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Syntheses and characterization of some 1, 2, 4-triazole derivatives as biological agents

RAM JANAM SINGH[1]* and DHARMENDRA KUMAR SINGH[2]

[1]Quality Control Laboratory, Indian Oil Corporation Limited,
Panipat Refinery Panipat, Haryana - 132 140 (India)
[2]Synthetic Research Laboratory, Department of Chemistry,
Veer Bahadur Singh Purvanchal University, Jaunpur - 222 002 (India).

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ABSTRACT

3-Alkyl -4-amino-4, 5-dihydro-1H-1, 2, 4-triazole-5-one (1) when condensed with di-(3-formyl phenyl)-terephthalate (2) yielded the corresponding novel di-[3-(3-alkyl-4,5-dihydro-1H-1,2,4-triazol-5-one-4-yl)-azomethinphenyl]-terephthalate (3). All the synthesized compounds were characterized by IR, PMR, Mass spectral data and elemental analyses. All newly synthesized compounds have been assayed for their antibacterial activity against *S. aureus, E. coli, B. subtilis and P. aeruginosa*.

Keywords: 4, 5-dihydro-1H-1, 2, 4-triazole-5-one, di-(3-formyl phenyl)-terephthalate, condensation, cyclization, antibacterial activity.

INTRODUCTION

The importance of triazole- derivatives lie in the field that these have occupied an unique position in heterocyclic chemistry due to their agricultural, industrial and biological activities[1]. The 1, 2, 4-triazole system has wide spread uses, and it has been considered as an interesting component in terms of antimicrobial activity[2]. Compounds containing 1, 2, 4-triazole moieties attached to a heterocyclic system are of wide interest because of their diverse biological activities[3]. In views of these observations and in continuation of our earlier work[4-14] on the syntheses of some 1,2,4- & 1,2,3- triazole derivatives, we now report the syntheses of some new di-[3-(3-alkyl-4, 5-dihydro-1H-1, 2, 4-triazol-5-one-4-yl)-azomethinphenyl]-terephthalate derived from 3-Alkyl -4-amino-4, 5-dihydro-1H-1, 2, 4-triazole-5-one with di-(3-formyl phenyl)-terephthalate.

MATERIAL AND METHODS

Melting and boiling points were determined on a Gallen Kamp apparatus in open capillaries and are uncorrected. IR spectra (KBr in cm^{-1}) were recorded on a Jasco FT-IR 5300 spectrophotometer and Proton magnetic resonance (PMR) spectra (DMSO-d6) on a Varion EM 390 spectrophotometer using TMS as an internal standard (chemical shift in d ppm). Mass spectra were recorded on Jeol JMS-D 300 mass spectrophotometer operating at 70 eV. The Purity of the compounds was checked by TLC using silica gel G and purified by column chromatography. All compounds showed satisfactory elemental analyses.

General Procedure for the preparation of di-(3-formyl phenyl)-terephthalate (2)

A mixture of 3-hydroxybenzaldehyde (0.01 mol), ethyl acetate (50 mL), terephthaloyl chloride

(0.01 mol) and triethylamine (0.01 mol) was stirred for one hour and then heated under reflux for 6 hours. The precipitate was filtered, washed with water and crystallized from aqueous ethanol (80%) to give **2** (yield 80%).

General Procedure for the preparation of di-[3-(3-alkyl-4, 5-dihydro-1H-1, 2, 4-triazol-5-one-4-yl)-azomethinphenyl]-terephthalate (3a-d)

A mixture of corresponding compound **1** (0.01 mol), acetic acid (30 mL) and di-(3-formyl phenyl)-terephthalate 2 (0.01 mol) was heated under reflux for 2 hours and then evaporated at 60 ^{0}C. The precipitate was filtered, washed with water and crystallized from aqueous ethanol (80%) to give **3a-d** (yield 70-80%).

(3a)

(yield 72%), m.p. 288 ^{0}C. Anal. calcd. for $C_{28}H_{22}N_8O_6$: C, 59.56; H, 3.86; N, 19.99%, Found : C, 59.61; H,3.85; N, 19.98%. IR (KBr): 3183(NH), 1730,1710 (C=O), 1612, 1590 (C=N), 1238(C-O), 820 (1,4-disustituted benzoid ring) and 692 cm^{-1} (1,3-disustituted benzoid ring) ; PMR: d 2.28 (6H, s, 2CH_3), 7.52-7.90 (8H, m, ArH), 8.35(4H, s, ArH), 9.77 (2H, s, 2N=CH) and 11.85 ppm (2H,s, 2NH); MS: m/z 299 (M^+) other peaks observed at 177, 147, 136, 129, 89, 69, 58 and 47.

(3b)

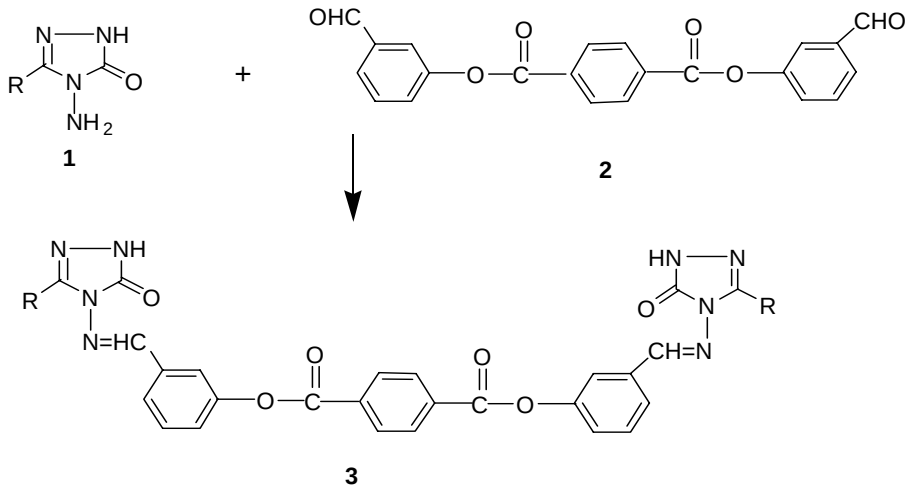
(yield 75%), m.p. 282^{0}C. Anal. calcd. for $C_{30}H_{26}N_8O_6$: C, 61.09; H, 4.39; N, 19.89%, Found : C, 61.05; H,4.41; N, 19.87%. IR (KBr): 3173 (NH), 1742,1708 (C=O), 1604, 1590 (C=N), 1236 (C-O), 805 cm^{-1} (1,4-disustituted benzoid ring) and 712 cm^{-1} (1,3-disustituted benzoid ring) ; PMR: d 1.33 (6H, t, 2CH_3), 3.05 (4H, q, 2CH_2), 7.62-7.90 (8H, m, ArH), 8.02-8.35 (4H, m, ArH), 9.76 (2H, s, 2N=CH) and 11.85 ppm (2H,s, 2NH); MS: m/z 296 (M^+) other peaks observed at 185, 168, 137, 128, 89, 67, 57 and 46.

(3c)

(yield 75%), m.p. 310 ^{0}C. Anal. calcd. for $C_{40}H_{30}N_8O_6$: C, 65.88; H, 4.33; N, 16.69%, Found : C, 65.89; H,4.32; N, 16.65%. IR (KBr): 3178(NH), 1741,1710 (C=O), 1606, 1574(C=N), 1238(C-O), 824 (1,4-disustituted benzoid ring) and 719 cm^{-1} (1,3-disustituted benzoid ring) ; PMR: d 4.05 (4H, s, 2CH_2), 9.71 (2H, s, 2N=CH) and 12.02 ppm (2H,s, 2NH); MS: m/z 292 (M^+) other peaks observed at 149, 139, 129, 128, 86, 68, 64 and 50.

(3d)

(yield 80%), m.p. 302 ^{0}C. Anal. calcd. for $C_{39}H_{28}N_8O_6$: C, 65.83; H, 4.34; N, 16.57%, Found : C, 65.87; H,4.31; N, 16.54%. IR (KBr): 3171(NH),



a) Methyl
b) Ethyl
c) Benzyl
d) Phenyl

Scheme 1: Synthetic pathway for the preparation of compounds 3a-d

1739, 1714 (C=O), 1599, 1575 (C=N), 1239 (C-O), 820 (1,3-disustituted benzoid ring), 716 cm^{-1} (1,3-disustituted benzoid ring) and 681 cm^{-1} (monosustituted benzoid ring); PMR: 7.50-7.57 (6H, m, ArH), 7.62-7.65 (2H, m, ArH), 7.72-7.82 (4H, m, ArH), 7.86-7.92 (4H, m, ArH), 8.33-8.35 (2H, m, ArH), 9.70 (2H, s, 2N=CH) and 12.32 ppm (2H,s, 2NH); MS: m/z 295 (M^+) other peaks observed at 153, 149, 138, 128, 88, 65, 60 and 53.

Antibacterial Activity

The antibacterial activity of synthesized compounds was investigated by employing the filter paper disc method [15-17]. Representative organisms selected for evaluation of antibacterial activity were *S. aureus, E. coli, B. subtilis* and *P. aeruginosa*. The antibacterial activity of each of the compounds was evaluated in triplicate at 100 µg $mL^{-1}$and 10 µg mL^{-1} concentrations. The compounds were tested as a solution or suspension in DMF (99.80 % anhydrous). An important and useful control drug Ampicillin was also tested under similar conditions, with view to compare the results.

The result indicates that all of the synthesized compounds showed moderate to strong activity against these bacterial strains (Table 1). It is abvious form the antibacterial screening results that the most of compounds have significant bacteriocide toxicity against *S. aureus, E. coli, B. subtilis and P. aeruginosa*.

Table 1:Evaluation of antibacterial activity of the synthesized compounds 3a-g

Compd.	Average zone of Inhibition/mm							
	S. aureus		*E. coli*		*B. subtilis*		*P.aeruginosa*	
	100 µg mL^{-1}	10 µg mL^{-1}	100 µg mL^{-1}	10 µg mL^{-1}	100 µg mL^{-1}	10 µg mL^{-1}	100 µg mL^{-1}	10 µg mL^{-1}
3a	22	20	17	16	18	16	19	17
3b	18	17	17	15	17	15	22	20
3c	23	21	18	15	16	15	16	16
3d	19	16	18	14	17	16	17	15
Standard (Ampicillin)	27	21	25	20	23	20	23	20
Control	00	00	00	00	00	00	00	00

RESULTS AND DISCUSSION

In the present work, 3-Alkyl -4-amino-4, 5-dihydro-1H-1, 2, 4-triazole-5-one (1) which is required as starting material were obtained in an one-pot reaction by heating corresponding ester ethoxycarbonylhydrazones and hydrazine hydrate under reflux conditions for 6 hours, which on cyclization affords 3-Alkyl -4-amino-4, 5-dihydro-1H-1, 2, 4-triazole-5-one (1). Di-[3-(3-alkyl-4, 5-dihydro-1H-1, 2, 4-triazol-5-one-4-yl)-azomethinphenyl]-terephthalate (3) which are novel compounds, were prepared by the reaction of corresponding compound 1 with di-(3-formyl phenyl)-terephthalate (2), which were synthesized by the reaction of 3-hydroxybezaldehyde with terephthaoyl chloride by using triethylamine (Scheme 1).

The structures of the synthesized compounds are confirmed by IR, PMR and MS spectral data and are further supported by correct elemental analyses (experimental part). These compounds were tested against various bacterial strains and the details are provided in the experimental section.

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