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Synthesis and characterization of 2,7-dioxo-9-(N-substituted phenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl esters

A. P. Rajput* and P. D. Girase†

** P.G. Research Center, Department of Chemistry, Z. B. Patil College, Dhule(M.S.), India*
† S. V. S's Dadasaheb Rawal College, Dondaicha, Dist. Dhule(M.S.), India

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ABSTRACT

A series of new 2,7-dioxo-9-(N-substituted phenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl esters ***2a-d*** *were prepared by condensation of diethylmalonate with 2,6-diamino-1-(N-substituted phenyl)-1,4-dihydropyridine-3,5-dicarbaldehydes* ***1a-d*** *which have been prepared according to our previous known procedure. The structures of the newly synthesized compounds have been confirmed on the basis of elemental analysis and spectral studies.*

Keywords: Dihdropyridines, Vilsmeier-Haack reaction, triaza-anthracenes.

INTRODUCTION

1,4-dihydropyridines and their derivatives are an important class of bioactive molecules in the pharmaceutical field[1]. The dihydropyridine heterocyclic ring is a common feature of a variety of bioactive compounds including anticonvulsant, antidiabetic, antianxiety, antidepressive, antitumor, analgesic, sedative, vasodilator, bronchodilator, hypnotic and anti-inflammatory agents [2].

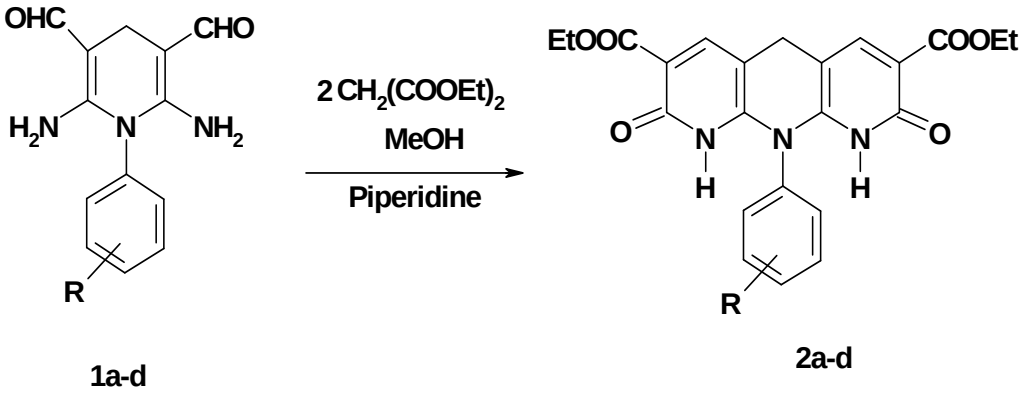
Diydropyridines are reported as calcium channel blockers[3] and are clinically useful agents for the treatment of cardiovascular diseases such as anginapectoris[4] and hypertension[5]. Similarly 1,8,9-triazaanthracenes[6,7] have great potential as useful ligands for metals and transition metals. In view of these findings, in continuation of our work and interest in V-H reaction[8-16], it was contemplated to synthesize some new triaza-anthracene derivatives **2a-d** (**Scheme-I**).

MATERIALS AND METHODS

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on FT-IR spectrophotometer. ^{1}HNMR spectra were recorded on varian USA Mercury plus 300 MHz NMR spectrometer with $CDCl_3$ as a solvent using TMS as internal reference (chemical shift in δ ppm). The starting compounds were synthesized according to our previous known procedure.

General procedure for synthesis of 2,7-dioxo-9-(N-substituted phenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl esters 2a-d.

To a solution of 2,6-diamino-1-(N-substituted phenyl)-1,4-dihydro-pyridine-3,5-dicarbaldehydes **1a-d** (1mmole) and diethyl malonate (20ml) in absolute methanol (30ml) was added 0.2ml piperidine and it was refluxed on water bath for 5-6 hrs. After cooling, the yellow solid separated was collected by filtration and recrystalized from ethanol to get a pure 2,7-dioxo-9-(N-substituted phenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl esters **2a-d (Scheme-I).**



1a-d **2a-d**

R, a = -H, b = -4Me, c = -4Cl, d = -2Me

(Scheme- I)

2,7-dioxo-9-(phenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl ester 2a:
M.F. $C_{23}H_{21}O_6N_3$; Yield 60%; faint yellow solid, mp 210-212^{0}C; IR (KBr): 3198 (NH), 2925 (CH_2), 1670, 1715 (C=O), 1475 (ArC=C), 1260 (C-N) cm^{-1}; ^{1}HNMR (DMSO-d6): δ 1.28 (t, J=7.0, 6H, 2CH_3), 3.81(s, 2H, CH_2), 4.30 (q, J=7.0, 4H, 2CH_2), 7.01-6.46 (m, Ar-H), 7.79 (s, 2H, 2CH), 12.80 (br s, 2H, 2NH).

2,7-dioxo-9-(4-methylphenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl ester 2b:
M.F. $C_{24}H_{23}O_6N_3$; Yield 64%; faint yellow solid, mp 222-224^{0}C; IR (KBr): 3200 (NH), 2920 (CH_2), 1660, 1730 (C=O), 1470 (ArC=C), 1242 (C-N) cm^{-1}; ^{1}HNMR (DMSO-d6): δ 1.27 (t, J=7.0, 6H, 2CH_3), 2.26 (s, 3H, CH_3), 3.55(s, 2H, CH_2), 4.32 (q, J=7.0, 4H, 2CH_2), 7.10-6.50 (m, Ar-H), 7.80 (s, 2H, 2CH), 12.78 (br s, 2H, 2NH).

2,7-dioxo-9-(4-chlorophenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl ester 2c:
M.F. $C_{23}H_{20}O_6N_3Cl$; Yield 58%; faint yellow solid, mp 201-203^{0}C; IR (KBr): 3178 (NH), 2920 (CH_2), 1687, 1735 (C=O), 1472 (ArC=C), 1244 (C-N) cm^{-1}; ^{1}HNMR (DMSO-d6): δ 1.32 (t, J=7.0, 6H, 2CH_3), 3.72 (s, 2H, CH_2), 4.28 (q, J=7.0, 4H, 2CH_2), 7.10-6.70 (m, Ar-H), 7.78 (s, 2H, 2CH), 12.82 (br s, 2H, 2NH).

2,7-dioxo-9-(2-methylphenyl)-1,2,7,8,9,10-hexahydro-1,8,9-triaza-anthracene-3,6-dicarboxylic acid diethyl ester 2d:
M.F. $C_{24}H_{23}O_6N_3$; Yield 60%; faint yellow solid, mp 192-194^{0}C; IR (KBr): 3202 (NH), 2924 (CH_2), 1650, 1740 (C=O), 1485 (ArC=C), 1255 (C-N) cm^{-1}; ^{1}HNMR (DMSO-d6): δ 1.29 (t, J=7.0, 6H, 2CH_3), 2.30 (s, 3H, CH_3), 3.81 (s, 2H, CH_2), 4.29 (q, J=7.0, 4H, 2CH_2), 7.02-6.46 (m, Ar-H), 7.79 (s, 2H, 2CH), 12.78 (br s, 2H, 2NH).

Antimicrobial activity:
The compounds **2a-d** were screened for their *in vitro* antimicrobial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Aspergillus niger* and *Candida albicans*. The agar diffusion

assay (Well method, Disc size 6mm, Hi media) was used. The compounds were tested at the concentration of 100µg/ml in DMF. The results were compared with respective standards Nystatin and Chloramphenicol. All the compounds showed moderate to good antimicrobial activity.

Table-1: Biological activities of Compounds 2a-d

Compound	*E. coli*	*P. aeruginosa*	*B. subtilis*	*S. aureus*	*A. niger*	*C. albicans*
2a	8.53	9.89	10.20	17.16	7.11	8.09
2b	-	9.96	15.30	13.30	7.13	8.23
2c	7.98	11.19	-	13.59	9.00	8.25
2d	-	-	10.90	13.30	-	-
Nystatin (100U/disc)	NA	NA	NA	NA	9.59	10.1
Chloramphenicol(10mcg/disc)	30.1	25.2	30.1	33.1	NA	NA

Diameter in mm calculated by Digital Vernier Calliper.
"-" means "no zone of inhibition", "NA" means "Not Applicable"

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