Efficient Synthesis of Dialkyl (2*Z*)-2-[(*E*)-1-Aryl-2-(3-arylquinoxalin-2-yl)ethenyl]but-2-enedioates

by **Issa Yavari***, **Anvar Mirzaei**, and **Loghman Moradi**

Chemistry Department, Tarbiat Modarres University, P. O. Box 14115-175, Tehran, Iran
(phone: +98-21-88006631; fax: +98-21-88006544; e-mail: yavarisa@modares.ac.ir)

The reaction of dialkyl acetylenedicarboxylates **4** with 1-aryl-2-[(3-arylquinoxalin-2(1*H*)-ylidene)-ethanones **3** in the presence of Ph_3P leads to dialkyl (2*Z*)-2-[(*E*)-1-aryl-2-(3-arylquinoxalin-2-yl)ethenyl]-but-2-enedioates **1** in good yields.

Introduction. – The quinoxaline ring system [1] is present in many natural and synthetic products exhibiting antitumor activity [2]. Quinoxalines have also been used for the synthesis of poly(phenylquinoxalines), which possess excellent thermal stabilities, low dielectric constants, high glass-transition temperatures, and good mechanical properties [3]. New living polymerization of 1,2-di(isocyano)arenes *via* (quinoxalinyl)palladium complexes have been reported [4]. The majority of quinoxaline derivatives are prepared by the reaction of benzene-1,2-diamine or an equivalent reagent with a 1,2-dicarbonyl compound [5][6].

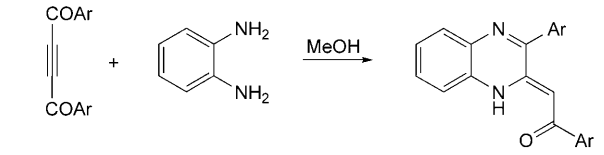
As part of our current studies on the development of new routes in the synthesis of heterocyclic systems [7], we now report a convenient one-pot synthesis of dialkyl (2*Z*)-2-[(*E*)-1-aryl-2-(3-arylquinoxalin-2-yl)ethenyl]but-2-enedioates of type **1**.

Results and Discussion. – Reaction of benzene-1,2-diamine with the corresponding 1,4-diarylbut-2-yne-1,4-dione **2** gave rise to the 1-aryl-2-[(3-arylquinoxalin-2(1*H*)-ylidene)ethanones **3**. The latter were then reacted with acetylenic esters of type **4** in the presence of Ph_3P in refluxing toluene to afford the target compounds **1** in good yields (*Scheme 1*). No products other than **1** were detected by NMR spectroscopy. The structures of **1a**–**1f** were deduced by elemental analysis, MS, IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy.

The ^{1}H-NMR spectrum of, *e.g.*, **1a** exhibited two *singlet*s at δ(H) 3.68 and 3.82 due to two MeO groups. The olefinic resonances were observed at δ(H) 5.68 and 7.01, along with characteristic *multiplet*s for the aromatic H-atoms. The ^{1}H-decoupled ^{13}C-NMR spectrum of **1a** showed 24 distinct signals, in agreement with the proposed structure. Unambiguous evidence for the proposed structure of **1a** was finally obtained by single-crystal X-ray-diffraction analysis. An ORTEP [8] diagram of **1a** is shown in the *Figure*. For details of the structure determination and refinement, see the *Exper. Part*.

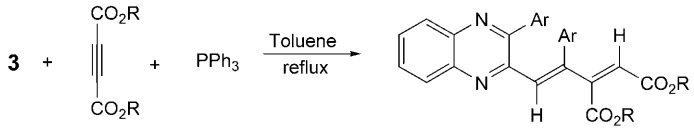
Mechanistically, it is conceivable that the reaction leading to **1** involves the initial formation of a zwitterionic 1:1 intermediate **5** of Ph_3P and the acetylenic compound (*Scheme 2*) [9–11]. The intermediate **5** is then protonated by the NH-acidic **3** to afford

Scheme 1



2	Ar
a	Ph
b	4-Me-C_6H_4

3	Ar
a	Ph
b	4-Me-C_6H_4



4	R
a	Me
b	Et
c	^{i}Pr
d	^{t}Bu

1	Ar	R
a	Ph	Me
b	Ph	Et
c	Ph	^{i}Pr
d	Ph	^{t}Bu
e	4-Me-C_6H_4	Me
f	4-Me-C_6H_4	Et

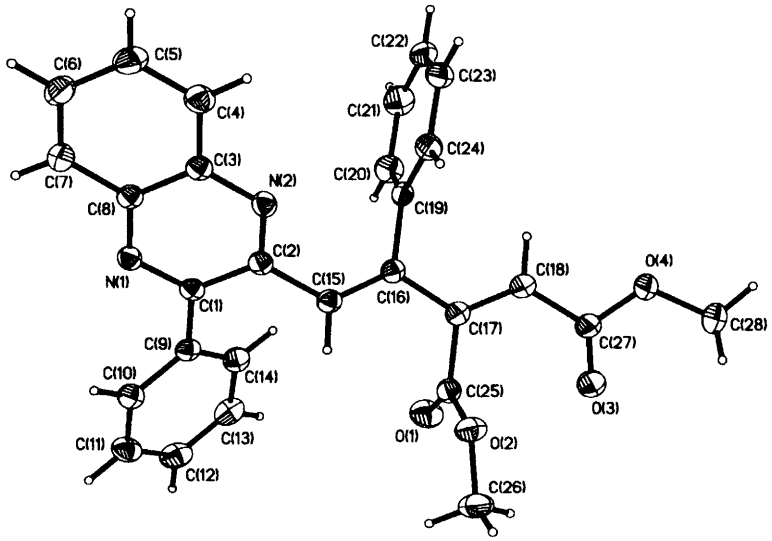
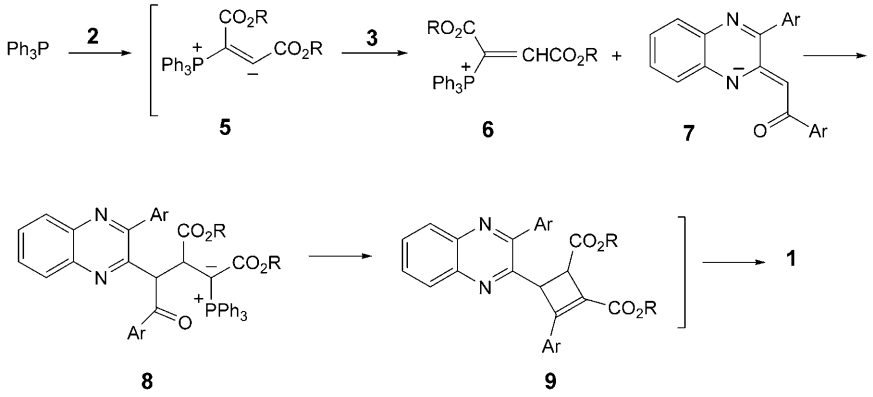


Figure. *X-Ray crystal structure of* **1a**. ORTEP-III Plot [8]; arbitrary atom numbering.

Scheme 2



6. The latter might be attacked by the C-atom of the bidentate anion **7** to afford the ylide **8**, which undergoes an intramolecular *Wittig* reaction to yield the cyclobutene derivative **9**. Compound **1** would then result from electrocyclic ring opening of **9**.

The advantage of the present procedure for the synthesis of the title compounds **1** is that the reaction can be performed under neutral conditions by simply mixing the starting materials.

Experimental Part

General. Benzene-1,2-diamine, Ph_3P, and the dialkyl acetylenedicarboxylates **4** were obtained from *Fluka* and used without further purification. M.p.: *Electrothermal-9100* apparatus; uncorrected. IR Spectra: *Shimadzu IR-460* spectrometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker DRX-500 AVANCE* instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp.; δ in ppm, J in Hz. EI-MS: *Finnigan-MAT-8430* mass spectrometer, at 70 eV; in m/z. Elemental analyses: *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Compounds **3**. To a stirred soln. of benzene-1,2-diamine (0.22 g, 2 mmol) in MeOH (10 ml) was added dropwise **2** (2 mmol) in MeOH, and the mixture was stirred for 4 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (CC) (SiO_2; hexane/AcOEt 5 :1) to afford the pure title compounds.

*1-Phenyl-2-(3-phenylquinoxalin-2(1*H*)-ylidene)ethanone* (**3a**). Yield: 0.62 g (95%). Pale-yellow powder. M.p. 75–77°. IR (KBr): 3050 (NH), 1578 (C=O), 1528, 1278, 750. ^1H-NMR: 6.50 (*s*, CH); 7.50–7.51 (*m*, 4 CH); 7.65–7.66 (*m*, 5 CH); 7.86–7.91 (*m*, 4 CH); 8.00 (*d*, ^3J=7.5, CH); 15.94 (*s*, NH). ^{13}C-NMR: 91.2 (CH); 119.7 (CH); 126.0 (CH); 126.6 (2 CH); 128.3 (2 CH); 128.8 (2 CH); 128.9 (2 CH); 129.3 (CH); 129.8 (CH); 130.8 (CH); 130.9 (CH); 132.2 (C); 137.3 (C); 137.4 (C); 138.2 (C); 147.7 (C); 156.8 (C); 181.2 (C=O). EI-MS: 324 (6, M^+), 247 (58), 219 (71), 218 (70), 105 (100), 77 (65), 76 (22). Anal. calc. for $C_{22}H_{16}N_2O$ (324.38): C 81.46, H 4.97, N 8.64; found: C 81.55, H 5.01, N 8.69.

*1-(4-Methylphenyl)-2-[3-(4-methylphenyl)quinoxalin-2(1*H*)-ylidene]ethanone* (**3b**). Yield: 0.48 g (70%). Pale-yellow powder. M.p. 80–82°. IR (KBr): 3050 (NH), 1578 (C=O), 1528, 1278, 750. ^1H-NMR: 2.38, 2.47 (2*s*, 2 Me); 6.41 (*s*, CH); 7.25 (*d*, ^3J=7.8, 2 CH); 7.36 (*d*, ^3J=7.8, 2 CH); 7.39 (*d*, ^3J=7.7, CH); 7.50 (*t*, ^3J=7.2, CH); 7.51 (*d*, ^3J=7.1, CH); 7.54 (*t*, ^3J=7.4, CH); 7.66 (*d*, ^3J=7.6, 2 CH); 7.71 (*d*, ^3J=7.6, 2 CH); 15.90 (*s*, NH). ^{13}C-NMR: 21.4, 22.7 (2 Me); 90.9, 119.2, 125.6 (3 CH); 126.7 (2 CH); 128.8 (2 CH); 129.2 (2 CH); 129.3 (CH); 129.4 (2 CH); 130.5 (CH); 131.8 (C); 133.3 (CH); 134.6, 135.7, 137.1, 139.9, 141.3, 147.4, 157.0 (7 C); 182.3 (C=O). EI-MS: 352 (8, M^+), 260 (5), 232 (68), 220 (30), 160 (10), (100), 105 (87), 77 (80), 65 (10). Anal. calc. for $C_{24}H_{20}N_2O$ (352.43): C 81.79, H 5.72, N 7.95; found: C 81.86, H 7.68, N 8.01.

General Procedure for the Preparation of Compounds **1**. To a stirred soln. of Ph_3P (0.57 g, 2.2 mmol) and **3** (0.65 g, 2 mmol) in toluene (10 ml), compound **4** (0.31 g, 2.2 mmol) in toluene (2 ml) was added dropwise, and the mixture was heated at reflux for 24 h. The solvent was removed under reduced pressure, and the residue was separated by CC (SiO_2; hexane/AcOEt 4 : 1) to afford the pure title compounds.

Dimethyl (2Z)-2-[(E)-1-Phenyl-2-(3-phenylquinoxalin-2-yl)ethenyl]but-2-enedioate (**1a**). Yield: 0.80 g (90%). Pale-brown powder. M.p. 126–128°. IR (KBr): 1726, 1724 (C=O); 1593; 1264; 1161; 757. ^{1}H-NMR: 3.68, 3.82 (2*s*, 2 MeO); 5.68 (*s*, CH); 6.97–6.98 (*t*, ^3J = 7.6, 2 CH); 7.01 (*s*, CH); 7.20–7.27 (*m*, 3 CH); 747–7.48 (*m*, 3 CH); 7.59–7.67 (*m*, 5 CH); 8.0 (*d*, ^3J = 8.2, CH). ^{13}C-NMR: 52.0, 52.6 (2 MeO); 121.4 (CH); 127.8 (C); 128.2 (2 CH); 128.4 (2 CH); 129.0 (CH); 129.1 (CH); 129.3 (CH); 129.6 (2 CH); 129.8 (CH); 129.9 (2 CH); 130.3 (CH); 132.3 (CH); 135.5, 137.8, 140.6, 140.7, 142.3, 148.6 (6 C); 151.0, 154.1 (2 C=N); 165.5, 168.0 (2 C=O). EI-MS: 450 (9, M^+), (3), 391 (8), 332 (34), 296 (86), 268 (28), 252 (83), 211 (84), 171 (100), 156 (42), 115 (18), 105 (14), 59 (85), 57 (87). Anal. calc. for $C_{28}H_{22}N_2O_4$ (450.49): C 74.65, H 4.92, N 6.22; found: C 74.72, H 4.98, N 6.29.

*Diethyl (2Z)-2-[(*E*)-1-Phenyl-2-(3-phenylquinoxalin-2-yl)ethenyl]but-2-enedioate* (**1b**). Yield: 0.70 g (75%). Pale-brown powder. M.p. 130–132°. IR (KBr): 1717, 1715 (C=O); 1591; 1261; 1168; 760. ^{1}H-NMR: 1.22 (*t*, ^3J = 7.2, Me); 1.26 (*t*, ^3J = 7.2, Me); 4.15 (*q*, ^3J = 7.2, CH_2O); 4.27 (*q*, ^3J = 7.2, CH_2O); 5.66 (*s*, CH); 6.99 (*d*, ^3J = 7.0, 2 CH); 7.12 (*s*, CH); 7.19–7.29 (*m*, 3 CH); 7.47–7.49 (*m*, 3 CH); 7.60–7.68 (*m*, 5 CH); 8.01 (*d*, ^3J = 8.2, CH). ^{13}C-NMR: 13.9, 14.1 (2 Me); 60.9, 61.8 (2 CH_2O); 121.9 (CH); 127.7 (C); 128.2 (2 CH); 128.5 (2 CH); 129.0, 129.1, 129.3 (3 CH); 129.6 (2 CH); 129.8 (CH); 129.9 (2 CH); 130.3, 132.0 (2 CH); 135.7, 137.9, 140.7, 142.7, 148.8 (5 C); 150.8, 154.1 (2 C=N); 165.0, 167.6 (2 C=O). EI-MS: 478 (6, M^+), 405 (30), 332 (19), 262 (16), 171 (64), 165 (31), 119 (100), 91 (22), 59 (30). Anal. calc. for $C_{30}H_{26}N_2O_4$ (478.54): C 75.30, H 5.48, N 5.85; found: C 75.41, H 5.51, N 5.92.

*Bis(1-Methylethyl) (2Z)-2-[(*E*)-1-Phenyl-2-(3-phenylquinoxalin-2-yl)ethenyl]but-2-enedioate* (**1c**). Yield: 0.68 g (70%). Pale-brown powder. M.p. 140–142°. IR (KBr): 1720, 1717 (C=O); 1593; 1268; 1097; 758. ^{1}H-NMR: 1.29 (*d*, ^3J = 7.0, 2 Me); 1.31 (*d*, ^3J = 6.8, 2 Me); 5.13 (*sept.*, ^3J = 6.8, CH); 5.28 (*sept.*, ^3J = 7.0, CH); 5.74 (*s*, CH); 7.10–7.11 (*d*, ^3J = 7.1, 2 CH); 7.24 (*s*, CH); 7.30–7.38 (*m*, 3 CH); 7.58–7.60 (*m*, 3 CH); 7.71–7.79 (*m*, 5 CH); 8.11 (*d*, ^3J = 8.2, CH). ^{13}C-NMR: 21.4, 21.7 (4 Me); 68.4, 69.6, 122.4 (3 CH); 127.6 (C); 128.1 (2 CH); 128.6 (2 CH); 128.9, 129.0, 129.3 (3 CH); 129.5 (2 CH); 129.7 (CH); 130.0 (2 CH); 130.2, 131.5 (2 CH); 135.9, 137.9, 140.6, 140.7, 143.0, 148.9 (6 C); 150.5, 154.1 (2 C=N); 164.4, 167.0 (2 C=O). EI-MS: 506 (7, M^+), 463 (15), 419 (48), 322 (80), 268 (28), 252 (83), 211 (84), 171 (100), 156 (34), 115 (18), 105 (44), 59 (44), 57 (57). Anal. calc. for $C_{32}H_{30}N_2O_4$ (506.59): C 75.87, H 5.97, N 5.53; found: C 75.92, H 5.93, N 5.60.

*Bis(1,1-Dimethylethyl) (2Z)-2-[(*E*)-1-Phenyl-2-(3-phenylquinoxalin-2-yl)ethenyl]but-2-enedioate* (**1d**). Yield: 0.72 g (72%). Pale-brown powder. M.p. 169–171°. IR (KBr): 1709, 1707 (C=O); 1594; 1273; 1135; 757. ^{1}H-NMR: 1.40, 1.42 (2*s*, 2 ^{t}Bu); 5.57 (*s*, CH); 7.0 (*d*, ^3J = 7.0, 2 CH); 7.12 (*s*, CH); 7.19–7.26 (*m*, 3 CH); 7.46–7.50 (*m*, 3 CH); 7.58–7.67 (*m*, 5 CH); 8.0 (*d*, ^3J = 8.2, CH). ^{13}C-NMR: 27.8, 28.1 (2 *Me*$_3$C); 81.0, 82.7 (2 Me$_3$*C*); 123.5 (CH); 127.5 (C); 128.1 (2 CH); 128.6 (2 CH); 129.0, 129.1, 129.2 (3 CH); 129.6 (2 CH); 129.7 (CH); 130.1 (2 CH); 130.2, 131.0 (2 CH); 136.3, 138.0, 140.6, 140.7, 143.4, 149.2 (6 C); 150.0, 154.2 (2 C=N); 164.4, 166.6 (2 C=O). EI-MS: 534 (5, M^+), 477 (10), 433 (27), 332 (39), 331 (30), 255 (5), 178 (3), 152 (3), 58 (100), 41 (28). Anal. calc. for $C_{34}H_{34}N_2O_4$ (534.65): C 76.38, H 6.41, N 5.24; found: C 76.45, H 6.32, N 6.48.

*Dimethyl (2Z)-2-[(*E*)-1-(4-Methylphenyl)-2-[3-(4-methylphenyl)quinoxalin-2-yl]ethenyl}but-2-enedioate* (**1e**). Yield: 0.56 (60%). Colorless powder. M.p. 126–128°. IR: 1722, 1720 (C=O); 1601; 1265; 1164; 755. ^{1}H-NMR: 2.42, 2.54 (2*s*, 2 Me); 3.80, 3.94 (2*s*, 2 MeO); 5.80 (*s*, CH); 6.93 (*d*, ^3J = 7.7, 2 CH); 7.10 (*d*, ^3J = 7.7, 2 CH); 7.19 (*s*, CH); 7.37 (*d*, ^3J = 7.8, 2 CH); 7.60 (*d*, ^3J = 7.8, 2 CH); 7.72 (*t*, ^3J = 7.1, CH); 7.77 (*t*, ^3J = 7.8, CH); 7.80 (*d*, ^3J = 8.0, CH); 8.10 (*d*, ^3J = 8.2, CH). ^{13}C-NMR: 21.2, 21.4 (2 Me); 51.9, 52.6 (2 MeO); 121.2 (CH); 128.8 (2 CH); 128.9, 129.0 (2 CH); 129.1 (2 CH); 129.4 (C); 129.5 (2 CH); 129.8 (2 CH); 130.1 (CH); 132.3, 132.4, 134.9, 137.5, 139.3, 140.5 (6 C); 140.7, 142.2, 149.0 (3 C); 151.2, 154.0 (2 C=N); 165.5, 168.2 (2 C=O). EI-MS: 478 (5, M^+), 420 (30), 419 (100), 359 (16), 243 (4), 165 (3), 119 (24), 91 (22), 59 (30). Anal. calc. for $C_{30}H_{26}N_2O_4$ (478.54): C 75.30, H 5.48, N 5.85; found: C 75.41, H 5.53, N 5.88.

*Diethyl (2Z)-2-[(*E*)-1-(4-Methylphenyl)-2-[3-(4-methylphenyl)quinoxalin-2-yl]ethenyl}but-2-enedioate* (**1f**). Yield: 0.64 g (65%). Colorless powder. M.p. 119–121°. IR (KBr): 1714, 1712 (C=O); 1600;

1262; 1177; 755. ^{1}H-NMR: 1.22 (*t*, ^3J=7.2, Me); 1.28 (*t*, ^3J=7.2, Me); 2.30, 2.43 (2*s*, 2 Me); 4.14 (*q*, ^3J=7.2, CH_2O); 4.30 (*q*, ^3J=7.2, CH_2O); 5.68 (*s*, CH); 6.85 (*d*, ^3J=7.7, 2 CH); 6.99 (*d*, ^3J=7.7, 2 CH); 7.11 (*s*, CH); 7.27 (*d*, ^3J=7.8, 2 CH); 7.50 (*d*, ^3J=7.8, 2 CH); 7.60 (*t*, ^3J=7.2, CH); 7.65 (*t*, ^3J=7.9, CH); 7.69 (*d*, ^3J=8.1, CH); 8.0 (*d*, ^3J=8.1, CH). ^{13}C-NMR: 13.8, 14.1, 21.2, 21.4 (4 Me); 60.9, 61.8 (2 CH_2O); 121.7 (CH); 128.8 (2 CH); 129.0, 129.1 (2 CH); 129.2 (2 CH); 129.4 (CH); 129.5 (2 CH); 129.9 (2 CH); 130.1, 132.1, 132.5 (3 CH); 135.1, 137.4, 139.3, 140.7, 140.9, 142.5, 149.2 (7 C); 151.1, 154.1 (2 C=N); 165.6, 167.9 (2 C=O). EI-MS: 506 (4, M^+), 433 (21), 360 (19), 296 (46), 268 (31), 252 (53), 211 (74), 171 (100), 156 (42), 115 (18), 105 (14), 59 (54), 57 (65). Anal. calc. for $C_{32}H_{30}N_2O_4$ (506.59): C 75.87, H 5.97, N 5.53; found: C 75.62, H 5.88, N 5.59.

X-Ray Crystal-Structure Determination of **1a**[1]). Structure-determination and refinement data: formula, $C_{28}H_{22}N_2O_4$, M_r 450.48; crystal size, $0.45\times0.30\times0.20$ mm^3; crystal system, monoclinic, a=11.741(3), b=7.224(2), c=26.500(8) Å, β=94.28(3); space group $P2_1/c$; Z=4, V=2241.4(11) Å^3, $D_{calc.}$=1.335 g cm^{-3}; R=0.0433 (for 3800 reflections), R_w=0.0850; $-2\le h\le14$; $-9\le k\le9$; $-33\le l\le33$; MoK_α radiation (λ=0.71073 Å); T=293(2) K.

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[1]) The crystallographic data of **1a** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication number CCDC-299057. Copies of the data can be obtained, free of charge, at http://www.ccdc.cam.ac.uk/data_request/cif.