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Synthesis of dialkyl 4-ethoxy-2,5-dihydro-1-(9,10-dihydro-9,10-dioxoanthracen-6-yl)-5-oxo-1*H*-pyrrole-2, 3-dicarboxylates

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Abstract: The reaction of dialkyl acetylenedicarboxylate with ethyl (9, 10-dihydro-9, 10-dioxoanthracen-6-ylcarbamoyl) formate in the presence of Ph_3P produces dialkyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1*H*-pyrrole-2, 3-dicarboxylate in fairly good yields. The structures of these products were deduced from their mass, ^{1}H NMR, ^{13}C NMR and FT-IR spectral data. Various features of this reaction will be presented and discussed.

Keywords: Intramolecular Wittig reaction, Triphenyl phosphine, Dialkyl acetylenedicarboxylate, Pyrrole.

Introduction

From the earliest days of modern structural theory of organic chemistry, quinones have been intimately associated with the chemistry of aromatic compounds [1−3]. Their importance in dye chemistry, in medicinal chemistry, in biological electron transport processes, and in other fields have been documented over the years [1−3]. 2-Amino-anthraquinone is an important intermediate in manufacturing of dyes and pharmaceuticals. The importance of the pyrrole nucleus in organic chemistry, especially in natural products such as hemoglobin, chlorophyll and mold metabolites is obvious [4, 5]. Thus, there is considerable current interest in the synthesis of this heterocyclic nucleus, scince five membered nitrogen heterocycles are the backbone of many biologically interesting compounds. There are several reports in the literature for the synthesis of pyrrole ring such as reaction of amines and enamines with γ-dicabonyl compounds [6] or reaction of α, β-unsaturated carbonyl compound with amines and nitroethane [7].

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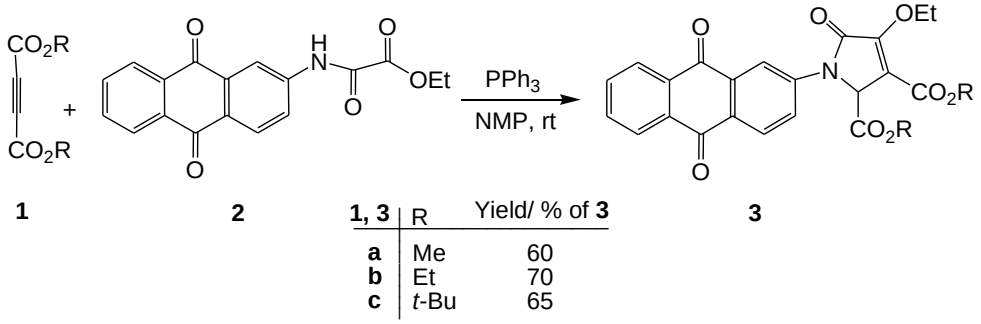
As a part of our studies on the development of new routes to heterocyclic and carbocyclic systems [8−11], herein we wish to report Synthesis of dialkyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1*H*-pyrrole-2, 3-dicarboxylates.

Results and discussion

We now report the reaction of dialkyl acetylenedicarboxylates **1** with ethyl (9, 10-dihydro-9, 10-dioxoanthracen-6-ylcarbamoyl) formate (**2**) in the presence of triphenylphosphine (Ph_3P). This reaction leads to dialkyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1*H*-pyrrole-2, 3-dicarboxylate **3a–3c** in fairly good yields (Scheme **1**).

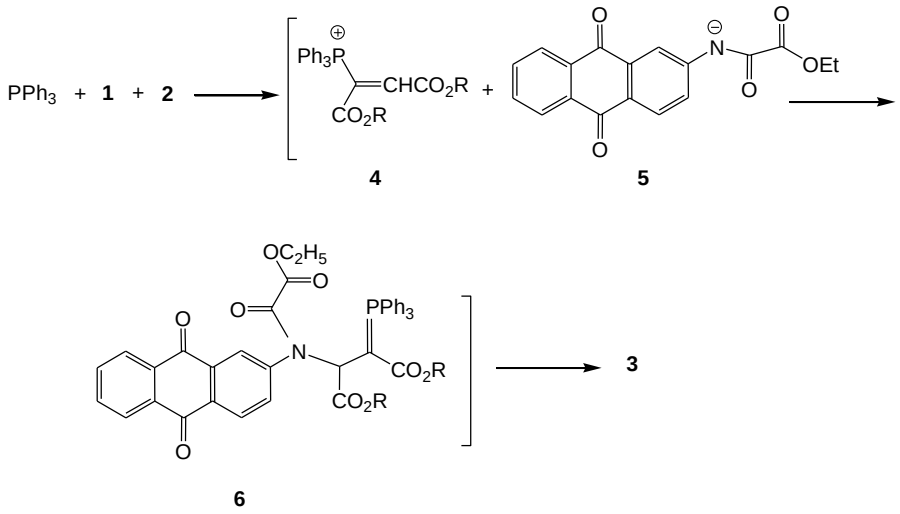
This reaction proceeded spontaneously at room temperature in CH_2Cl_2 and was finished within 24 h. The ^{1}H and ^{13}C NMR spectra of the reaction mixtures clearly indicated the formation of **3**. The structures of compounds **3a–3c** were deduced from their elemental analyses and their IR, ^{1}H and ^{13}C NMR spectra. The mass spectra of these compounds are fairly similar and display molecular ion peaks at appropriate *m/z* values.

Other fragmentations involved the loss of the ester moieties.



1, 3	R	Yield/ % of 3
a	Me	60
b	Et	70
c	*t*-Bu	65

Scheme 1. Synthesis of **3** from **1** and **2** mediated by Ph_3P



Scheme 2. A plausible mechanism for the formulation of **3**

Although we have not yet established the mechanism for the reaction between Ph_3P and **1** in the presence of **2** in an experimental manner, a possible explanation is proposed in Scheme **2**. It is reasonable to assume that **3** results from the initial addition of Ph_3P to the acetylenic ester and subsequent protonation of the 1:1 adduct by the NH-acid to produce **4**. Then the positively charged ion **4** is attacked by the nitrogen atom of the conjugate base of the NH-acid **5** to form the phosphorane **6**, which is converted to **3** *via* an intramolecular Wittig reaction [12, 13].

Experimental

2-Amino-anthraquinone, dialkyl acetylene dicarboxylates and Ph_3P were obtained from Fluka (Buchs, Switzerland) andused without further purification. Melting points were measured on an Electrothermal 9100 apparatus. The ^1H, and ^{13}C NMR spectra were measured at 300, and 75 MHz, respectively, on a Bruker 300-AVANCE FT-NMR instrument with $CDCl_3$ as solvent.

Preparation of ethyl (9, 10-dihydro-9, 10-dioxoanthracen-6-ylcarbamoyl)formate (2):

To a stirred solution of 0.44 g 2-amino-anthraquinone (2 mmol) in 5 mL of NMP was added dropwise a solution of 0.27 g of ethyl oxalyl chloride (2 mmol) in 2 mL of NMP at room temperature. Reaction was completed within 1 hr. The solvent was removed and the product was obtained as light green powder; m.p. 232-234°C; yield: 0.58 g (90%). IR (KBr) (υ_{max}/cm^{-1}): 1728, 1707, 1673, and 1593 (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (3 H, *t*, $^3J_{HH}$ = 7 Hz, Me), 4.33 (2 H, *q*, $^3J_{HH}$ = 7 Hz, OCH_2), 7.90–7.93 (2 H, *m*, 2 CH), 8.19–8.26 (4 H, *m*, 4 CH), 8.66 (1 H, *s*, CH), 11.39 (1 H, *s*, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (Me), 63.5 (OCH_2), 118.3 (CH), 126.1 (CH), 127.5 (C), 127.7 (CH), 129.1 (CH), 129.9 (CH), 133.9 (2 CH), 134.9 (C), 135.3 (2 C), 143.8 (C), 156.9 and

160.8 (2 C=O amide and ester), 182.3 and 183.2 (2 C=O) ppm. MSEI: *m/z* (%): 323 (M^+, 66), 250 (100), 223 (51), 208 (67), 180 (61), 151 (66), 76 (31), 29 (29).

Preparation of dimethyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1H-pyrrole-2, 3-dicarboxylate (3a). Typical Procedure:

To a stirred solution of 0.52 g of Ph_3P (2 mmol) and 0.64 g ethyl (9, 10-dihydro-9, 10-dioxo anthracen-6-ylcarbamoyl) formate (2 mmol) in 20 mL of CH_2Cl_2 was added dropwise a solution of 0.28 g of dimethyl acetylenedicarboxylate (2 mmol) in 5 mL of CH_2Cl_2 and refluxed. After 24 h the solvent was removed under reduced pressure and the viscous residue was purified by recrystallization to give a light brown powder; m.p. 130-132°C; yield: 0.54 g (60%). IR (KBr) (υ_{max}/cm^{-1}): 1749, 1728, 1710, 1673, and 1593 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (3 H, *t*, $^3J_{HH}$ = 7.1 Hz, Me), 3.73 (3 H, *s*, MeO), 3.88 (3 H, *s*, MeO), 4.84 (2 H, ABX_3, OCH_2), 5.59 (1 H, *s*, NCH), 7.44–7.49 (2 H, *m*, 2 CH), 7.64–7.71 (4 H, *m*, 4 CH), 8.80–8.83(1 H, *m*, CH) ppm. ^{13}C NMR (75MHz, $CDCl_3$): δ = 16.1 (Me), 53.1 (MeO), 54.1 (MeO), 60.5 (NCH), 69.0 (OCH_2), 113.0 (O-C-*C*), 126.1 (CH), 127.6 (CH), 129.4 (C), 132.9 (CH), 133.9 (CH), 134.7 (CH), 134.9 (CH), 135.1 (CH), 135.2 (C), 135.5 (C), 136.1 (C), 142.3 (N-C), 156.9 (OC=*C*), 162.8, 165.5, and 168.9 (3 C=O amide and ester), 182.7 and 182.9 (2 C=O) ppm. MSEI: *m/z* (%): 449 (M^+, 20), 390 (30), 330 (56), 277 (17), 234 (100), 207 (34), 151 (55), 59 (40), 29 (47).

Diethyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1H-pyrrole-2, 3-dicarboxylate (3b):

Dark red powder; m.p. 150–152°C; yield: 0.67 g (70%). IR (KBr) (υ_{max}/cm^{-1}): 1745, 1708, 1677, 1645, and 1592 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (3 H, *t*, $^3J_{HH}$ = 7 Hz, Me), 1.35 (3 H, *t*, $^3J_{HH}$ = 7 Hz, Me), 1.45 (3 H, *t*, $^3J_{HH}$ = 7 Hz, Me), 4.12 (2 H, *q*, $^3J_{HH}$ = 7 Hz, OCH_2), 4.29 (2 H, ABX_3, OCH_2), 4.79 (2 H, ABX_3, OCH_2), 5.57 (1 H, *s*, NCH), 7.80–7.83 (2 H, *m*, 2 CH), 8.31–8.40 (4 H, *m*, 4 CH), 8.37 (1 H, *s*, CH), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ= 14.4 (Me), 14.5 (Me), 16.0 (Me), 60.8 (NCH), 61.8 (OCH_2), 63.0 (OCH_2), 69.6 (OCH_2), 113.0 (O-C=*C*), 117.5 (CH), 124.8 (CH), 125.8 (C), 127.7 (CH), 129.4 (CH), 129.7 (CH), 130.6 (CH), 133.9 (CH), 134.4 (C), 134.7 (C), 134.9 (C), 142.3 (N-C), 154.0 (O-C=*C*), 161.7, 164.3, and 167.7 (3 C=O amide and ester), 182.4 and 182.8 (2 C=O) ppm.

Di-tert-butyl 4-ethoxy-2, 5-dihydro-1-(9, 10-dihydro-9, 10-dioxoanthracen-6-yl)-5-oxo-1H-pyrrole-2, 3-dicarboxylate (3c):

Brownish green powder; m.p. 147–150°C; yield: 0.69 g (65%). IR (KBr) (υ_{max}/cm^{-1}): 1740, 1728, 1708, 1677, and 1648 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (9 H, *s*, CMe_3), 1.45 (3 H, *t*, $^3J_{HH}$ = 7 Hz, Me), 1.58 (9 H, *s*, CMe_3), 4.46 (2 H, ABX_3, OCH_2), 5.39 (1 H, *s*, NCH), 7.81–7.84 (2 H, *m*, 2 CH), 8.31–8.34 (2 H, *m*, 2 CH), 8.35 (1 H, *s*, CH), 8.35–8.48 (2 H, *m*, 2 CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.0 (Me), 28.6 (C*Me*$_3$), 29.6 (C*Me*$_3$), 62.0 (NCH), 69.0 (OCH_2), 83.1 (*C*Me$_3$), 83.4 (*C*Me$_3$), 117.6 (O-C=*C*), 125.8 (CH), 127.7 (CH), 129.3 (C), 130.4 (CH), 133.9 (CH), 134.0 (CH), 134.4 (CH), 134.4 (CH), 134.7 (C), 134.8 (C), 137.9 (C), 142.6 (N-C), 153.3 (O-C=*C*), 160.9, 164.8, and 166.5 (3 C=O amide and ester), 182.4 and 182.9 (2 C=O) ppm.

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