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A Synthesis of Novel Perinaphthenones from Acetylenic Esters and Acenaphthoquinone–Malononitrile Adduct in the Presence of Triphenylphosphine

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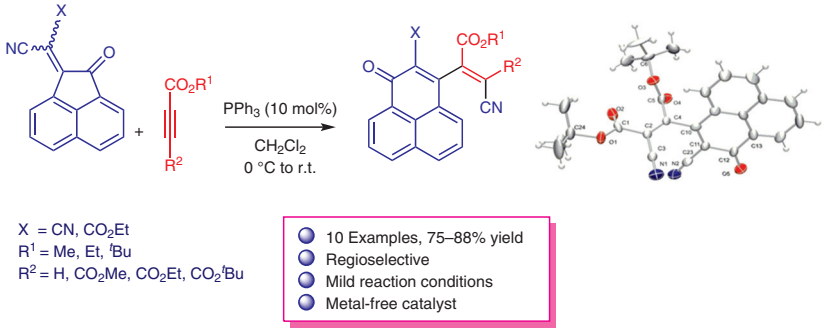


Received: 16.06.2018
Accepted after revision: 25.07.2018
Published online: 23.08.2018
DOI: 10.1055/s-0037-1610253; Art ID: st-2018-b0264-l

Abstract A facile protocol involving Tebby zwitterions (PPh_3-acetylenic esters) and the Knoevenagel condensation product of acenaphthylene-1,2-dione with malononitrile or ethyl cyanoacetate for the selective synthesis of a new series of perinaphthenone derivatives is described. Triphenylphosphine plays a catalytic role in these transformations. The structure of a typical product was confirmed by X-ray crystallography. The merits of this method include high yields of products, good atom economy, and a metal-free catalyst.

Key words perinaphthenones, acenaphthylenedione, alkynoate esters, triphenylphosphine, malononitrile

The yellow dye perinaphthenone (**A**; 1*H*-phenalen-1-one) is an aromatic ketone used as a singlet oxygen sensitizer in photochemistry and photobiology.[1] Some natural perinaphthenone derivatives, for example **B**–**E** (Figure 1), have been reported and their photodynamic fungicidal activity has been demonstrated.[2–4] The synthesis of novel fungicides based on the structures of perinaphthenone-type natural products is considered to be a promising strategy.[4]

The α,β-unsaturated carbonyl group in perinaphthenone is responsible for its remarkable photophysical and photochemical properties. The nature of the lowest singlet and triplet excited states of aromatic ketones (n, π*) or (π, π*) is highly dependent on the interaction between the carbonyl group and the arene system.[5–7]

Some derivatives of 1-oxo-1*H*-phenalene-2,3-dicarbonitrile have important applications as molecular fluorescent sensors and as anticancer drugs.[8] The synthesis these derivatives has some similarities to that of the new compounds described in this letter.

During our previous studies on applications of trivalent phosphorus nucleophiles in syntheses of organic compounds,[9–12] we discovered a novel reaction between acetylenic esters and the Knoevenagel condensation product of acenaphthylene-1,2-dione[13] with malononitrile or ethyl cyanoacetate (**1** and **2**, respectively) in the presence of triphenylphosphine as a catalyst in dry CH_2Cl_2 at 0 °C to room temperature, which led to a new series of perinaphthenones in moderate to good yields.[14]

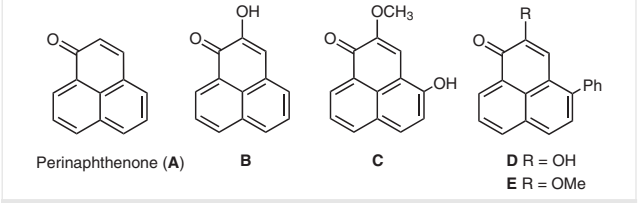
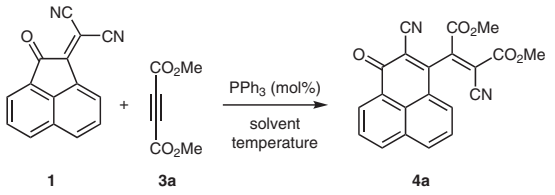


Figure 1 Perinaphthenone (**A**) and some natural perinaphthenone derivatives **B**–**E**

Initially, we studied the effects of the amount of PPh_3, the temperature, and various solvents on the reaction of DMAD (**3a**) with adduct **1** as a model reaction. First, the effects of various amounts of PPh_3 in CH_2Cl_2 at 0 °C to room temperature were investigated (Table 1, entries 1–7). The use of 10 mol% of PPh_3 gave product **4a** in 84% yield (entry 2). We then tested the effects of EtOH, MeCN, THF, and toluene as solvents (entries 8–16), but none gave an improved yield of the product. Therefore, the best reaction conditions for this transformation are CH_2Cl_2 as solvent in the presence of 10 mol% of PPh_3 at 0 °C to room temperature.

With the optimal reaction conditions in hand, we proceeded to explore the substrate scope of this reaction. The Knoevenagel condensation products of acenaphthylene-1,2-dione with malononitrile or ethyl cyanoacetate (**1** and **2**, respectively) were successfully applied in the reaction to give perinaphthenone derivatives **4a–j** in satisfactory yields (Table 2).[14]

Table 1 Optimization of the Reaction Conditions for the Preparation of Perinaphthenone Derivative **4a**[a]

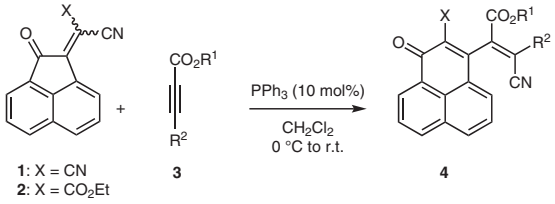


1 **3a** **4a**

Entry	PPh_3 (mol%)	Solvent	Temp (°C)	Yield[b] (%)
1	5	CH_2Cl_2	0 to r.t	72
2	10	CH_2Cl_2	0 to r.t	84
3	20	CH_2Cl_2	0 to r.t	67
4	30	CH_2Cl_2	0 to r.t	61
5	40	CH_2Cl_2	0 to r.t	58
6	50	CH_2Cl_2	0 to r.t	64
7	100	CH_2Cl_2	0 to r.t	78
8	10	EtOH	0 to r.t	75
9	10	EtOH	0 to r.t then reflux	69
10	10	THF	0 to r.t	68
11	10	THF	0 to r.t then reflux	60
12	10	MeCN	0 to r.t	74
13	10	MeCN	0 to r.t then reflux	69
14	10	Toluene	0 to r.t	72
15	10	Toluene	0 to r.t then reflux	69
16	10	CH_2Cl_2	0 to r.t then 40	76

[a] Reaction conditions: **1** (1 mmol), **3a** (1 mmol), solvent (5 mL), 12 h.
[b] Isolated yield.

Table 2 Synthesis of Perinaphthenone Derivatives **4a–j**[a]



1: X = CN
2: X = CO_2Et
3
4

Entry	X	R^1	R^2	Product	Yield[b] (%)
1	CN	Me	CO_2Me	**4a**	84
2	CN	Et	CO_2Et	**4b**	80
3	CN	^{t}Bu	CO_2-*t*-Bu	**4c**	75
4	CN	Me	H	**4d**	85
5	CN	Et	H	**4e**	88
6	CO_2Et	Me	CO_2Me	**4f**	86
7	CO_2Et	Et	CO_2Et	**4g**	83
8	CO_2Et	*t*-Bu	CO_2-*t*-Bu	**4h**	81
9	CO_2Et	Me	H	**4i**	88
10	CO_2Et	Et	H	**4j**	86

[a] Reaction conditions: **1** or **2** (1 mmol), **3** (1 mmol), CH_2Cl_2 (5 mL), 12 h.
[b] Isolated yield.

The structures of products **4a–j** were fully assigned from their IR, ^{1}H NMR, ^{13}C NMR, and mass spectra. The IR spectrum of **4a** revealed the presence of carbonyl (1728 and 1654 cm^{-1}) and nitrile groups (2194 cm^{-1}). The ^{1}H NMR spectrum of **4a** showed signals for two methoxy groups at δ = 3.94 and 4.02 ppm. The ^{13}C NMR spectra clearly showed signals for CN, CO_2R, and C=O groups in the appropriate regions of the spectrum.

The structure of compound **4c** was also confirmed by single-crystal X-ray analysis (Figure 2).[15] Similar structures were assumed for derivatives **4a**, **4b**, and **4f–h** on the basis of the similarities of their NMR spectra. The olefinic protons of compounds **4d**, **4e**, **4i**, and **4j** appeared at about δ = 7.10–7.43 ppm, which is consistent with an *E*-geometry of the double bond.[16]

A plausible mechanism for the formation of perinaphthenone derivatives **4a–j** is shown in Scheme 1. It is conceivable that the initial addition of PPh_3 to the acetylenic ester **3** affords the reactive zwitterionic intermediate **5**. Next, addition of intermediate **5** to the Knoevenagel condensation product **1** or **2** gives intermediate **6**. On the basis of a mechanism reported in the literature,[17] we propose a reaction path involving cyclization to provide intermediate **7**. This intermediate, is converted into **9** by ring expansion and elimination of a cyanide ion. This cyanide ion then undergoes Michael addition to intermediate **9** to afford adduct **10**, which is converted into product **4** by a retro-Michael elimination of PPh_3.

In conclusion, we succeeded in regioselective syntheses of perinaphthenone derivatives through the reaction of acetylenic esters with the Knoevenagel condensation products of acenaphthylene-1,2-dione with malononitrile or ethyl cyanoacetate in the presence of PPh_3 (10 mol%) as a catalyst at 0 °C to room temperature in dry CH_2Cl_2. The synthesis is simple and versatile, and the new compounds have potential applications as dyes or drug precursors. The pres-

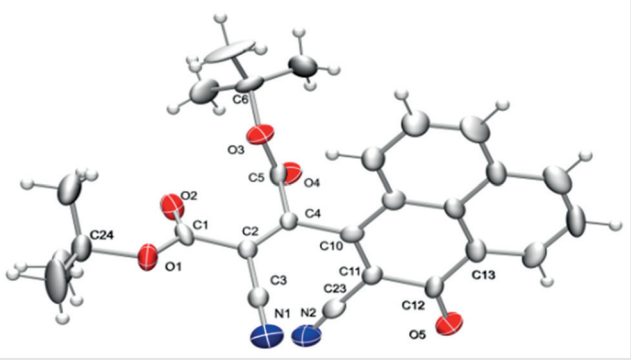
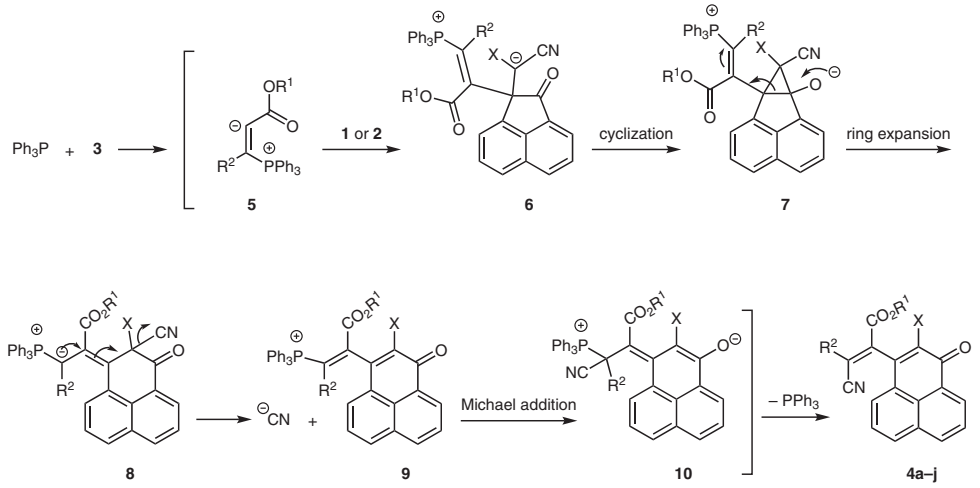


Figure 2 X-ray crystal structure of compound **4c**



Scheme 1 Plausible mechanism for the formation of products **4a–j**

ent method has the advantage that the reaction is carried out under mild and metal-free conditions. The reported method might serve as a convenient strategy for preparing a variety of perinaphthenone derivatives.

Funding Information

We gratefully acknowledge the financial support from the Research Council of Tarbiat Modares University.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610253.

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(14) **1*H*-Phenalen-1-one Derivatives 4a–j; General Procedure**
A mixture of PPh_3 (0.026 g, 0.1 mmol) and CH_2Cl_2 (5 mL) at 0 °C was added dropwise over 10 min to a stirred solution of the appropriate Knoevenagel adduct **1** or **2** (1 mmol) and acetylenic ester **3** (1 mmol) in CH_2Cl_2 (5 mL). The mixture was then allowed to warm to r.t. and stirred for 12 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography [silica gel, hexane–EtOAc (2:1)].

Dimethyl 2-Cyano-3-(2-cyano-1-oxo-1*H*-phenalen-3-yl)but-2-enedioate (4a)
Yellow solid; yield: 0.31 g (84%); mp 185–190 °C. IR (KBr): 3057, 2952, 2194 (CN), 1728 (C=O), 1654 (C=O), 1571, 1437 ($C=C_{Ar}$), 1255, 1008, 778 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H, MeO), 4.02 (s, 3 H, MeO), 7.77 (t, ^3J = 7.5 Hz, 1 H Ar-H), 7.92 (t, ^3J = 7.5 Hz, 1 H Ar-H), 8.13 (d, ^3J = 7.5 Hz, 1 H, Ar-H), 8.26 (d, ^3J = 8.0 Hz, 1 H Ar-H), 8.30 (d, ^3J = 8.0 Hz, 1 H Ar-H), 8.78 (d, ^3J = 7.5 Hz, 1 H Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 53.9 (2 × MeO), 111.1 (CN), 111.8 (CN), 112.3 (C), 113.0 (C), 122.5 (C), 126.7 (CH), 126.8 (C), 127.9 (CH), 131.2 (C), 131.9 (C), 132.5 (CH), 133.6 (CH), 136.3 (CH), 136.7 (CH), 150.5 (C), 153.1 (C), 158.6 (C=O), 162.1 (C=O), 177.7 (C=O). EI-MS: *m/z* (%) = 372 (M^+, 82), 313 (53), 299 (48), 272 (51), 255 (100), 226 (50), 200 (32). Anal. Calcd for $C_{21}H_{12}N_2O_5$ (372.34): C, 67.74; H, 3.25; N, 7.52. Found: C, 67.95; H, 3.32; N, 7.61.

Dimethyl 2-Cyano-3-[2-(ethoxycarbonyl)-1-oxo-1*H*-phenalen-3-yl]but-2-enedioate (4f)
Yellow solid; yield: 0.36 g (86%); mp 180–185 °C. IR (KBr): 3055, 2988, 2214 (CN), 1727 (C=O), 1625 (C=O), 1588, 1370 ($C=C_{Ar}$), 1269, 780 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ = 1.25 (t, ^3J = 7.0 Hz, 3 H Me), 3.28 (s, 3 H, MeO), 3.52 (s, 3 H, MeO), 4.48 (q, ^3J = 7.0 Hz, 2 H, CH_2O), 7.73 (t, ^3J = 7.5 Hz, 1 H Ar-H), 7.88 (t, ^3J = 7.5 Hz, 1 H Ar-H), 8.10 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 8.31 (d, ^3J = 8.0 Hz, 1 H Ar-H), 8.33 (d, ^3J = 8.0 Hz, 1 H Ar-H), 8.64 (d, ^3J = 7.5 Hz, 1 H Ar-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8 (Me), 52.0, 52.7 (2 × MeO), 64.6 (CH_2O), 114.6 (CN), 122.9 (C), 126.1 (CH), 126.5 (CH), 127.1 (C), 127.6 (C), 128.4 (C), 128.5 (CH), 128.7 (CH), 129.2 (C), 131.3 (C), 131.9 (CH), 133.6 (CH), 149.1 (C), 150.7 (C), 158.3 (C=O), 161.8 (C=O), 162.3 (C=O), 187.2 (C=O). EI-MS: *m/z* (%) = 419 (M^+, 91), 360 (62), 345 (53), 318

(52), 301 (100), 275 (42), 246 (25), 202 (34). Anal. Calcd for $C_{23}H_{17}NO_7$ (419.10): C, 65.87; H, 4.09; N, 3.34. Found: C, 65.99; H, 4.16; N, 3.41.

(15) **X-Ray Crystal-Structure Determination of 4c**

The X-ray diffraction measurements were carried out on STOE IPDS 2T diffractometer with graphite-monochromated Mo Kα radiation. A single crystal suitable for X-ray analysis was grown from DMSO solution, mounted on a glass fiber, and used for data collection. Compound **4c** crystallizes in the monoclinic crystal system with a = 1062.8(2) pm, b = 1862.6(4) pm, c = 1278.5(3) pm, β = 109.11(3)°; cell volume = 2.3914(10) nm^3. Orientation matrices for data collection were obtained by least-square refinement of 12379 diffraction data for compound **4c**. The diffraction data were collected in a series of ω scans with 1° oscillations and were integrated by using the *Stoe X-AREA* software package.[18] A numerical absorption correction was applied by using *X-Red32* software. The structure was solved by direct methods and subsequent difference Fourier maps and then refined on F^2 by a full-matrix least-squares procedure using anisotropic displacement parameters. Atomic factors are from the International Tables for X-ray Crystallography. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. All refinements were performed by using the *X-STEP32*, *SHELXL-2014*, and *WinGX-2013.3* programs.[19] CCDC 1502615 contains the supplementary crystallographic data for compound **4c**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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