Asian Journal of Chemistry Vol. 15, Nos. 3 & 4 (2003), 1373–1379

Reactions of Cyclic Oxalyl Compounds, Reaction of Some Furan-2,3-diones with Various Hydrazine Derivatives

İLHAN ÖZER İLHAN, YUNUS AKÇAMUR, EMİN SARIPINAR* and ERTUĞRUL ASLAN

Department of Chemistry, University of Erciyes, Kayseri-38039, Turkey
E-mail: emin@erciyes.edu.tr Fax: 00 90 352 4374933

Furan-2,3-diones (**1a–c**) react with various hydrazines (**2a–d**) in boiling benzene to yield the pyrazole-3-carboxylic acids (**3a–c**) and the 1,2-dihydropyridazine-3,4-diones (**6a–d**). The structures of all products were confirmed by elemental analysis, IR, ^{1}H- and ^{13}C-NMR spectroscopic measurements. Thermal decomposition of 4-benzoyl-1-(2,4-dinitrophenyl)-5-phenyl-1H-pyrazole-3-carboxyl ic acid (**3b**) leads to the formation of [1-(2,4-dinitrophenyl)-5-phenyl-1H-pyrazol-4-yl]phenylmethanone (**5**). The pyrazole-3-carboxylic acid chloride (**4**) was obtained from the reaction of **3a** and thionyl chloride.

Key Words: Furan-2,3-diones; Pyrazole-3-carboxylic acids; 1,2-Dihydropyridazine-3,4-diones; Michael-type addition; Cyclocondensation.

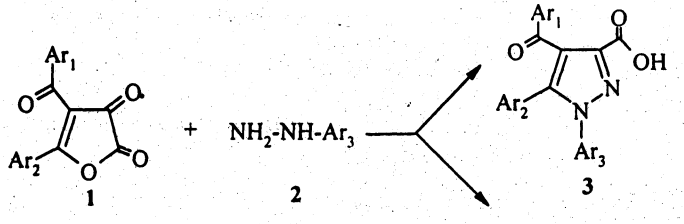
INTRODUCTION

Recently, reactions of cyclic oxalyl compounds have been reported to give substituted heterocyclic compounds[1]. The reactions of 4-benzoyl-5-phenylfuran-2,3-dione with several semicarbazones, ureas and their thio-analogues and oximes have been reported in different solvents and at various temperatures[2]. The general reactivity of 4-benzoyl-5-phenylfuran-2,3-dione and the mechanism of the reactions with NH-nucleophiles have recently been reviewed with semi-empirical (AM1 and PM3) calculations[3]. The reactions are generally initiated by the nucleophilic attack of the nitrogen atom of semicarbazone or urea, directed on to the oxygen atom of the furan cycle. The reaction of the furan-2,3-dione **1a**, obtained easily from dibenzoylmethane and oxalyl dichloride[1a], with various phenyl hydrazones and phenylhydrazines leads to pyrazole carboxylic acids and pyridazinones[4]. In general, the pyrazole nucleus and its chemistry[5] have found considerable attention during the decades due to outstanding biological activities such as antipyretic, analgetic, antifungal and anti-inflammatory activities[6], as well as to interesting properties in commercially important dyestuffs[7].

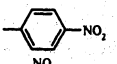
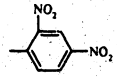
In the present study, we carried out reactions between various hydrazine and furan-2,3-dione derivatives and prepared a new series of substituted pyrazole carboxylic acids and the 1,2-dihydropyridazine-3,4-diones.

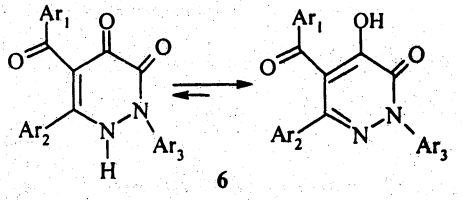
The reactions of the furan-2,3-diones **1a, c** with hydrazine derivatives **(2a–c)** (**Scheme-1**) yields 1H-pyrazole-3-carboxylic acid derivatives **(3a–c)** in boiling benzene. The structures of synthesized compounds were assigned on the basis of analytical as well as spectroscopic data. Product **3a** obtained in 50% yield by treating **1a** with *p*-nitrophenylhydrazine **(2a)** and refluxing in boiling benzene for 4 h. In the IR spectra of compound **3a**, the —OH absorption bands of —COOH groups were found to be at *ca.* 3050–2400 cm^{-1}. The C=O absorption was at 1760 cm^{-1}. The ^{13}C NMR signals were found to be at 193.16 (t, J = 4.5 Hz, PhCO) and 160.86 (s, COOH), and the ^{1}H NMR signals were at δ = 11.30 (broad, OH), and δ = 8.45–7.35 (m, Ar—H) and elemental analysis data confirm the structure of **3a**.

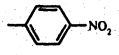
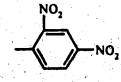
Scheme-1

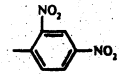
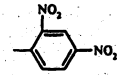
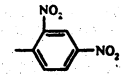


1	Ar_1	Ar_2
a	Ph-	Ph-
b	*p*-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-
c	CH_3CH_2O-	Ph-

2	Ar_3
a	
b	
c	-H
d	-Ph



3	Ar_1	Ar_2	Ar_3
a	Ph-	Ph-	
b	Ph-	Ph-	
c	CH_3CH_2O-	Ph-	H

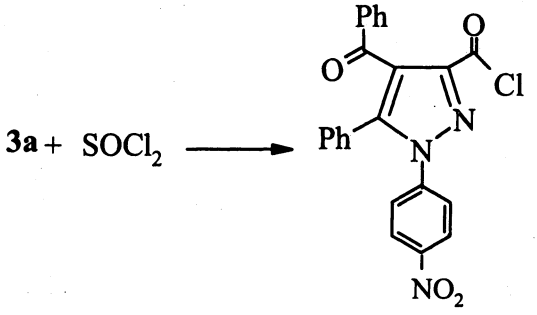
6	Ar_1	Ar_2	Ar_3
a	*p*-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-	Ph-
b	*p*-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-	
c	Ph-	Ph-	
d	CH_3CH_2O-	Ph-	

Akçamur *et al.*[4b] reported that the N-unsubstituted pyrazolo-pyridazine derivative was formed from 4-benzoyl-5-phenylfuran-2,3-dione **(1a)** and hydrazine hydrate **(2c)** during a one-pot reaction probably occurring *via* a pyrazole carboxylic acid intermediate. In this study, when the reaction of the ethyl-4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate[1c] **(1c)** with **2c** (**Scheme-1**) was

carried out, instead of pyrazolo-pyridazine derivative 4-(ethoxycarboyl)-5-phenyl-1H-pyrazole-3-carboxylic acid **(3c)** was obtained. The characteristic strong IR absorption band at 3300–2550 cm^{-1}, the ^{13}C NMR signals at 165.58 (s, COOH), 162.06 (ester CO), 62.44 (CH_2), and 15.47 (CH_3) and the ^1H NMR signals at δ = 10.39 ppm showed the presence of —COOH and the corresponding signals in CH_3 and CH_2 protons were determined at 1.19 and 4.21 ppm, respectively.

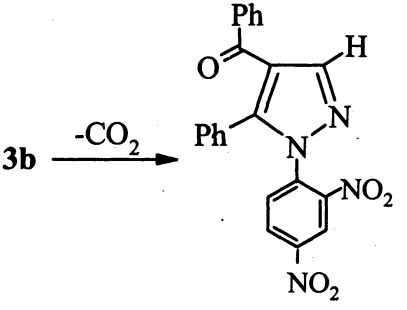
4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid chloride **(4)**, obtained from the reaction of **3a** with $SOCl_2$ in 30% yield is remarkably stable (m.p. 167°C). The C=O absorption at 1775 and 1680 cm^{-1}, and the ^{13}C NMR signals at 192.54 (t, J = 4.6 Hz, PhCO) and 159.50 (s, COCl) were found.

Scheme-2



4

Scheme-3



5

[1-(2,4-Dinitrophenyl)-5-phenyl-1H-pyrazol-4-yl]phenylmethanone **(5)** was found to form after **3b** was heated at 225°C and decarboxylated. The peak at 7.95 in the ^1H NMR spectrum was thought to belong to C3-H. The ^{13}C NMR signals were found to be at 191.30 (t, J = 4.9 Hz, PhCO); 157.75 (t, J = 3.4 Hz, C5) and 149.38 (C3).

As well as pyridazine-3-one derivatives **(6a–d)** were formed during the reaction of the furan-2,3-diones **(1a–c)** with hydrazine derivatives **(2a–d)**. 5-(4-Methoxy-

benzoyl)-6-(4-methoxyphenyl-2-phenyl-1,2-dihydropyridazine-3,4-dione[1d] (**6a**), was synthesized during the reaction of **1b** with phenylhydrazine (**2d**). The IR and NMR data of compound **6a** indicate the existence of tautomerism in this compound. In the IR spectra of compound **6a**, broad O—H or N—H were observed at 3400–2850 cm^{-1} and the C=O absorption bands are found to be at about 1720 and 1650 cm^{-1}. The ^1H NMR peak of **6a** observed at 9.22 ppm belongs to the —OH in the enol form. The peaks at 10.42 ppm are thought to represent the —NH in the other tautomer form. The enol structure of **6a** should be stabilized by intramolecular hydrogen bonding. The ^{13}C NMR signals were found to be at 191.16 (t, J = 3.5 Hz, ArCO), 161.34 (s, C-3), 147.40 (s ,C-4), 144.23 (t, J = 3.1 Hz, C-6) and 114.63 (s, C-5) and elemental analysis data confirm the structure of **6a**.

EXPERIMENTAL

Solvents were dried by refluxing the appropriate drying agent and distilled before use. Melting points were determined on the electrothermal 9200 apparatus and are uncorrected. Microanalyses were performed on a Carlo-Erba elemental analyser, model 1108; the results agree favourably with the calculated values. IR spectra were recorded on a Shimadzu model 435 V-04 spectrometer, using potassium bromide discs. ^1H and ^{13}C NMR spectra were recorded on a Gemini-Varian 200 instrument. The chemical shifts are reported in ppm from tetramethylsilane and given in δ units.

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid (3a)

4-Benzoyl-5-phenylfuran-2,3-dione (**1a**) (0.5 g, 1.798 mmol) and *p*-nitrophenylhydrazine (**2a**) (0.277 g, 1.798 mmol) were refluxed in benzene for 4 h. The solvent was evaporated and the remaining oily residue was treated with ether to give a yellow crude product which was recrystallized from acetic acid; yield 0.37 g (50%); m.p. 249°C; IR (KBr): ν = 3050–2400 ν(OH), 1760 cm^{-1} ν(C=O); ^1H NMR (DMSO, δ): 11.30 (broad, COOH), 8.45–7.35 (m, 14H, Ar—H); ^{13}C NMR (DMSO, δ): 193.16 (t, J = 4.5 Hz, PhCO), 160.86 (s, COOH), 151.35 (t, J = 3.7 Hz, C5), 146.15 (s, C3), 136.60–128.81 (m, Arom. C), 125.92 (s, C4). Elemental analysis: found (calcd.): [C = 67.05 (66.83), H = 3.70 (3.63), N = 9.91 (10.16)].

4-Benzoyl-1-(2,4-dinitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic-acid(3b)

4-Benzoyl-5-phenylfuran-2,3-dione (**1a**) (0.5 g, 1.798 mmol) and 2,4-dinitrophenylhydrazine (**2b**) (0.356 g, 1.798 mmol) were refluxed in benzene for 2 h. The solvent was evaporated and the remaining oily residue was treated with cyclohexane. The resulting yellow crude product was filtered and recrystallized from toluene and allowed to dry on P_2O_5; yield 0.41 g (50%;, m.p. 223–224°C; IR (KBr): ν = 3100–2400 ν(COOH), 1720, 1660 cm^{-1} ν(C=O); ^1H NMR (DMSO, δ): 9.05-7.17 (m, 14H, Ar—H); ^{13}C NMR ($CDCl_3$, δ): 196.13 (PhCO), 158.91 (COOH), 156.41 (C5), 147.12 (C3), 140.49–122.06 (Arom. C), 122.96 (C4). Elemental analysis: found (calcd.): [C = 60.23 (60.26), H = 3.09 (3.07), N = 12.19 (12.22)].

4-(Ethoxycarboyl)-5-phenyl-1H-pyrazole-3-carboxylic acid (3c)

Ethyl-4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate **(1c)** (0.5 g, 2.03 mmol) and hydrazine hydrate **(2c)** (0.125 mL, 2.03 mmol) were refluxed in benzene for 1 h or stirred in benzene at room temperature for 24 h. The solvent was evaporated and the remaining oily residue was treated with *n*-hexane and ether and stirred for 24 h in order to give a white product which was recrystallized from *n*-butanol and allowed to dry on P_2O_5; yield 0.38 g (71%;, m.p. 284°C; IR (KBr): ν = 3450–3300 ν(NH), 3300–2550 ν(COOH); 1680 cm^{-1} ν(C=O); ^1H NMR (DMSO, δ): 10.39 (—OH) (—NH not observed), 7.61–7.51 (m, 6H, Ar—H), 4.21 (q, O—CH_2), 1.19 (t, CH_3); ^{13}C NMR (DMSO, δ): 165.58 (COOH), 162.06 (O—C=O), 147.29 (C5), 131.55 (C3), 131.20–112.79 (Arom. C), 109.210 (C4), 62.44 (CH_2), 15.47 (CH_3). Elemental analysis: found (calcd.): [C = 59.78 (59.96), H = 4.53 (4.64), N = 10.75 (10.81)].

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid chloride (4)

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid **(3a)** (0.1 g, 2.42 mmol) and thionyl chloride (0.17 ml, 2.42 mmol) were refluxed on a steam bath for 4.5 h. After cooling, the crude precipitate was filtered off and recrystallized from carbon tetrachloride and allowed to dry on P_2O_5; yield 0.031 g (30%); m.p.: 167°C; IR (KBr): ν = 1775, 1680 cm^{-1} ν(C=O); ^1H NMR ($CDCl_3$, δ): 8.54–7.27 (m, 14H, Ar—H); ^{13}C NMR ($CDCl_3$, δ): 192.54 (t, J = 4.6 Hz, PhCO), 159.50 (s, COC1), 153.60 (s, C3), 150.02 (t, J = 3.6 Hz, C5), 138.0—126.63 (m, Arom. C), 122.18 (s, C4). Elemental analysis: found (calcd.): [C = 63.68 (63.96), H = 3.29 (3.24), N = 10.05 (9.72)].

[1-(2,4-Dinitrophenyl)-5-phenyl-1H-pyrazol-4-yl]phenylmethanone (5)

4-Benzoyl-1-(2,4-dinitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid **(3b)** (0.5 g, 1.09 mmol) on an oil-bath was heated up to 224°C until the yellow product turned to brown. The crude product was recrystallized from methanol and left to dry on P_2O_5; yield 0.21 g (46%); m.p. 208°C; IR (KBr): ν = 1660 cm^{-1} ν(C=O); ^1H NMR ($CDCl_3$, δ): 7.95 (s, C3-H), 8.6—7.10 (m, 13H, Ar—H); ^{13}C NMR ($CDCl_3$, δ): 191.30 (t, J = 4.9 Hz, PhCO), 157.75 (t, J = 3.4 Hz, C5), 149.38 (C3), 145.18–125.07 (m, Arom. C), 123.23 (s, C4). Elemental analysis: found (calcd.): [C = 63.77 (63.77), H = 3.34 (3.38), N = 13.23 (13.53)].

5-(4-Methoxybenzoyl)-6-(4-methoxyphenyl)-2-phenyl-1,2-dihydropyridazine-3,4-dione (6a)

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)furan-2,3-dione **(1b)** (0.2 g, 0.59 mmol) was dissolved in 35 mL benzene. (0.058 mL, 0.59 mmol) phenylhydrazine **(2d)** was added dropwise into it in ice-salt bath. It is advised that having finished dropping phenylhydrazine the mixture should be stirred for 1–2 h. The solvent was evaporated and the remaining oily residue was treated with ether. The oily residue was dissolved in dry ether. Cyclohexane was then added into the dissolved dry ether. The yellow precipitate was washed thoroughly in petroleum ether; yield 0.1 g (40%); m.p. 142°C; IR (KBr): ν = 3400–2850 (broad) ν(O—H or N—H),

1720 and 1650 cm^{-1} ν(C=O); ^1H NMR (DMSO δ): 10.42 and 9.22 (broad, —NH and —OH, tautomers, respectively), 7.78–6.74 (m, 12H, Ar—H), 3.87 and 3.63 (6H, $2CH_3O$); ^{13}C NMR (DMSO, δ): 191.16 (t, J = 3.5 Hz, ArCO), 161.34 (s, C3), 147.40 (s, C4), 144.23 (t, J = 3.1 Hz, C6), 133.61–115.03 (m, Aromatic C), 114.63 (s, C5), 57.34 and 56.79 (q, CH_3O). Elemental analysis: found (calcd.): [C = 70.21 (70.09), H = 4.72 (4.67), N = 6.74 (6.54)].

2-(2,4-Dinitrophenyl)-5-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-1,2-dihydropyridazine-3,4-dione (6b)

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)furan-2,3-dione **(1b)** (0.2 g, 0.59 mmol) and 2.4-dinitrophenylhydrazine **(2b)** (0.116 g, 0.59 mmol) were refluxed in benzene for 10 h. The solvent was evaporated and the precipitated oily residue was washed with ethyl alcohol and the remaining yellow crude product was recrystallized from benzene, yield 0.17 g (55%); m.p. 191°C; IR (KBr): ν = 3500 and 3350 ν(broad O—H, N—H), 1695, 1650 cm^{-1} ν(C=O); ^1H NMR (DMSO, δ): 11.70 and 10.18 (broad, —NH and —OH, tautomers, respectively), 9.03–6.45 (m, 11H, Ar—H), 3.87 and 3.68 (6H, $2CH_3O$); ^{13}C NMR (DMSO, δ): 191.69 (ArCO), 161.76 (C3), 146.90 (C4), 145.24 (C6), 136.36–115.62 (Aromatic C), 108.52 (C5), 57.53 and 57.01 (CH_3O). Elemental analysis: found (calcd.): [C = 58.14 (57.91), H = 3.47 (3.47), N = 11.12 (10.81)].

5-Benzoyl-2-(2,4-dinitrophenyl)-6-phenyl-1,2-dihydropyridazine-3,4-dione (6c)

4-Benzoyl-5-phenylfuran-2,3-dione **(1a)** (0.5 g, 1.798 mmol) and 2,4-dinitrophenylhydrazine **(2b)** (0.356 g, 1.798 mmol) were refluxed in benzene for 30 min. The precipate was filtered and recrystallized from xylene and allowed to dry on P_2O_5; yield 0.31 g (38%;, m.p.: 180–181°C; IR (KBr): ν = 3500 and 3360 ν(O—H and N—H), 1780, 1720 and 1660 cm^{-1} ν(C=O); ^1H NMR ($CDCl_3$, δ): 9.75 and 8.80 (broad, —NH and —OH tautomers, respectively), 9.15–7.10 (13H, Ar—H). Elemental analysis: found (calcd.): [C = 60.55 (60.26), H = 3.08 (3.07), N = 12.14 (12.22)].

Ethyl-1-(2,4-dinitrophenyl)-5,6-dioxo-3-phenyl-1,2-dihydropyridazine-4-carboxylate (6d)

Ethyl-4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate **(1c)** (0.5 g, 2.03 mmol) and 2,4-dinitrophenyl hydrazine **(2b)** (0.4 g, 2.03 mmol) were stirred in benzene at room temperature for 12 h. The solvent was evaporated. The remaining oily residue was then treated with *n*-hexane and ether and stirred for 24 h to give a yellow product which was recrystallized from toluene and allowed to dry on P_2O_5; yield 0.64 g (74%); m.p.: 124–126°C; IR (KBr): ν = 3450 and 3300 ν(O—H, N—H), 1740, 1651 cm^{-1} ν(C=O); ^1H NMR (DMSO, δ): 10.29 and 9.4, (broad, —NH and —OH tautomers, respectively), 8.78–7.10 (8H, Ar—H), 4.11 (O—CH_2), 1.10 (CH_3); ^{13}C NMR (DMSO, δ): 177.80 (C4), 175.67 (C3), 165.23 and 115.94 (Aromatic C); 159.36 (C6), 108.21 (C5). Elemental analysis: found (calcd.): [C = 53.33 (53.50), H = 3.53 (3.31), N = 13.11 (13.19)].

ACKNOWLEDGEMENT

The authors are grateful for the financial support by Research Foundation of Erciyes University (Kayseri, Turkey).

REFERENCES

1. (a) E. Ziegler, M. Eder, C. Belegratis and E. Prewedourakis, *Monatsh Chem.*, **98**, 2249 (1967); (b) G. Kollenz, C.O. Kappe and H.A. El-Nabey, *Heterocycles*, **32**, 669 (1991); (c) R.W. Saalfrank, T. Lutz, B. Hörner, J. Gündel, K. Peters and H. G. Von Schnering, *Chem. Ber.*, **124**, 2289 (1991); (d) E. Saripinar, Y. Güzel, Z. Önal, İ.Ö. İlhan and Y. Akaçmur, *J. Chem. Soc. Pak.*, **22**, 308 (2000).
2. (a) G. Kollenz, E. Ziegler, W. Ott and H. Igel, *Z. Naturforsch*, **31B**, 1511 (1976); (b) W. Ott, E. Ziegler and G. Kollenz, *Synthesis*, **7**, 477; (c) Y. Akçamur, B. Altural, E. Saripinar, G. Kollenz, C.O. Kappe, E. M. Peters and H.G. Von Schnering, *J. Heterocyclic Chem.*, **25**, 1419 (1988); (d) B. Altural, Y. Akçamur, E. Saripinar, İ. Yildirim and G. Kollenz, *Monatsh Chem.*, **120**, 1015 (1989); (e) Y. Akçamur and G. Kollenz, *Oppi Briefs*, **9** (1987).
3. (a) İ. Yildirim, E. Saripinar, Y. Güzel, Ş. Patat and Y. Akçamur, *J. Mol. Struct. (Theochem)*, **334**, 165 (1995); (b) E. Saripinar, İ. Yildirim, Y. Güzel and Y. Akçamur, *Monatsh. Chem.*, **127**, 505 (1996); (c) İ. Yildirim, M. Tezcan, Y. Güzel, E. Saripinar and Y. Akamur, *Tr. J. Chem.*, **20**, 27 (1996).
4. (a) Y. Akçamur, G. Penn, E. Ziegler, H. Sterk, G. Kollenz, K. Peters, E.M. Peters and H.G. von Schnering, *Monatsh Chem.*, **117**, 231 (1986); (b) Y. Akçamur, A. Şener, A.M. İpekoğlu and G. Kollenz, *J. Heterocyclic Chem.*, **34**, 221 (1997).
5. (a) A.N. Kost and I.I. Grandberg, *Adv. Heterocyclic Chem.*, **6**, 347 (1966); (b) M.P. Sammes and A.R. Katritzky, *Adv. Heterocyclic Chem.*, **34**, 1, 38 (1983); (c) J. Elguero, in: A.R. Katritzkyand C.W. Rees (Eds.), Comprehensive Heterocyclic Chem., Vol 4, Pergamon Press, Oxford Ch. 4, p. 4 (1984); (d) R.S. Theobald, in: S. Coffey and M.F. Ansell (Eds.), Rodd's Chemistry of Carbon Compounds, 2nd Edn., Vol IV (c), Elsevier Science Publishers, Amsterdam p. 1 (1986); (e) M. H. Elnagdi, G.E.H. Elgemeie and F.A.E. Abd-Elaal, *Heterocycles*, **23**, 3121 (1985); (f) S.T. Mullins, in: S. Coffey and M.F. Ansell (Eds.), Rodd's Chemistry of Carbon Compounds, Suppl. of Vol IV (c/d) , Elsevier Science Publishers, Amsterdam, p. 1 (1994).
6. (a) L. Knorr, *Ber.*, **17**, 549 (1884); (b) A.E. Heming and W.C. Kuzell, *Antibiot. Chemother.*, **3**, 634 (1953); (c) E. Hermann and J. Gabliks, *Cancer Chemother. Rept.*, **14**, 85 (1961); (d) H.J. Ha, S.J. Oh, S.K. Lee and C.E. Song, *Korean J. Med. Chem.*, **6** (1996); (e) B. Maggio, G. Daidone, D. Raffa, S. Plescia, L. Mantione, V.M.C. Cutuli, N.G. Mangano and A. Eur Caruso, *J. Med. Chem.*, **36**, 737 (2001).
7. (a) G.A. Hanson, *Bull. Soc. Chim. Belgium*, **67**, 707 (1958); (b) O. Neunhoeffer, G. Alsdorf and H. Ulrich, *Chem. Ber.*, **92**, 252 (1959); (c) E.E. Baroni and K.A. Kovyrzina, *Zh. Obshch. Khim.*, **31**, 1641 (1961).

(*Received*: 5 December 2002; *Accepted*: 2 April 2003) AJC-3034