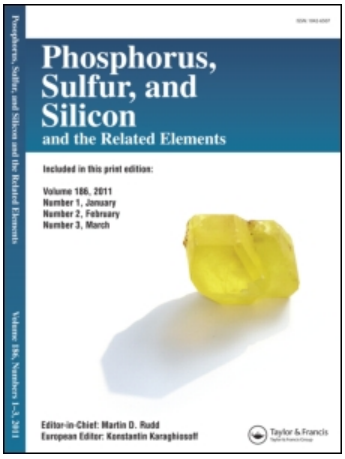

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The reaction of ethyl 9,10-dihydro-9,10-dioxoanthracen-1-yl-carbamoyl-formate with dialkyl acetylenedicarboxylates in the presence of triphenylphosphine leads to dialkyl 4-ethoxy-2,5-dihydro-1-(9,10-dihydro-9,10-dioxoanthracen-1-yl)-5-oxo-1H-pyrrole-2,3-dicarboxylates in fairly good yields. A dynamic NMR effect is observed as a result of restricted rotation around the single bond linking the anthraquinone moiety and the heterocyclic ring system, which is attributed to the interaction between the pyrrole residue and the peri C═O group.

Keywords Intramolecular Wittig reaction; *peri* interaction; restricted rotation; triphenylphosphine

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] 1-Amino-anthraquinone

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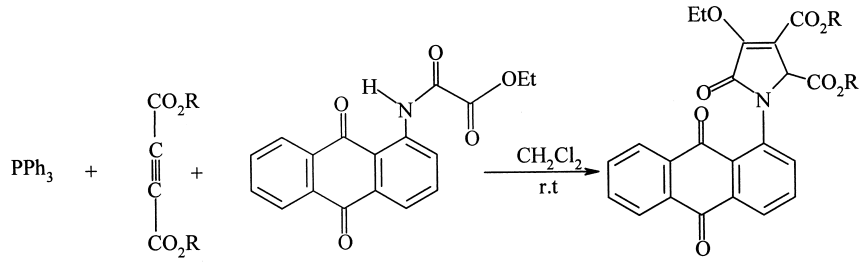
is an important intermediate in manufacturing of dyes and pharmaceuticals. The importance of the pyrrole nucleus in organic chemistry, especially in natural products such as hemoglobin, chlorophyll and mold metabolites is obvious.[4,5] As part of our current studies on the development of new routes to heterocyclic and carbocyclic systems,[6–9] we now report the reaction of dialkyl acetylenedicarboxylates **1** with ethyl 9,10-dihydro-9,10-dioxoanthracen-1-yl-carbamoylformate (**2**) in the presence of triphenylphosphine. This reaction leads to dialkyl 4-ethoxy-2,5-dihydro-1-(9,10-dihydro-9,10-dioxoanthracen-1-yl)-5-oxo-1*H*-pyrrole-2,3-dicarboxylates **3a–3c** in fairly good yields (see Scheme 1).

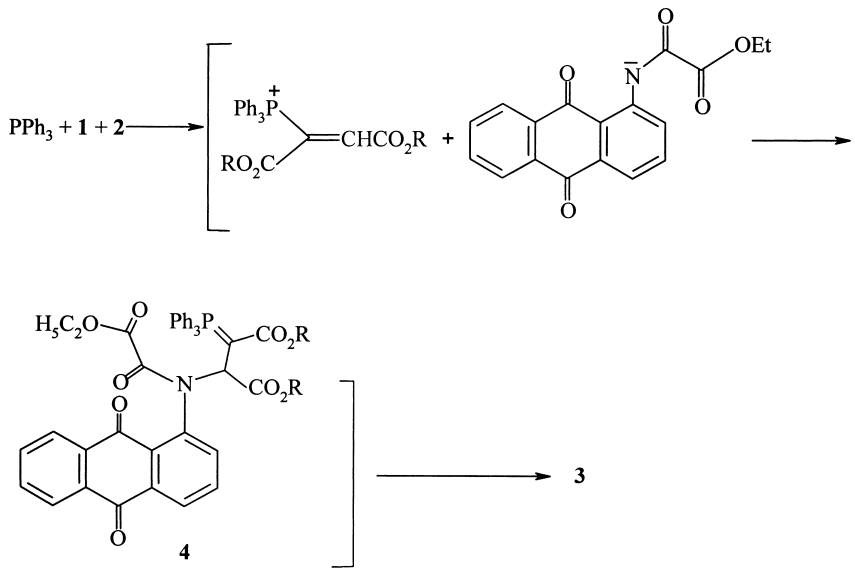


1, 3	R	%Yilelds of 3
a	Me	60
b	Et	70
c	t-Bu	65

SCHEME 1 Synthesis of 3 from 1 and 2 mediated by triphenylphosphine.

This reaction proceeded spontaneously at room temperature in CH_2Cl_2 and was finished within 24 hours. The ^1H 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, ^1H and ^{13}C NMR spectra. The mass spectra of these compounds are fairly similar and display molecular ion peaks at appropriate *m/z* values. Any other fragmentation involved the loss of the ester moieties.

Although we have not yet established the mechanism for the reaction between triphenylphosphine 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 triphenylphosphine to the acetylenic ester and subsequent protonation of the 1:1 adduct by the NH-acid. Then the positively charged ion is

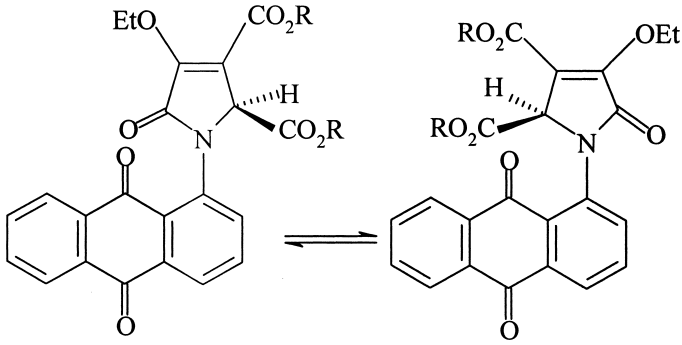


SCHEME 2 Aplaussible mechanism for formulation of 3.

attacked by the nitrogen atom of the conjugate base of the NH-acid to form the phosphorane **4**, which is converted to **5** via an intramolecular Wittig reaction.[10]

Compounds **3a–3c** exhibit atropisomerism at room temperature because of hindered rotation around the carbon-nitrogen bond linking the anthraquinone moiety and the pyrrole ring system, which is the result of interaction of the pyrrole moiety with the *peri* C=O group.[11–13] Thus, the ^{1}H NMR spectrum of **3a** reveals that one of the methoxy signals is quite broad at 298 K, while the other methoxy resonance remains sharp. The broad line sharpens at low temperature and a new weak resonance appears at about 450 Hz upfield to the major resonance. The maximum exchange broadening at half peak height ($w_{1/2\,\max}$) of the methoxy resonance at 298 K is 5 Hz. Since the $w_{1/2\,\max}$ for a two site system with very unequal populations is given by P_B ($|\upsilon_A - \upsilon_B|$), where P_B is the fractional population of the minor conformer that calculated to be populated to the extent of 7% at this temperature.[14,15] A line-shape calculation carried out with $P_B = 7\%$, $k = 130\ s^{-1}$, and with the chemical shift differences for methoxy groups at 230 K, reproduces well the observed spectrum at 278 K. The free-energy of activation ($\Delta G^{\#}$) and ΔG° for the *N*-aryl bond rotation in **3a** is then 66.2 ± 2 kJ mol^{-1} and 6.2 ± 2 kJ mol^{-1}, respectively.

The dynamic NMR effect for **3a** can be attributed to restricted rotation around the aryl-nitrogen single bond[6–9] as a result of the steric effect of the carbonyl group at the *peri* position (Scheme 3).



SCHEME 3 Atropisomerism in compound 3.

The presented reaction of **2** with dialkyl acetylendicarboxylates in the presence of triphenylphosphine provide a simple one-pot entry into the synthesis of dialkyl 4-ethoxy-2,5-dihydro-1-(9,10-dihydro-9,10-dioxoanthracen-1-yl)-5-oxo-1*H*-pyrrole-2,3-dicarboxylates of potential interest. Dynamic NMR effects are observed in the ^{1}H NMR spectra of **3a** and attributed to restricted rotation around the aryl-nitrogen bond.

EXPERIMENTAL

1-Amino-anthraquinone, dialkyl acetylenedicarboxylates and triphenylphosphine were obtained from Fluka (Buchs, Switzerland) and used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. ^{1}H, 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. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Hewlet-Packard MSD 5973 mass spectrometer. IR spectra were measured on a Bomem MB-100 FT-IR spectrometer.

Preparation of Ethyl 9,10-Dihydro-9,10-dioxoanthracen-1-yl-carbamoyl-formate (2)

To a stirred solution of 0.44 g 1-amino-anthraquinone (2 mmol) in 20 mL of acetone was added drop wise a solution of 0.27 g of ethyl oxalyl

chloride (2 mmol) in 10 mL of acetone at room temperature. Reaction was completed within 1 hr. The solvent was removed and the product was obtained as golden yellow crystals; m.p. 198–200°C; yield: 0.58 g (90%).

IR (KBr) (υ_{max}/cm^{-1}): 1736, 1720, 1668, and 1645 (C=O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (3 H, t, $^3J_{HH}$ = 7 Hz, CH_3), 4.53 (2 H, q, $^3J_{HH}$ = 7 Hz, OCH_2), 7.83–7.88 (2 H, m, 2 CH), 7.90 (1H, t, $^3J_{HH}$ = 8 Hz, CH), 8.19 (1 H, dd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, CH), 8.31 (1 H, m, CH), 8.41 (1 H, m, CH), 9.18 (1 H, dd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, CH), 13.76 (1 H, br s, NH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4 (CH_3), 64.3 (OCH_2), 124.3 (CH), 126.4 (CH), 127.5 (CH), 128.1 (CH), 132.5 (CH), 133.1 (C), 134.6 (C), 134.9 (CH), 136.3 (CH), 140.4 (C), 156.0 and 160.8 (2 C=O, amide and ester), 182.8 and 187.0 (2 C=O) ppm.

MS (EI, 70 eV), *m/z* (%): 323 (M^+, 3).

Anal. Calcd for $C_{18}H_{13}NO_5$ (323.3): C, 66.87; H, 4.05; N, 4.33%. Found C, 66.81; H, 4.08; N, 4.30%.

Preparation of Dimethyl 4-Ethoxy-2,5-dihydro-1-(9,10-dihydro-9,10-dioxoanthracen-1-yl)-5-oxo-1*H*-pyrrole-2,3-dicarboxylate (3a). Typical Procedure

To a stirred solution of 0.52 g of triphenylphosphine (2 mmol) and 0.64 g ethyl 9,10-dihydro-9,10-dioxoanthracen-1-yl-carbamoyl-formate (2 mmol) in 20 mL of CH_2Cl_2 was added drop wise a solution of 0.28 g of dimethyl acetylenedicarboxylate (2 mmol) in 5 mL of CH_2Cl_2 at room temperature. After 24 h the solvent was removed under reduced pressure and the viscous residue was purified by column chromatography (Merck silica gel 60, 230-400 Mesh ASTM) using *n*-hexane-EtOAc 2:3 as eluent. The solvent was removed under reduced pressure and the pure product obtained as light yellow crystals; m.p. 139-142°C; yield: 0.54 g (60%).

IR (KBr) (υ_{max}/cm^{-1}): 1748, 1725, 1711, 1672, and 1643 (C=O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (3 H, t, $^3J_{HH}$ = 7 Hz, CH_3), 3.67 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 4.86 (2 H, ABX_3, OCH_2), 5.24 (1 H, br s, NCH), 7.57 (1 H, dd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, CH), 7.80–7.83 (2 H, m, 2 CH), 7.87 (1H, t, $^3J_{HH}$ = 8 Hz, CH), 8.20 (1 H, m, CH), 8.29 (1 H, m, CH), 8.48 (1 H, dd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.1 (CH_3), 52.4 (OCH_3), 53.3 (OCH_3), 62.7 (OCH_2), 69.0 (OCH_2), 113.4 (O–C=*C*), 127.4 (CH), 127.8 (CH), 129.4 (CH), 132.9 (C), 134.4 (C), 134.9 (C), 134.7 (CH), 134.9 (CH), 135.1 (CH),, 135.6 (C), 136.1 (C), 137.4 (CH), 154.8 (O–*C*=C), 162.8, 165.5, and 168.9 (3 C=O, ester and amide), 182.7 and 182.9 (2 C=O) ppm.

MS (EI, 70 eV), *m/z* (%): 449 (M^+, 7).

Anal. Calcd for $C_{24}H_{19}NO_8$ (449.4): C, 64.14; H, 4.26; N, 3.12%. Found C, 64.10; H, 4.22; N, 3.10%.

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

Light yellow crystals; m.p. 128–131°C; yield: 0.67 g (70%).

IR (KBr) (υ_{max}/cm^{-1}): 1750, 1727, 1716, 1679, and 1646 (C=O).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.13$ (3 H, t, $^3J_{HH} = 7$ Hz, CH_3), 1.33, (3 H, t, $^3J_{HH} = 7$ Hz, CH_3), 1.48 (3 H, t, $^3J_{HH} = 7$ Hz, CH_3), 4.12 (2 H, q, $^3J_{HH} = 7$ Hz, OCH_2), 4.26 (2 H, ABX_3, OCH_2), 4.86 (2 H, ABX_3, OCH_2), 5.21 (1 H, br s, NCH), 7.59 (1 H, dd, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 2$ Hz, CH), 7.79–7.82 (2 H, m, 2 CH), 7.84 (1H, t, $^3J_{HH} = 8$ Hz, CH), 8.20 (1 H, m, CH), 8.28 (1 H, m, CH), 8.47 (1 H, dd, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 2$ Hz, CH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4 (CH_3), 14.5 (CH_3), 16.0 (CH_3), 61.4 (OCH_2), 62.4 (OCH_2), 62.9 (OCH_2), 69.1 (OCH_2), 113.7 (O–C=*C*), 127.4 (CH), 127.9 (CH), 129.3 (CH),, 129.9 (C), 132.8 (C), 134.3 (C), 134.5 (CH), 135.0 (CH), 135.6 (CH), 135.9 (C), 136.3 (C), 137.6 (CH), 155.0 (O–*C*=C), 162.2, 168.5, and 170.0 (3 C–O, ester and amide), 182.8 and 182.8 (2 C=O) ppm.

MS (EI, 70 eV), *m/z* (%): 477 (M^+, 4).

Anal. Calcd for $C_{26}H_{23}NO_8$ (477.4): C, 65.40; H, 4.86; N, 2.93%. Found C, 65.32; H, 4.83; N, 2.96%.

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

Light yellow crystals; m.p. 131–134°C; yield: 0.69 g (65%).

IR (KBr) (υ_{max}/cm^{-1}): 1744, 1717, 1709, 1678, and 1655 (C=O).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.32$ (9 H, s, CMe_3), 1.46 (3 H, t, $^3J_{HH} = 7$ Hz, CH_3), 1.49 (9 H, s, CMe_3), 4.82 (2 H, ABX_3, OCH_2), 5.05 (1 H, br s, NCH), 7.64 (1 H, dd, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 2$ Hz, CH), 7.82–7.85(2 H, m, 2 CH), 7.86 (1H, t, $^3J_{HH} = 8$ Hz, CH), 8.22 (1 H, m, CH), 8.29 (1 H, m, CH), 8.5 (1 H, dd, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 2$ Hz, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 16.0$ (CH_3), 28.6 (CMe_3), 29.6 (CMe_3), 63.9 (OCH_2), 68.7 (OCH_2), 82.4 (CMe_3), 83.2 (CMe_3), 116.1 (O–C=*C*), 127.3 (CH), 127.9 (CH), 129.1 (CH),, 129.9 (C), 132.9 (C), 134.2 (C), 134.6 (CH), 135.1 (CH), 135.9 (CH), 136.1 (C), 136.5 (C), 137.9 (CH), 155.0 (O–*C*=C), 162.6, 166.5, and 169.0 (3 C=O, ester and amide), 182.6 and 182.9 (2 C=O) ppm.

MS (EI, 70 eV), *m/z* (%): 533 (M^+, 3).

Anal. Calcd for $C_{30}H_{31}NO_8$ (533.5): C, 67.53; H, 5.86; N, 2.63%. Found C, 67.56; H, 5.82; N, 2.60%.

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