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Synthesis and Characterization of Some New Heterocyclic Compounds Derived from 1,3-bis(4-nitrophenyl) prop-2-en-1-one.

Farah H. Hussein, Abbas F. Abbas, and Mouayed A. Hussein*.

Collage of Science, University of Basrah, Basrah Iraq.

ABSTRACT

An efficient and practical synthesis of four compounds of isoxazole,pyrazoline , pyrimidine-2-ol and pyrimidine-2-thiol derivatives structures was achieved through cyclization of hydroxylamine,hydrazine hydrate, urea and thiourea with α,β--unsaturated ketones (chalcones) using sodium hydroxide or glacial acetic acid as catalyst under thermal conditions. These compounds have been characterized by FT-IR, GC-Mass and ^{1}H NMR spectroscopy.

Keywords: Chalcone , heterocyclic, nitro compounds

Corresponding author

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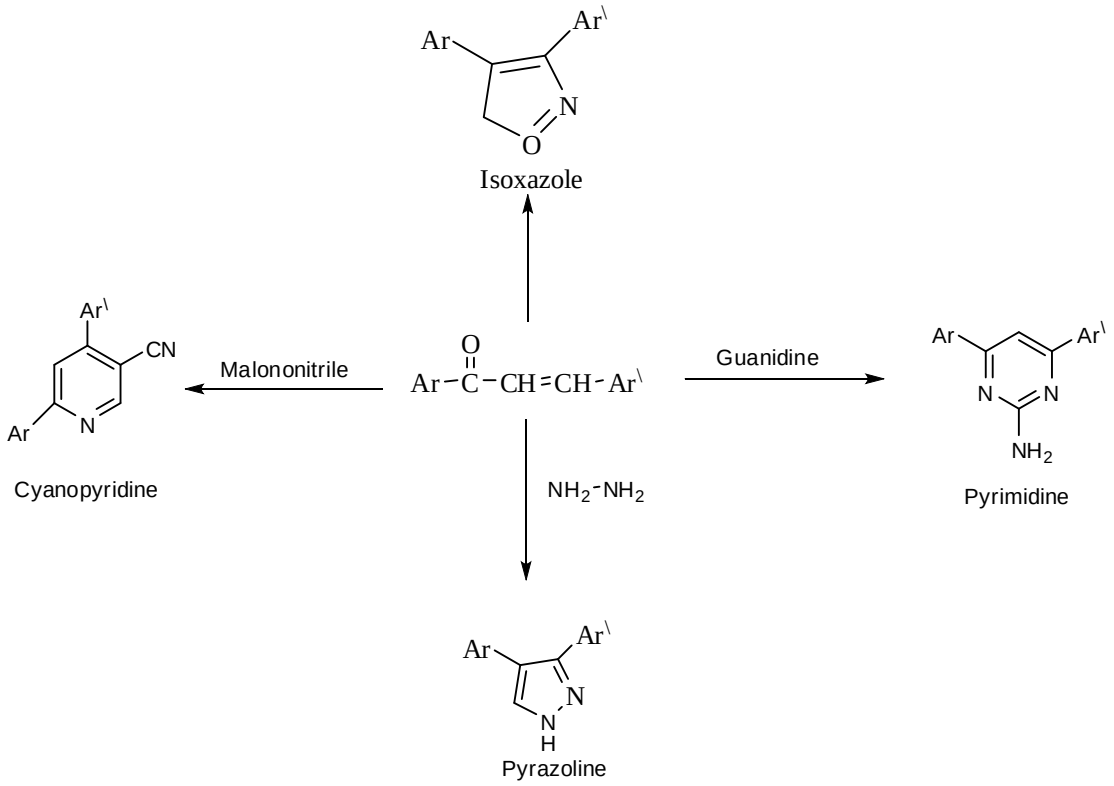
INTRODUCTION

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones. The name “Chalcones” was given by Kostanecki and Tambor [1]. These compounds are also known as benzalacetophenone or benzylidene acetophenone. In chalcones, two aromatic rings are linked by an aliphatic three carbon chain. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed.

Chalcones are -unsaturated ketone containing the reactive ketoethylenic group –CO-CH=CH-. These are coloured compounds because of the presence of the chromophore -CO-CH=CH-, which depends in the presence of other auxochromes. Different methods are available for the preparation of chalcones[2-4] .The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with aryl aldehyde in the presence of alcoholic alkali[5]. Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines isoxazoles and pyrimidines having different heterocyclic ring systems.[6-9]



EXPERIMENTAL

General. Melting points were uncorrected. FT.IR-8400,SHIMADZU. NMR spectra were acquired with a Bruker Ultra Shield (^{1}H : 300 MHz) (University of AL-al-Bayt,Jordan). The chemical shifts were referenced to tetra methyl silane (TMS) as an internal standard. GC mass spectra were acquired with Shimadzu Qp5050A. (University of AL-al-Bayt,Jordan).

Synthesis of 3,5-bis(4-nitrophenyl)-4,5-dihydroisoxazole (2a)

To a stirred solution of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) (which was prepared as mentioned in the literature) [10] (1.0 mmol) in 10 ml EtOH (96 %) was added hydroxylamine hydrochloride (2.0 mmol) and 10% NaOH (2.5 ml) at room temperature. The reaction mixture was heated to reflux overnight. The progress of the reaction was monitored by TLC (benzene/methanol, 9:1). The EtOH was removed under reduced pressure and the residue was recrystalized from EtOH to afford the pure products and gave a 73% yield with a m.p. (310 d)^{o}c. The GC-Mass analysis for $C_{15}H_{11}N_3O_5$ (m/z = 313) ; FT-IR spectra (KBr pellet) υ(cm^{-1}) 1153 (N-O stretching of isoxazole ring), 3002 (C–H stretching of aromatic ring), 1267 (C–N stretching of isoxazole ring), 1068 (C-O

stretching of isoxazole ring), 2880 (C-H stretching of aliphatic ring), $\delta_H(CDCl_3)$ (3.350-3.360) ppm (2H,d,6,6\); (4.545-4.677) ppm (1H,t,7); (7.765-7.788) ppm (2H,d,3) ; (8.011-8.175) ppm (6H,m,1,2,4).

Synthesis of 3,5-bis(4-nitrophenyl)-4,5-dihydro-1H-pyrazole (2b)

To a stirred solution of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) (which was prepared as mentioned in the literature) [10] (1.0 mmol) in 10 ml EtOH (96 %) was added hydrazine hydrate (2.0 mmol) and glacialaceticacid (2.5 ml) at room temperature. The reaction mixture was heated to reflux overnight. The progress of the reaction was monitored by TLC (benzene/methanol, 9:1). The EtOH was removed under reduced pressure and the residue was recrystalized from EtOH to afford the pure products and gave a 78% yield with a m.p. (190 d)°c. The GC-Mass analysis for $C_{15}H_{12}N_4O_4$ (m/z = 312) ; FT-IR spectra (KBr pellet) $\upsilon(cm^{-1})$ 3242 (N-H stretching of pyrazoline ring), 3051 (C–H stretching of aromatic ring), 1259 (C–N stretching of pyrazoline ring), $\delta_H(CDCl_3)$ (3.350-3.360) ppm (2H,d,6,6\); (3.845-3.945) ppm (1H,t,7); 6.670 ppm (1H,s,5); (7.765-7.788) ppm (2H,d,3) ; (8.011-8.175) ppm (6H,m,1,2,4).

Synthesis of 4,6-bis(4-nitrophenyl)pyrimidin-2-ol (2c)

To a stirred solution of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) (which was prepared as mentioned in the literature) [10] (1.0 mmol) in 10 ml EtOH (96 %) was added urea (2.0 mmol) and 10% NaOH (2.5 ml) at room temperature. The reaction mixture was heated to reflux overnight. The progress of the reaction was monitored by TLC (benzene/methanol, 9:1). The EtOH was removed under reduced pressure and the residue was recrystalized from EtOH to afford the pure products and gave a 70% yield with a m.p. (330 d)°c. The GC-Mass analysis for $C_{16}H_{10}N_4O_5$ (m/z = 338) ; FT-IR spectra (KBr pellet) $\upsilon(cm^{-1})$ 1076 (C-O stretching), 3095 (C–H stretching of aromatic ring), 3360 (O–H stretching), $\delta_H(CDCl_3)$ 7.959 ppm (1H,s,3); (8.140-8.152) ppm (4H,d,2); (8.475-8.497) ppm (4H,d,1); 11.009 ppm (1H,s,4)

Synthesis of 4,6-bis(4-nitrophenyl)pyrimidine-2-thiol (2d)

To a stirred solution of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) (which was prepared as mentioned in the literature) [10] (1.0 mmol) in 10 ml EtOH (96 %) was added thiourea (2.0 mmol) and 10% NaOH (2.5 ml) at room temperature. The reaction mixture was heated to reflux overnight. The progress of the reaction was monitored by TLC (benzene/methanol, 9:1). The EtOH was removed under reduced pressure and the residue was recrystalized from EtOH to afford the pure products and gave a 71 % yield with a m.p. (320 d)°c. The GC-Mass analysis for $C_{16}H_{10}N_4O_4S$ (m/z = 354) ; FT-IR spectra (KBr pellet) $\upsilon(cm^{-1})$ 3095 (C–H stretching of aromatic ring), 2200 (S–H stretching), $\delta_H(CDCl_3)$ 8.019 ppm (1H,s,3); (8.140-8.152) ppm (4H,d,2); (8.475-8.497) ppm (4H,d,1); 11.959 ppm (1H,s,4)

RESULTS AND DISCUSSION

Treatment of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) with hydroxylamine hydrochloride or hydrazine hydrate in boiling ethanol gave isoxazole or pyrazoline compounds 2a,2b) respectively , after purification by recrystallization from ethanol, pure isoxazole and pyrazoline compounds as shown in (scheme 1) in (73-78)% yield. The structures of these products were established from their GC-Mass, FT-IR, and ^1H NMR spectra. The FT-IR spectra of isoxazole compound (2a) were characterized by the disappearance of the absorption band that was attributed to the (C=O) stretching which appeared at (1710) cm^{-1}. These fact confirmed the correct expected chemical structure of these compounds. The IR spectrum of isoxazole compound (2a) showed a peak at 1153 cm^{-1} which related to (N-O) stretching of isoxazole ring , a peak at 1276 cm^{-1} which appeared due to (C-N) stretching of isoxazole ring and a peak at 1068 cm^{-1} which appeared due to (C-O stretching of isoxazole ring). While, the C-H stretching aromatic rings showed a peak within the range 3002 cm^{-1}.

The FT-IR spectrum of pyrazoline compounds were characterized by the disappearance of the absorption band that was attributed to the (C=O) stretching which appeared at (1710) cm^{-1}. These fact confirmed the correct expected chemical structure of these compounds. The IR spectrum of pyrazoline compound (2b) showed a peak at 1259 cm^{-1} which appeared due to (C-N) stretching of pyrazoline ring and a peak at 3242 cm^{-1} which appeared due to (N-H stretching of pyrazoline ring). While, the C-H stretching aromatic rings showed a peak within the range 3051 cm^{-1}.

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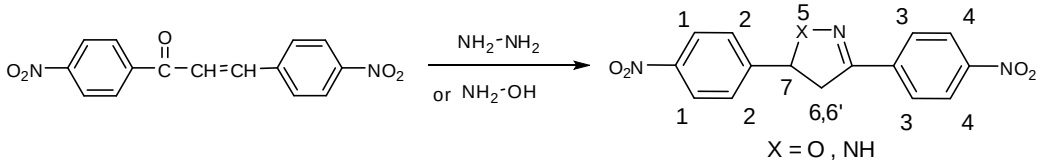
Treatment of 1,3-bis(4-nitrophenyl)prop-2-en-1-one (1a) with urea or thiourea in boiling ethanol gave pyrimidine-2-ol or pyrimidine-2-tiol compounds 2c,2d) respectively , after purification by recrystallization from ethanol, pure pyrimidine-2-ol or pyrimidine-2-tiol compounds as shown in (scheme 2) in (70-71)% yield. The structures of these products were established from their GC-Mass, FT-IR, and ^{1}H NMR spectra. The FT-IR spectra of pyrimidine-2-ol compound (2c) were characterized by the disappearance of the absorption band that was attributed to the (C=O) stretching which appeared at (1710) cm^{-1}. These fact confirmed the correct expected chemical structure of these compounds. The IR spectrum of pyrimidine-2-ol compound (2c) showed a peak at 1076 cm^{-1} which related to (C-O) stretching, a peak at 3360 cm^{-1} which appeared due to (O-H) stretching . While, the C-H stretching aromatic rings showed a peak within the range 3095 cm^{-1}.

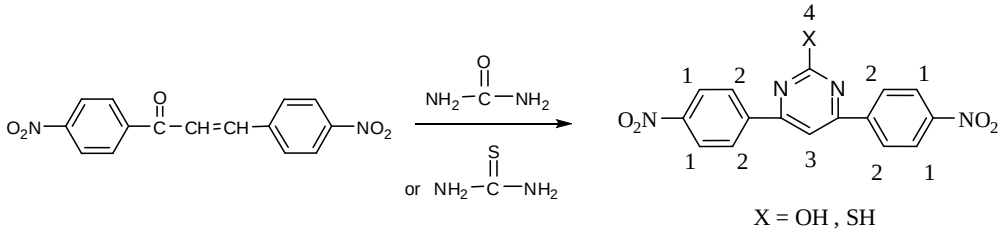
The FT-IR spectrum of pyrimidine-2-thiol compounds were characterized by the disappearance of the absorption band that was attributed to the (C=O) stretching which appeared at (1710) cm^{-1}. These fact confirmed the correct expected chemical structure of these compounds. The IR spectrum of pyrimidine-2-thiol compound (2d) showed a peak at 2200 cm^{-1} which appeared due to (S-H) stretching . While, the C-H stretching aromatic rings showed a peak within the range 3095 cm^{-1}.

The ^{1}H NMR spectra of isoxazole,pyrazoline,pyrimidine-2-ol and pyrimidine-2-thiol compounds are shown in figures (1-4). All the ^{1}H NMR spectra of isoxazole,pyrazoline,pyrimidine-2-ol and pyrimidine-2-thiol compounds were characterized [11-13] In compounds (2a,2b) by the presence protons (7) of isoxazole and pyrazoline ring showed triplet signals within the range (3.845-4.677) ppm because interaction with two protons in (6 and 6\) position and showed doublet signals within the range (3.350-3.360) ppm which appeared to protons in (6and 6\) position because interaction with protons in (7) position , while the aromatic protons showed multiplet signals within the range (8.011-8.175) ppm due to six protons in positions (1,2,4).The other two aromatic proton in position 3 showed doublet signals within the range (7.715-7.788) ppm because interaction with proton in position 4. In compound 2b showed singlet signal within the range 6.670 ppm which appeared to proton NH in pyrazoline ring (proton in position 5). These peaks confirmed the correct expected chemical structure of isoxazole and pyrazoline compounds.

In compounds (2c,2d) by the presence protons (4) of pyrimidine-2-ol and pyrimidine-2-thiol ring showed singlet signal within the range (11.009-11.759) ppm , while the aromatic protons showed doublet signals within the range (8.475-8.497) ppm due to four protons in positions (1) because interaction with proton in position (2).The other four aromatic protons in position (2) showed doublet signals within the range (8.140-8.152) ppm because interaction with proton in position (1) and showed singlet signal within the range 7.959 ppm which appeared to proton in position (3). These peaks confirmed the correct expected chemical structure of isoxazole and pyrazoline compounds



Scheme (1)



Scheme (2)

REFERENCES

[1] S. V. Kostanecki and Tambor, J. Chem Ber., 1899; 32: 1921
[2] H. Rupe and D. Wasserzug, J. Chem Ber., 1901;34; 3527
[3] S. A. Hermes, Chem Ber., 1969;70: 96422
[4] D. S. Breslow and C. R. Houser, Chem Ber., 1940;62: 2385
[5] K. Kazauki, K. Hitayama, S. Yokomor and T. Soki, Chem Abstr., 1976; 85:, 591()
[6] M. A. El.Hashah; M. El-Kady; M. A. Saiyed and A. A. Elaswy, Egypt. J. Chem., 1985;27:715
[7] L. S. Crawley and W. J. Fanshawe, J. Heterocyclic chem., 1977; 14: 531
[8] E. C. Taylor and R. W. Morrison, J. Org. Chem., 1967;32: 2379
[9] P. S. Utale, P. B. Raghuvanshi and A. G. Doshi, Asian J. Chem., 1998; 10: 597
[10] I. Karamana, H. Gezegenb, M. B. G_rdereb, A. Dingilb, Ceylan , J. chemistry & biodiversity , 2010, 7 pp.400-408
[11] R.M. Silverstien, F.X.Webster, D.J.Kiemle "Spectrometric Identification of Organic Compounds", sixth ed., John Wiley and Sons, New Yourk, USA, 2005.
[12] J.W.Cooper, Spectroscopic Techniques for Organic Chemistry, John Wiley and Sons, New Yourk, USA,1980.
[13] R.L.Shriner, C.K.Hermann, "Spectroscopic Techniques for Organic Chemistry", John Wiley and Sons, New Yourk, USA, 2004.