Monatshefte für Chemie 134, 1093–1098 (2003)
DOI 10.1007/s00706-003-0021-5

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Synthesis and Dynamic NMR Spectroscopic Study of Dialkyl 4-Ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1*H*-pyrrole-2,3-dicarboxylates

Issa Yavari*, **Mehdi Adib, Shahrzad Abdolmohammadi,** and **Mansoreh Aghazadeh**

Department of Chemistry, University of Tarbiat Modarres, P.O. Box 14115-175, Tehran, Iran

Received December 6, 2002; accepted December 11, 2002
Published online June 12, 2003

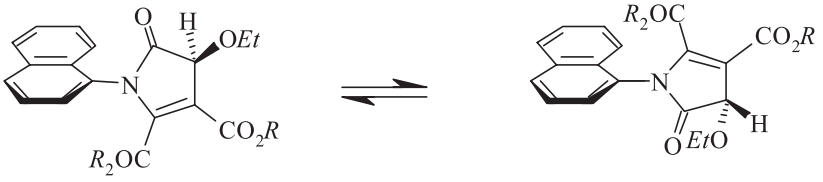
Summary. Protonation of the reactive 1:1 intermediate produced in the reaction between triphenylphosphine and dialkyl acetylenedicarboxylates with ethyl 2-(1-naphthylamino)-2-oxoacetate, leads to a vinylphosphonium salt, which undergoes intramolecular *Wittig* reaction to produce dialkyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1*H*-pyrrole-2,3-dicarboxylates in excellent yields. A dynamic NMR effect is observed in the ^{1}H NMR spectra of the title compounds as a result of restricted rotation around the single bond linking the naphthalene moiety and the heterocyclic system, which is attributed to the *peri* interaction between the pyrrole residue and the *peri* CH group. The free energy of activation ($\Delta G^{\neq}$) for this process is 58 ± 2 kJ mol^{-1}.

Keywords. *Peri* interaction; Hindered rotation; Stereochemistry; Rotational isomers; Intramolecular *Wittig* reaction; Triphenylphosphine.

Introduction

Peri interactions in suitably substituted naphthalenes have attracted the attention of organic chemists since the elegant works of *House* and coworkers in the 1960s [1–4]. Hindered 1-substituted naphthalene derivatives such as dialkyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1*H*-pyrrole-2,3-dicarboxylates (**1**) adopt a twisted conformation, *i.e.*, the pyrrole moiety is not coplanar with the naphthalene ring. In fact, compound **1** possesses a conformational stereogenic axis and, in addition, a configurational stereogenic center. This molecule adopts two distinct *syn*, *anti* conformations, due to restricted rotation around the *Ar*–N bond. As a consequence, **1** is expected to exist as a pair of *syn*, *anti* diastereomeric conformers of different stabilities

* Corresponding author. E-mail: isayavar@yahoo.com



(anti)-**1** *(syn)*-**1**

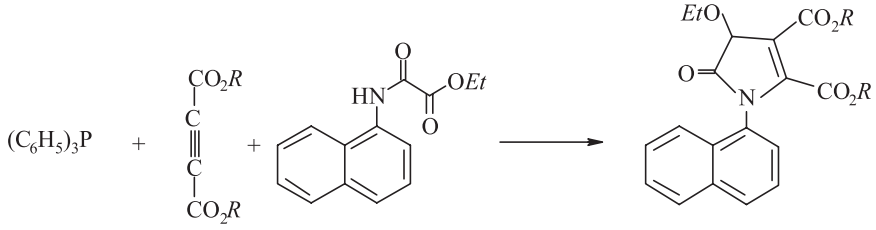
Scheme 1

(Scheme 1). We wish to report the detection of these atropisomers by NMR spectroscopy at low temperatures.

Results and Discussion

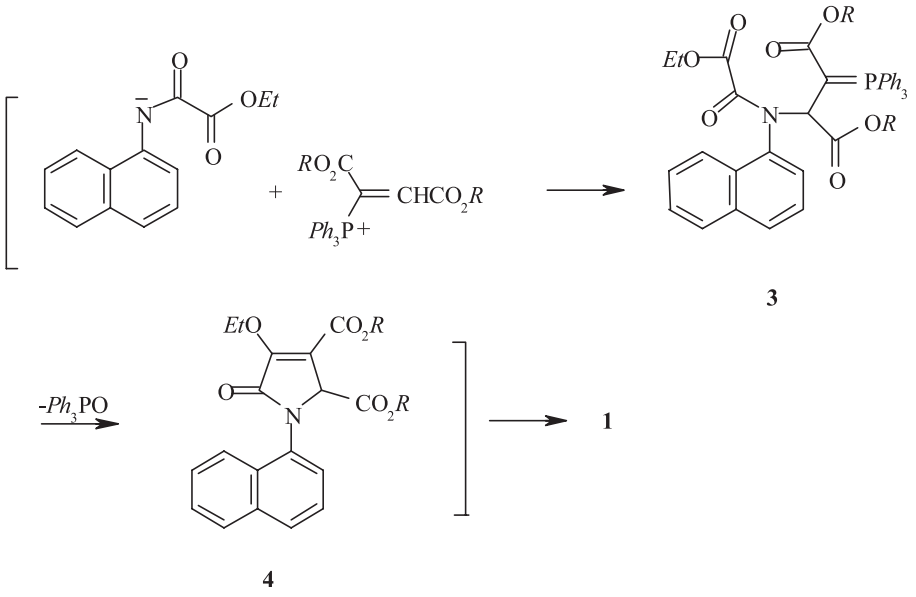
Compound **1** is readily prepared *via* an intramolecular *Wittig* reaction. Thus, triphenylphosphine and dialkyl acetylenedicarboxylates **2** in the presence of a strong NH-acid, such as ethyl 2-(1-naphthylamino)-2-oxoacetate undergo a smooth reaction at ambient temperature to produce a phosphorus ylide. This in turn experiences an intramolecular *Wittig* reaction [5] under the reaction conditions employed to produce dialkyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1*H*-pyrrole 2,3-dicarboxylates **1** (Scheme 2). No other product could be detected by NMR spectroscopy. Compounds **1a**–**1c** exhibit atropisomerism at ambient temperatures because of hindered rotation around the carbon–nitrogen bond between the naphthalene moiety and the pyrrole ring system, which is the result of *peri* interaction of the pyrrole moiety with the *peri* CH group.

The structures of compounds **1a**–**1c** were deduced from their elemental analyses and their high-field ^{1}H and ^{13}C NMR and IR spectral data. The mass spectra of these compounds displayed molecular ion peaks at $m/z = 369$, 397, and 453. Initial fragmentations involved the loss of ester moieties and scission of the heterocyclic ring system.



	R		*R*
2a:	*Me*	**1a**:	*Me*
2b:	*Et*	**1b**:	*Et*
2c:	*tBu*	**1c**:	*tBu*

Scheme 2



Scheme 3

Although we have not yet established the mechanism of the reaction between triphenylphosphine and dialkyl acetylenedicarboxylates in the presence of ethyl 2-(1-naphthylamino)-2-oxoacetate in an experimental manner, a possible explanation is proposed in Scheme 3. On the basis of the well-established chemistry of trivalent phosphorus nucleophiles [6–9], it is reasonable to assume that **1** 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 might be attacked by the conjugate base of the NH-acid to form phosphorane **3**, which is converted to pyrrole derivative **4**. Compound **4** apparently isomerises under the reaction conditions employed to produce the 5-oxo-4,5-dihydropyrrole ring system **1** (see Scheme 3).

^{13}C NMR spectroscopy was used to distinguish structure **1** from the primary adduct, the 5-oxo-2,5-dihydropyrrole derivative **4**. Thus, each of the products exhibited a methine carbon resonance at about $\delta = 68$–69 ppm. The chemical shift of the methine carbon in **4** is expected to appear at about $\delta = 52$–56 ppm [10, 11]. The most noteworthy feature of the ^{1}H NMR spectrum of **1a** in $CDCl_3$ solution at 20°C is the presence of several broad signals (see Fig. 1). Near 60°C the broad lines become sharper. Decreasing the temperature leads to decoalescence of the methoxy and the methine signals. The ^{1}H NMR spectrum at -50°C is consistent with the presence of two conformational diastereoisomers in 54:46 ratio (see Fig. 1). This dynamic effect is interpreted in terms of a restricted rotation around the *Ar*–N bond.

Although an extensive lineshape analysis in relation to the dynamic NMR effect observed for **1** was not undertaken in the present work, the variable temperature spectra are sufficient to calculate the free energy barrier as well as enthalpy and entropy of activation for the restricted *Ar*–N bond rotation. From the coalescence of the methoxy and methine protons and using the expression $k = \pi\Delta\nu/\sqrt{2}$ [12], the first-order rate constants (k) were calculated (see Table 1).

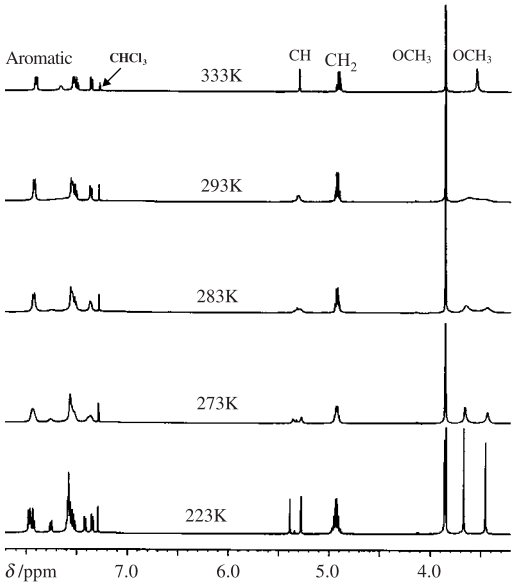


Fig. 1. Variable temperature 500 MHz ^{1}H NMR spectra of **1a** in $CDCl_3$

Table 1. Selected ^{1}H chemical shifts (at 500.1 MHz, in ppm, Me_4Si) and activation parameters of **1** in $CDCl_3$

	T_c/K	δ_{CO_2R} ppm		δ_{CHO} ppm		$\Delta\nu$/Hz	k/s^{-1}	E_A[a] kJ mol^{-1}	$\Delta H^{\neq b}$ kJ mol^{-1}	$\Delta S^{\neq c}$ J mol^{-1}	$\Delta G^{\neq d}$ kJ mol^{-1}
1a	259	3.85	3.86			5.00	11.10				
	283			5.28	5.39	55.01	122.14				
	295	3.45	3.67			110.02	244.28	55.70	53.68	− 15.93	58.73
1b	287			5.24	5.35	55.01	122.14				
	299	0.82	1.09			135.03	302.63	53.45	51.55	− 26.11	58.97
1c	288			5.09	5.24	75.02	166.56				
	299	0.95	1.28			165.03	374.05	51.16	49.87	− 29.95	58.52

[a] E_A was obtained from the slope of the linear plot of $\ln k$ versus T^{-1}; [b] $\Delta H^{\neq} = E_A - RT$; [c] $\Delta S^{\neq} = R(\ln A - \ln ek_BT/h)$; [d] $\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq}$

Application of the absolute rate theory with a transmission coefficient of **1** gives a free energy of activation ($\Delta G^{\neq}$) of 58 ± 2 kJ mol^{-1} for **1a**, where all known sources of errors are estimated and included [13]. Similar dynamic NMR effects were observed for compounds **1b** and **1c** (see Table 1). The $\Delta G^{\neq}$ values measured for **1a**–**1c** are about one-half of the value reported for the 1,8-disubstituted naphthalene in Ref. [4].

Experimental

Dialkyl acetylenedicarboxylates, triphenylphosphine, ethyl oxalyl chloride, and 1-naphthylamine were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O-Rapid analyzer. The experimental data were in good agreement

with the calculated values. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution) with a Bruker DRX-500 AVANCE spectrometer at 500.1 and 125.8 MHz. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Chromatography columns were prepared from Aldrich silica gel, 70–230 mesh.

General Procedure for the Preparation of **1**

To a magnetically stirred solution of 0.52 g of triphenylphosphine (2 mmol) and 0.70 g of ethyl 2-(1-naphthylamino)-2-oxoacetate (2 mmol) in 6 cm^3 of CH_2Cl_2 was added dropwise a mixture of 0.28 g of dimethyl acetylenedicarboxylate (2 mmol) in 4 cm^3 of CH_2Cl_2 at $-5°C$ for 10 min. The reaction mixture was then allowed to warm up to room temperature and stirred for 6 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography using hexane:ethyl acetate = 2:1 as eluent. The solvent was removed under reduced pressure.

Dimethyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**1a**, $C_{20}H_{19}NO_6$)

Colorless crystals, mp 143–145°C (from 1:1 hexane:ethyl acetate = 1:1), yield 0.66 g (90%); IR (KBr) $\bar{\nu}_{max}$ = 1738, 1690, and 1630 (C=O) cm^{-1}; MS: m/z (%) = 369 (M^+, 12); ^{1}H NMR (298 K): δ = 1.46 (t, J = 7.0 Hz, OCH_2CH_3), 3.50 (br s, OCH_3), 3.81 (s, OCH_3), 4.89 (q, J = 7.0 Hz, OCH_2CH_3), 5.29 (br s, OCH), 7.34 (dd, J = 7.3, 1.0 Hz, CH), 7.46 (d, J = 8.2 Hz, CH), 7.48–7.53 (m, 2CH), 7.65 (br, CH), 7.85 (d, J = 8.0 Hz, CH), 7.88 (d, J = 8.0 Hz, CH) ppm; ^{13}C NMR (298 K): δ = 15.75 (OCH_2CH_3), 52.04 (OCH_3), 52.81 (br, OCH_3), 63.44 (br, OCH_2), 68.75 (OCH), 112.81 (N–C=*C*), 121–123 (very br, CH), 123.5–126 (very br, CH), 125.46 and 126.65 (2CH), 127.24, 128.61, and 129.67 (3br, 3CH), 130.17 (br, C), 132.08 (very br, C), 134.56 (C), 154.46 (very br, C), 162.28 (C=O), 164.69 (very br, C=O), 168.15 (br, C=O) ppm.

Diethyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**1b**, $C_{22}H_{23}NO_6$)

Colorless crystals, mp 79–82°C (from hexane:ethyl acetate = 1:1), yield 0.73 g (92%); IR (KBr) $\bar{\nu}_{max}$ = 1711 and 1633 (C=O) cm^{-1}; MS: m/z (%) = 397 (M^+, 35), 324 (29), 278 (15), 250 (80), 154 (100), 127 (27), 44 (26); ^{1}H NMR (298 K): δ = 0.65–1.20 (br, OCH_2CH_3), 1.31 and 1.48 (2t, J = 7.1 Hz, $2OCH_2CH_3$), 3.75–4.20 (br, OCH_2CH_3), 4.24–4.33 (m, ABX_3, OCH_2CH_3), 4.89 (q, J = 7.1 Hz, OCH_2CH_3), 5.28 (br, OCH), 7.37 (d, J = 7.2 Hz, CH), 7.49 (d, J = 7.8 Hz, CH), 7.52–7.54 (m, 2CH), 7.65 (br, CH), 7.88 (d, J = 7.8 Hz, CH), 7.90 (d, J = 7.8 Hz, CH) ppm; ^{13}C NMR (298 K): δ = 13.77 (br, OCH_2CH_3), 14.11 and 15.67 ($2OCH_2CH_3$), 61.01 and 61.95 ($2OCH_2CH_3$), 63.63 (br, OCH_2CH_3), 68.83 (OCH), 112.95 (N–C=*C*), 121–124 (very br, CH), 124.5–125.5 (very br, CH), 125.38 and 126.60 (2CH), 127.16, 128.54, and 129.56 (3br, 3CH), 130.20 (br, C), 132.12 (very br, C), 134.53 (C), 154.05 (very br, CH), 161.71 (C=O), 165.15 (very br, C=O), 167.63 (br, C=O) ppm.

Di-tert-butyl 4-ethoxy-1-(1-naphthyl)-5-oxo-4,5-dihydro-1H-pyrrole-2,3-dicarboxylate (**1c**, $C_{26}H_{31}NO_6$)

Colorless crystals, mp 134–136°C (from hexane:ethyl acetate 1:1), yield 0.82 g (90%); IR (KBr) $\bar{\nu}$ = 1738, 1706, and 1627 (C=O) cm^{-1}; MS: m/z (%) = 453 (M^+, 2), 353 (4), 324 (2), 297 (20), 250 (20), 154 (17), 57 (75), 44 (100); ^{1}H NMR (298 K): δ = 0.9–1.4 (very br, CMe_3), 1.47 (t, J = 7.0 Hz, OCH_2CH_3), 1.53 (s, CMe_3), 4.86 (m, ABX_3, OCH_2), 5.15 (br, OCH), 7.40 (d, J = 7.2 Hz, CH), 7.4–7.6 (m, 3CH), 7.6–7.8 (br, CH), 7.88 (d, J = 7.8 Hz, 2CH) ppm; ^{13}C NMR (298 K): δ = 15.66

(OCH_2CH_3), 27.49 (br, CMe_3), 28.15 (CMe_3), 64.80 (br, OCH_2CH_3), 68.43 (OCH), 82.03 and 82.63 ($2CMe_3$), 115.26 (N–C=*C*), 121–125 (very br, CH), 125.24 (CH), 125–126 (very br, CH), 126.49 (CH), 126.93, 128.41, and 129.25 (3br, 3CH), 130.14 (br, C), 132.50 (very br, C), 134.46 (C), 153.86 (very br, C), 160.90 (C=O), 164.95 (very br, C=O), 166.24 (br, C=O) ppm.

References

[1] House HO, Magin RW, Thompson HW (1963) J Org Chem **28**: 2403; House HO, Bashe RW (1965) J Org Chem **30**: 2942; House HO, Bashe RW (1967) J Org Chem **32**: 784; House HO, Campbell WJ, Gil M (1970) J Org Chem **35**: 1815; House HO, Koepsell DG, Campbell WJ (1972) J Org Chem **37**: 1003
[2] Clough RL, Robrets JD (1976) J Am Chem Soc **98**: 1018
[3] Gasparrini F, Lunazzi L, Misiti D, Villani C (1995) Acc Chem Res **28**: 163
[4] Yavari I, Adib M, Jahani-Moghaddam F (2002) Monatsh Chem **133**: 1431
[5] Zbiral E (1974) Synthesis 775; Becker KB (1980) Tetrahedron **36**: 1717
[6] Johnson AW (1966) Ylid Chemistry, Academic Press, New York
[7] Quin LD (2000) A Guide to Organophosphorus Chemistry, Wiley Interscience, New York
[8] Corbridge DEC (1995) Phosphorus: An Outline of its Chemistry, Biochemistry and Technology, Elsevier, Amsterdam
[9] Yavari I, Adib M, Esnaashari M (2001) Monatsh Chem **132**: 1557; Yavari I, Adib M (2001) Tetrahedron **57**: 5873
[10] Yavari I, Ramazani A, Esmaili AA (1997) J Chem Res (S) 208
[11] Yavari I, Esmaili AA, Ramazani A, Bolbol-Amiri AR (1997) Monatsh Chem **128**: 927
[12] Günther H (1995) NMR Spectroscopy, 2nd ed, Wiley, New York, Chapt 9
[13] Anet FAL, Anet R (1975) In: Cotton FA, Jackman LM (eds) Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York, p 543