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Antibacterial and Antifungal Study of Synthesised Anthracenyl Based Triazole Cycloadducts

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ABSTRACT

Bioactive anthracenyl based triazole cycloadduct compounds which were prepared from 9-anthracenyl methyl azide as electron rich dipole and activated electron deficient dipolarophiles under mild condition. Reaction proceeded regioselectively to form one regioisomer with good yield. Anthracenyl triazole based cycloadduct were screened for antibacterial and antifungal activity.

Key words: Cycloaddition, Triazoline, Antibacterial, 9-anthracenyl methyl chloride, 9-anthracenyl methyl azide.

INTRODUCTION

1,2,3-triazolines were reported to be herbicidal active anticonvulsants[1] and antiischemic agents[2] as rational drug design. Also triazolines are use synthetic intermediates in synthesis of natural products[3] and drugs.[4-7] Dipolar cycloaddition reaction of azide with olefinic dipolarophile is an excellent tool for construction of triazoline ring.

Cycloaddition with conjugated electron pair olefins such as ethyl acrylate.[8] Similarly, azides add to acrylamide[9] acrylonitrile,[10] methyl acrylate,[11] methyl crotonate and ethylideneacetone[12] regiospecifically to give adducts.

MATERIAL AND METHODS

All reactants and solvent were purchased from S.D. Fine chemicals. The test cultures were brought from National Chemical Laboratory (NCL) Pune, India. The cultures were maintained at 40^{0}C.

Synthesis of anthracenyl triazoline based cycloadducts 9-anthracenyl methyl chloride (1) (1 eq.) used as starting material for synthesizing 9-anthracenyl methyl azide (2) using sodium azide (2 eq.) using dry Dimethyl Sulfoxide at room temperature under mild condition and easy to work out because sodium azide is easily soluble in water during work up. Further 9-anthracenyl methyl azide

react with traditional activated dipolarophile without using any catalyst.

Azide (2) (0.1mmol) was mixed with excess of methyl acrylate/ acrylonitrile (excess i.e. 8-10ml) and allowed to stir at room temperature to give cycloadduct 3a/3b respectively. After stirring of 6-8 hours the excess of cycloadduct3a/3b was removed by evaporation and product 3a/3b obtained was purified by column chromatography. For cycloadduct3c, azide (2) (0.1 mmol) was charged with N-methyl maleimide in refluxing toluene for 4-5 hours, after completion of reaction as indicated on tlc for consumption of starting material, solvent was evaporated and cycloadduct was purified by percolating through silica gel bed.

RESULTS AND DISCUSSION

All the cycloadducts were characterised by disappearance of azide peak (two stretching bands at 2094 and 2133 cm^{-1} absorption IR specturm) in IR spectrum and appearance of protons of triazolenic protons in PMR scan. Cycloadducts were further confirmed by respective molecular ion peak in mass scan. Spectral characterisation have been summarized in Table I. We had studied antibacterial activity while antifungal activities were not seen. The best antibacterial activity was seen for compound 3a, 3b and 3c showed comparative inhibition zone compared to one of the reference standard Tetracycline for the bacterial culture of *E.coli* and *B. subtilis*. Conclusively, anthracenyl based triazoline cycloadducts were found to show remarkable antibacterial activity and reaction proceeded regioselectively to form1, 4 isomer under mild conditions with satisfactory bioactivity. Formation of 1,4 isomer revealed that azide might have imparted highest molecular orbital (HOMO) and dipolarophile might have imparted lowest unoccupied molecular orbital(LUMO).

Antibacterial Study

Cycloadduct (3a, 3b and 3c) synthesized were screened for to check their bioactivities. The test cultures were brought from national chemical laboratory (NCL) Pune, India. The cultures were maintained at 40^0C. The prepared cycloadduct were screened against both Gram +ve and Gram –ve bacteria. The gram +ve bacteria selected was *B. subtilis*.

Table 1: Spectral characterization of cycloadduct 3a, 3b and 3c

Cycloadduct	M. P. (^{0}C)	Yield (%)	IR(cm^{-1}, KBr)	PMR (300 MHz, $CDCl_3$ ppm) δ	M/S (m/z)
3a	75	76.00	1213,1434,1678,1741,2950	3.11-3.31(dt,9.9HZ, 12.3Hz,2H), 3.76(s,3H),4.79(t,12.3Hz,1H),5.71(d,14.7Hz,1H),6.08 (d,14.7Hz,1H),7.48-7.61(m,4H), 8.06d,8.4Hz,2H),8.45(d,8.7Hz,2H), 8.51 (s,1H)	319(MIP), 291,276,208, 191(base peak), 152,16,94,75,65,50
3b	122	80.17	893,1098,1446,1623,2247	3.166-3.212(dd,11.4HZ, 2H), 4.744(t,11.7Hz,1 H),5.784 (d,14.7Hz,1H),6.012 (d,14.7Hz,1H),7.058-7.637 (m, 4H),8.063 (d,8.1Hz ,2H), 8.349(d,9Hz,2H),8.549 (s,1H)	284(MIP), 258, 191(base peak), 102,94
3c	194^{0}C	78.34	1284, 1450, 1694, 1771, 2925, 3067	2.532(s, 3H), 3.276-3.373(m, 1H), 4.705-4.760(m, 2H), 5.057(d, 12.6Hz, 1H), 7.103-7.454(m, 9H).	—-

The gram –ve bacteria selected were *E.coli* and *Pseudomonas aeruginosa*. The reference standards used for bacterial cultures were Streptomycin and Tetracycline. Cycloadducts were insoluble in water and therefore dissolved in Dimethylsulfoxide and used. All the bacterial cultures were exposed to Dimethylsulfoxide to see whether Dimethylsulfoxide exhibits any activity for that Whatmann filter paper discs were dipped in Dimethylsulfoxide and placed at the centre of plates spread with the cultures. No zone of inhibition was seen indicating that Dimethylsulfoxide did not show any antibacterial or antifungal activity.

Procedure

The inoculum density of all the bacterial cultures was adjusted to 10^8cfu/ml by counting under haemocytometer slide. The inoculum was prepared by suspending the cultures in sterile saline. This was then followed by plate method where in agar plates were seeded with 0.6ml of the bacterial suspension and exposed to the different concentrations of the test substances. Approximate dilutions of the test substances were added to wells bored in plates. Following incubation the average zone of inhibition of the cycloaddducts was measured in millimeteres. However, minimum inhibitory concentration (MIC) values could not be obtained because the zone sizes obtainedfor the compounds could not be compared to the zone sizes of the standard antibiotics and its concentration used. The results of antibacterial study in terms of zone of inhibition recorded in millimetres for cycloadducts are discussed in the Table 2.

Table 2: Antibacterial activity of anthracenyl based triazole cycloadducts (3a, 3b and 3c)

S. No.	Cycloadduct	Zone of inhibition(mm)		
		E.coli	***P.aeruginosa***	***B.subtilis***
1	3a	12	15	16
2	3b	13	13	17
3	3c	12	13	14
4	Streptomycin(10mcg/disc)	19	23	23
5	Tetracycline(30mcg/disc)	12	30	14

Antifungal Activity

Number of experiments was set up to study antifungal activity. However none of the compounds (3a, 3b and 3c) demonstrated any antifungal activity even at high concentrations (5000 mcg/ml). Fungal culture selected for study were *Aspergillus niger* and *Trichoderma spp*. The reference standards chosen were AmphotericinB and Ketoconazole.

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