin-Elmer Raman Station 400 dispersive Raman spectrometer equipped with an InGaAs detector (operating range $3500\text{--}200\text{ cm}^{-1}$) at a resolution of 4 cm^{-1} with Nd:YAG laser excitation (1064 nm). The NMR spectra were registered on a Bruker AMX-400 instrument (400.26 MHz (^1H), 100.68 MHz (^{13}C)) in acetone- d_6 .

Syntheses

General procedure for the synthesis of esters 1. In the case of compounds **1a–c**, **1e**, a solution of 0.01 mol of 3-phenylpropionaldehyde in 0.012 mol of the corresponding alkyl cyanoacetate was stirred with 3 g of basic Al_2O_3 (pH = 9.5) until the exothermic effect ceased and the mass solidified. The reaction mixture was left at $20\text{ }^\circ\text{C}$ for 12 h and then extracted with dichloromethane. The solvent was removed under vacuum. The resulting residue was crystallized from hexane. The synthesis of compound **1d** was carried out upon addition of 3 mL of absolute dioxane using 6 g of Al_2O_3 .

Methyl (*E*)-2-cyano-5-phenylpent-2-en-4-ynoate (1a). ^1H NMR: δ 3.90 (s, 3H, OMe), 7.37–7.61 (m, 5H, H_{Ar}), 7.54 (s, 1H, =CH) ppm. ^{13}C NMR: δ 53.4 (OMe), 85.2 (C6), 111.3 (C5), 113.7 (C=N), 114.2 (C8), 120.6 (C1), 128.6 (C3 and C3'), 131.0 (C4), 132.8 (C2 and C2'), 136.8 (=CH), 161.45 (C=O) ppm.

Ethyl (*E*)-2-cyano-5-phenylpent-2-en-4-ynoate (1b). ^1H NMR: δ 1.34 (t, 3H, Me, $J = 7.2$ Hz), 4.35 (q, 2H, OCH_2 , $J = 7.2$ Hz), 7.50–7.65 (m, 5H, H_{Ar}), 7.67 (s, 1H, =CH) ppm.

Allyl (*E*)-2-cyano-5-phenylpent-2-en-4-ynoate (1c). ^1H NMR: δ 4.81 (d, 2H, OCH_2 , $J = 5.6$ Hz), 5.30 (dd, 1H, *cis*-H in =CH₂, $J = 1.4/11.2$ Hz), 5.43 (dd, 1H, *trans*-H in =CH₂, $J = 1.4/13.2$ Hz), 6.03 (m, 1H, =CH (All)), 7.50–7.65 (m, 5H, H_{Ar}), 7.71 (s, 1H, =CH) ppm.

Propargyl (*E*)-2-cyano-5-phenylpent-2-en-4-ynoate (1d). ^1H NMR: δ 3.19 (t, 1H, $\equiv\text{CH}$, $J = 5.6$ Hz), 4.96 (d, 2H, OCH_2 , $J = 5.6$ Hz), 7.50–7.66 (m, 5H, H_{Ar}), 7.73 (s, 1H, =CH) ppm.

Hexadecyl (*E*)-2-cyano-5-phenylpent-2-en-4-ynoate (1e). ^1H NMR: δ 0.88 (t, 3H, Me, $J = 7.2$ Hz), 3.97 (q, 2H, OCH_2 , $J = 7.2$ Hz), 7.42–7.55 (m, 5H, H_{Ar}), 7.28 (s, 1H, =CH) ppm.

General procedure for the synthesis of amides 2. A solution of 0.01 mol of 3-phenylpropionaldehyde and 0.01 mol of the corresponding cyanoacetamide in 3 mL of dry *N*-methylpyrrolidone (NMP) was stirred with 5 g of basic Al₂O₃ until the exothermic effect ceased and the mass solidified. The reaction mixture was left at 20 °C for 12 h and then extracted with NMP. The resulting solution was poured into water. The precipitate obtained was collected by filtration and recrystallized from a toluene–hexane mixture.

(*E*)-2-Cyano-*N*-methyl-5-phenylpent-2-en-4-ynamide

(2a). ¹H NMR: δ 2.90 (q, 3H, Me, *J* = 4.8 Hz), 7.47–7.62 (m, 7H, 5H_{Ar} + =CH + NH) ppm. ¹³C NMR: δ 27.0 (NMe), 85.2 (C6), 109.0 (C5), 118.1 (C8), 115.7 (C9), 120.8 (C1), 128.5 (C3 and C3'), 130.6 (C4), 132.6 (C2 and C2'), 134.2 (C7), 159.4 (C=O) ppm.

(*E*)-2-Cyano-*N*-allyl-5-phenylpent-2-en-4-ynamide (2c).

¹H NMR: δ 4.20 (m, 2H, CH₂NH), 5.24 (m, 2H, *cis*- and *trans*-H in =CH₂), 5.87 (m, 1H, =CH (All)), 6.30 (br. s, 2H, NH) 7.37–7.60 (m, 5H, H_{Ar}), 7.57 (s, 1H, =CH) ppm.

(*E*)-2-Cyano-*N*-phenyl-5-phenylpent-2-en-4-ynamide

(2f). ¹H NMR: δ 7.18–7.77 (m, 10H, H_{Ar}) 7.69 (s, 1H, =CH), 9.43 (br. s, 1H, NH) ppm.

(*E*)-2-Cyano-5-phenylpent-2-en-4-ynamide (2g).

¹H NMR: δ 6.30 (br. s, 2H, NH₂), 7.44–7.65 (m, 5H, H_{Ar}), 7.67 (s, 1H, =CH) ppm.

(*E*)-5-Phenyl-2-(piperidine-1-carbonyl)pent-2-en-4-

ynenitrile (2h). ¹H NMR: δ 1.66 (br. s) and 3.58 (m) (10H, piperidyl), 7.35–7.57 (m, 5H, H_{Ar}), 7.08 (s, 1H, =CH) ppm.

Conclusions

(*E*)-2-Cyano-5-phenylpent-2-en-4-ynoic acid esters and *N*-substituted amides were obtained by the Knoevenagel condensation between 3-phenylpropionaldehyde and the corresponding cyanoacetates or cyanoacetamides in the presence of basic alumina used as a catalyst. The new esters and amides were characterized by the NMR, IR, and Raman spectra, as well as elemental analysis.

Acknowledgements

This work was performed with financial support from the Ministry of Science and Higher Education of the Russian Federation using the equipment of the Center for Molecular Composition Studies of INEOS RAS (agreement no. 075-03-2023-642).

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