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Synthesis of some biologically active 2,5-diazido-1-(N-substituted phenyl-1H-pyrole-3,4-dicarbaldehydes and their transformation in to multivariant functionalities

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ABSTRACT

Azides are considered very important biologically useful compounds [1]. Their derivatives are used in rubber vulcanization, polymer cross linking, dyes, tire, pharmaceuticals, foaming of plastics, herbicides and pesticides [1].Many Azide compounds show mutagenic activities[2,3].

Keywords: Azide, Vilsmeier-Haack Reaction, Dicarbaldehydes.

INTRODUCTION

The chemistry of azides has attracted the attention of many chemists, since many of these compounds play an important role in organic chemistry[5,6].Azides[8] present themselves as energy rich and flexible intermediates among many synthetic precursors and have continued to attract immense interest. Azides can be considered as a masked amino group and is used for amine protection. Azides as dipoles undergo cycloaddition reaction with olefinic species popularly known as Huisgen reaction[9].They are also important intermediates in multicomponent reactions[10]. As a result of these useful applications a various Azide derivatives have been developed by different co-workers.[11-13]

MATERIALS AND METHODS

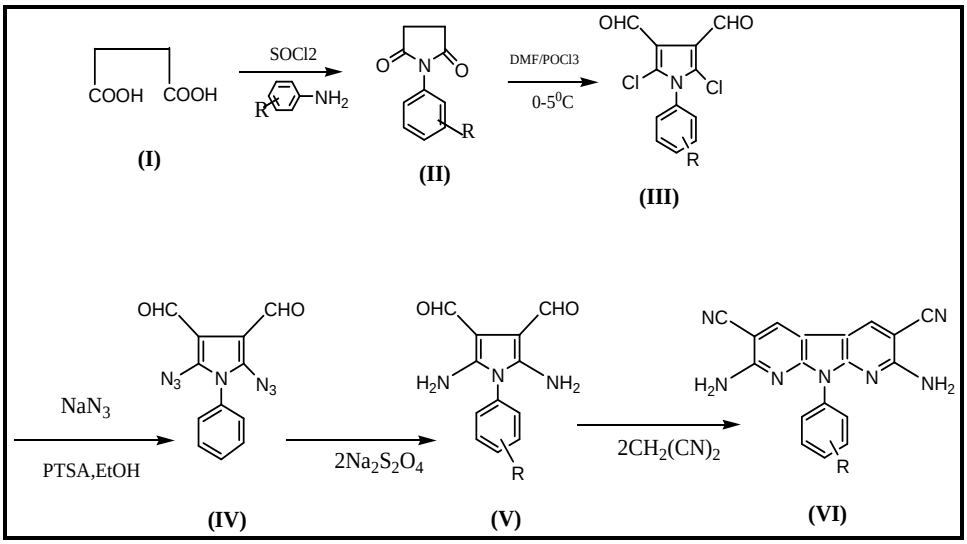
All melting points were determined in open capillary & are uncorrected. I.R. spectra were Recorded on Perkin-Elmier spectrum. H^1NMR were recorded on Bruker DRX 500MHz.NMR spectrometer with DMSO-d_6 as a solvent using TMS as internal reference . (chemical shift in δ ppm).

General Procedure For Synthesis Of 2,5-diazido -1-phenyl -1-(N-substituted phenyl) -1H-pyrrole-3,4-dicarbaldehydes.

To a solution of III (1mmole) in absolute ethanol (10 ml), P-toluenesulphonic acid (2mmole) and sodium azide (3mmole) were added and the reaction mixture was heated under reflux for 3 hr. After completion of the reaction ,the reaction mixture was poured in to ice-cooled water and the resulting precipitate was filtered, dried and purified

by recrystallisation from aq. Ethanol which afforded pure 2,5-diazido-1-phenyl-1-(N-substituted phenyl)-1H-pyrrole-3,4-dicarbaldehydes.

REACTION SCHEME



(IVa) 2,5-diazido-1-phenyl-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula : $C_{12}H_7O_2N_7$, Physical nature : whitish Yield(%) : 72%; M.P(^{0}C) : 68-70 ^{0}C Molecular Weight : 281 ; IR: (KBr)cm^{-1} 2854 (CHO), 2108(N_3), 1658(>C=O), 1442 (Ar C=C), 1247 (C-N). ; H^1NMR (300MHz,DMSO-d_6,δppm) 7.63-7.32 (m, Ar-H), 10.07 (s,2H,2CHO).; C^{13}NMR : 191 (2CHO), 119 (C-N), 120-130(Ar-CH) ; Elemental Analysis: Calculated : C-51.24,H-2.49,N-34.87. Found,C-51.20,H-2.45,N-34.85.

(IVb) 2,5-diazido-1-(2-chloro phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula : $C_{12}H_6O_2N_7Cl$; Physical nature : whitish Yield(%) : 73 %; M.P(^{0}C) : 44 ^{0}C Molecular Weight : 315.5 ; IR(KBr)cm^{-1} : 2858 (CHO), 2100 (N_3), 1652 (>C=O), 1440 (Ar C=C), 1242 (C-N).; H^1NMR (300MHz, DMSO-d_6,δppm) : 7.60-7.38 (m,Ar-H), 10.12 (s,2H,2CHO). ; C^{13}NMR : 193 (2CHO), 116 (C-N), 125-130 (Ar-CH).; Elemental Analysis: Calculated C-45.64,H-1.90,N-31.06. Found,C-45.60,H-1.85,N-31.00.

(IVc) 2,5-diazido-1-(4-chloro phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula : $C_{12}H_6O_2N_7Cl$, Physical nature : whitish Yield(%) : 71 % ; M.P(^{0}C) : 93 ^{0}C ; Molecular Wight : 315.5 **;** IR(KBR)cm^{-1} : 2859 (CHO), 2125 (N_3), 1660 (>C=O), 1449 (Ar C=C), 1250 (C-N). ; ^{1}NMR (300MHz, DMSO-d_6, δppm) : 7.65-7.35 (m,Ar-H), 10.20 (s,2H,2CHO). ; C^{13}NMR **:** 198 (2CHO),120 (C-N), 122-135 (Ar-CH) ; Elemental Analysis: Calculated C-45.64,H-1.90,N-31.06. Found,C-45.60,H-1.88,N-31.00.

(IVd) 2,5-diazido-1-(3-chloro phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula : $C_{12}H_6O_2N_7Cl$, Physical nature : yellowish Yield(%) : 90; M.P(^{0}C) : 46-50 ^{0}C Molecular Weight : 315.5 ; IR(KBr)cm^{-1} : 2854 (CHO), 2108 (N_3), 1658 (>C=O), 1442 (Ar C=C), 1247 (C-N). H^1NMR(300MHz,DMSO-d_6,δppm) : 7.63-7.32 (m,Ar-H), 10.07 (s,2H,2CHO). C^{13}NMR : 191 (2CHO), 119 (C-N), 120-130 (Ar-CH) Elemental Analysis: Calculated,C-45.64,H-1.90,N-31.06.Found,C-45.60,H-1.85,N-31.00.

(IVe) 2,5-diazido-1-(3-methoxy phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula : $C_{13}H_9O_3N_7$ Physical nature : whitish Yield(%) : 88 %; M.P(^{0}C) : 38-42 ^{0}C Molecular Weight : 311 ; IR(KBr)cm^{-1} : 2850 (CHO), 2120 (N_3), 1660 (>C=O), 1440 (Ar C=C), 1250 (C-N).; H^1NMR (300MHz,DMSO-d_6,δppm): 2.40(s,3H,CH_3), 7.63-7.32 (m, Ar-H), 10.07 (s,2H,2CHO). ; C^{13}NMR : 189 (2CHO), 118 (C-N), 121-130 (Ar-CH), 55.9 (-OCH_3).; Elemental Analysis: Calculated C-50.16,H-2.89,N-31.51.Found,C-50.12,H-2.85,N-31.49.

(**IVf) 2,5-diazido-1-(4-methyl phenyl)-1H-pyrrole-3,4-dicarbaldehyde**.:
Molecular formula : $C_{13}H_9O_2N_7$: Physical nature : whitish Yield(%) : 80%; M.P(^{0}C) : 48-50 ^{0}C Molecular Weight : 295 IR(KBr)cm^{-1} : 2845 (CHO), 2125 (N_3), 1670 (>C=O), 1450 (ArC=C), 1252 (C-N). H^{1}NMR (300MHz, DMSO-d_6,δppm) : 2.45(s,3H,CH_3) 7.60-7.30 (m,Ar-H) ,10.12 (s,2H,2CHO). C^{13}NMR 187 (2CHO), 115 (C-N), 123-130 (Ar-CH), 52.9 (-CH_3). Elemental Analysis: Calculated C-52.92,H-3.05,N-33.22.Found,C-52.90,H-3.00,N-33.20.

General procedure for synthesis of 2,5-diamino-1-(N-substituted phenyl)-1H-pyrrol-3,4- dicarbaldehydes.
Sodium dithionite (6mmole) was added in portions to a stirred solution of 2,5-diazido-1-(N- substituted phenyl)-1H-pyrrole-3,4-dicarbaldehydes IVa-f(1mmole) in a mixture of methanol (15ml) and water (5ml).The solution was stirred at room temperature for 3-4 hrs. The reaction mixture was poured in to ice cold water. The precipitated solid was collected by filtration, washed well with water, dried and recrystallised from ethanol to get a pure 2-5-diamino-1-(N-substituted phenyl)-1H pyrrole-3,4-dicarbaldehydes.

(**Va) 2,5-diamino-1-phenyl-1H-pyrrole-3,4- dicarbaldehyde**.
Molecular formula : $C_{12}H_{11}O_2N_3$ Physical nature : whitish Yield(%) : 85% M.P(^{0}C) : 298 ^{0}C Molecular Weight : 229 IR(KBr)cm^{-1} : 3325-3138 (NH_2), 2852 (CHO), 1660 (>C=O), 1442 (Ar C=C), 1249 (C-N). H^{1}NMR (300MHz, DMSO-d_6,δppm) : 7.54-7 (m,Ar-H), 9.61 (CHO), 4.0 (-NH_2). C^{13}NMR **:** 191 (CHO), 119 (C-N), 120-130 (Ar-CH). Elemental Analysis: Calculated C-62.88,H-4.80,N-18.34.Found,C-62.80,H-4.75,N-18.30.

(**Vb) 2,5-diamino-1-(2-chloro phenyl)-1H-pyrrole-3-dicarbaldehyde**.
Molecular formula: $C_{12}H_{10}O_2N_3Cl$ Physical nature : whitish Yield(%) : 82 % M.P(^{0}C) : 300 ^{0}C Molecular Weight : 263.5 IR(KBr)cm^{-1} : 3355-3140 (NH_2), 2848 (CHO), 1661 (>C=O), 1448 (ArC=C), 1242 (C-N). H^{1}NMR(300MHz,DMSO-d_6,δppm) : 7.48-7 (m,Ar-H), 9.55 (CHO), 4.10 (-NH_2). C^{13}NMR : 198 (CHO), 112 (C-N), 125-135 (Ar-CH). Elemental Analysis: Calculated C-54.64,H-3.79,N-15.93.Found,C-54.60,H-3.75,N-15.90.

(Vc) 2,5-diamino-1-(4-chloro phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula: $C_{12}H_{10}O_2N_3Cl$ Physical nature : whitish Yield(%) : 75 % M.P(^{0}C) : 280 ^{0}C Molecular Weight : 263.5 IR(KBr)cm^{-1} : 3329-3139 (NH_2), 2858 (CHO), 1660 (>C=O), 1448 (ArC=C), 1245(CN). H^{1}NMR (300MHz, DMSO d_6,δppm) : 7.49-7 (m,Ar-H), 9.70 (CHO), 4.5 (-NH_2). C^{13}NMR : 189 (CHO), 122 (C-N), 128-138 (Ar-CH). Elemental Analysis: CalculatedC-54.64,H-3.79,N-15.93,Found,C-54.60,H-3.75,N-15.90.

(Vd) 2,5-diamino-1-(3-chloro phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula: $C_{12}H_{10}O_2N_3Cl$ Physical nature : whitish Yield(%) : 72 % M.P(^{0}C) : 305^{0}C Molecular Weight : 263.5 IR(KBr)cm^{-1} : 3315-3128 (NH_2), 2845 (CHO), 1670 (>C=O), 1440 (Ar C=C), 1241 (C-N). H^{1}NMR(300MHz,DMSO-d_6,δppm) : 7.59-7 (m,Ar-H), 9.61 (CHO), 4.8 (-NH_2). C^{13}NMR : 198 (CHO), 115 (C-N), 123-133 (Ar-CH). Elemental Analysis: Calculated C-54.64,H-3.79,N-15.93.Found,C-54.62,H-3.75,N-15.90.

(Ve) 2,5-diamino-1-(3-methoxy phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula: $C_{13}H_{13}O_3N_3$ Physical nature : whitish Yield(%) : 77 % M.P(^{0}C) : 310 ^{0}C Molecular Weight : 259 IR(KBr)cm^{-1} : 3324-3138 (NH_2), 2842 (CHO), 1666 (>C=O), 1446 (Ar C=C), 1250 (C-N). H^{1}NMR(300MHz,DMSO-d_6,δppm) : 7.46-7 (m,Ar-H), 9.68 (CHO), 4.8 (-NH_2). C^{13}NMR : 199 (CHO), 166 (C-N), 122-132 (Ar-CH). Elemental Analysis: Calculated C-60.23,H-5.01,N-16.21.Found,C-60.20,H-5.00,N-16.19.

(Vf) 2,5-diamino-1-(4-methyl phenyl)-1H-pyrrole-3,4-dicarbaldehyde.
Molecular formula: $C_{13}H_{13}O_2N_3$ Physical nature : whitish Yield(%) : 71 % M.P(^{0}C) : 315 ^{0}C Molecular Weight : 243 IR(KBr)cm^{-1} : 3325-3138 (NH_2), 2852 (CHO), 1660 (>C=O), 1442 (Ar C=C), 1249 (C-N). H^{1}NMR (300MHz, DMSO-d_6,δppm) : 7.54-7 (m,Ar-H), 9.61 (CHO), 4.0 (-NH_2). C^{13}NMR : 191 (CHO), 119 (C-N), 120-130 (Ar-CH). Elemental Analysis: Calculated C-64.25,H-5.34,N-17.28.Found,C-64.20,H-5.30,N-17.23.

General procedure for the synthesis of 2,7-diamino-9-(N-substituted phenyl)-9H-carbazole-3,6-dicarbonitriles.
Triethylamine (4mmole,0.40 gm) was added to a solution of 2,5-diamino-1-(N-substituted phenyl)-1H-pyrrole-3,4-dicarbaldehyde (1mmole) and malononitrile (2.5 mmole) in absolute ethanol (10 ml). The solution was stirred at

room temperature for 3 hrs. The resulting solid product was collected by filtration, dried and recrystallised from ethanol to afford a pure 2,7-diamino-9-(N-substituted phenyl)-9H-carbazole-3,6-dicarbonitriles.

(VIb) 2,7-diamino-9-(2-chloro phenyl)-9H-carbazole-3,6-dicarbonitrile.
Molecular formula: $C_{18}H_{10}N_7Cl$ Physical nature : whitish Yield(%) : 70 % M.P(^{0}C) : 295 ^{0}C Molecular Weight : 359.5 IR(KBr)cm^{-1} : 3335-3228 (NH_2), 2228 (CN), 1478 (Ar C=C), 1254 (C-N). H^1NMR(300MHz,DMSO-d_6, δppm) : 7.48-7 (m,Ar-H), 4.6 (s,4H,2NH_2). C^{13}NMR : 112 (CN), 159 (C-N), 123-133 (Ar-CH). Elemental Analysis: Calculated C-60.08,H-2.78,N-27.26. Found,C-60.00,H-2.75,N-27.24.

(VI-e) 2,7-diamino-9-(3-methoxy phenyl)-9H-carbazole-3,6-dicarbonitrile .
Molecular formula: $C_{19}H_{13}N_7OCl$ Physical nature : whitish Yield(%) : 72% M.P(^{0}C) : 140-145^{0}C Molecular Weight :390.5 IR(KBr)cm^{-1}: 3325-3220 (NH_2), 2225 (CN), 1472 (Ar C=C), 1244 (C-N). H^1NMR(300MHz,DMSO-d_6,δppm):7.54-7 (m,,Ar-H), 4.1 (s,4H,2NH_2). C^{13}NMR :117 (CN), 157 (C-N), 120-130 (Ar-CH). Elemental Analysis: Calculated C-58.38,H-3.32,N-25.09.Found,C-58.35,H-3.30,N-25.00,.

Table-1 shows physical data of compounds Synthesized:

Compounds	R	Molecular Formula	M.P(^{0}C)	Yield(%)
Iva	H	$C_{12}H_7O_2N_7$	68-70	72
IVb	2-Cl	$C_{12}H_6O_2N_7Cl$	44	73
IVc	4-Cl	$C_{12}H_6O_2N_7Cl$	93	71
IVd	3-Cl	$C_{12}H_6O_2N_7Cl$	46-50	90
IVe	3-OCH_3	$C_{13}H_9O_3N_7$	38-42	88
IVf	4-CH_3	$C_{13}H_9N_7O_2$	48-50	80
Va	H	$C_{12}H_{11}O_2N_3$	298	85
Vb	2-Cl	$C_{12}H_{10}O_2N_3Cl$	300	82
Vc	4-Cl	$C_{12}H_{10}O_2N_3Cl$	280	75
Vd	3-Cl	$C_{12}H_{10}O_2N_3Cl$	305	72
Ve	3-OCH_3	$C_{13}H_{13}O_3N_3$	310	77
Vf	4-CH_3	$C_{13}H_{13}N_3O_2$	315	71
VIb	2-Cl	$C_{18}H_{10}N_7Cl$	295	70
VIe	3-OCH_3	$C_{19}H_{13}N_7OCl$	140-145	72

BIOLOGICAL TESTING OF COMPOUNDS.
Heterocyclic diazido & diamino compounds IV(a-f),V(a-f),VI(a-b) were evaluated for antibacterial activity against Escherichia coli (Ec), Pseudomona aeruginosa (PA), Staphylococcus aureus (SA), and anti fungal activity against Bacillus subtillis (BS), Candida albicans (CA).

The results were obtained in the form of clearing zone and were after the period of incubation (37^{0c} for 24 hrs). The zone of inhibition was measured in mm and data is presented in table 2.

The Compounds IV d & e and V d & e showed moderate antibacterial activity against EC,PA & SA.Compounds IV a & b Showed antibacterial activity against SA & antifungal activity against BS.

Media used
For bacteria : Nutrient agar (Hi-media)
For yeast : MGYP
Inoculum size :
Bacteria : 1 x 10 bacteria per ml.
Yeast : 1 x 10 cells per ml
❖ concentration of compound
(Prepared in ethanol) 100 µ gm 1 disc
❖ method used
(disc method, disc size 6mm)
"__" means no zone of inhibition.

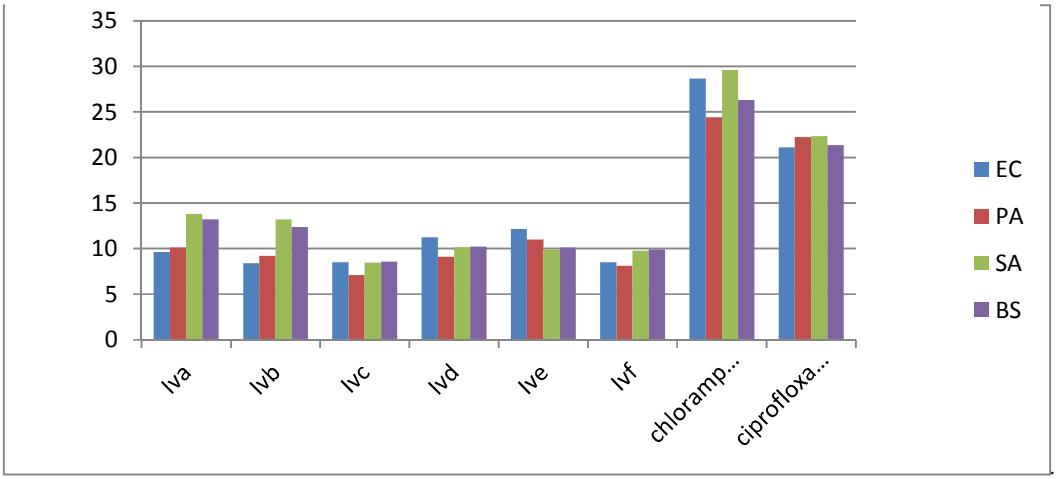
CULTURES USED:

	Culture name	Culture code
ES	*Escherichia coli*	NMC 1209
PA	*Pseudomonas aeruginosa*	NCIM 2036
SA	*Staphylococcus aureus*	NCIM 2079
BS	*Bacillus subtilis*	NICM 2250

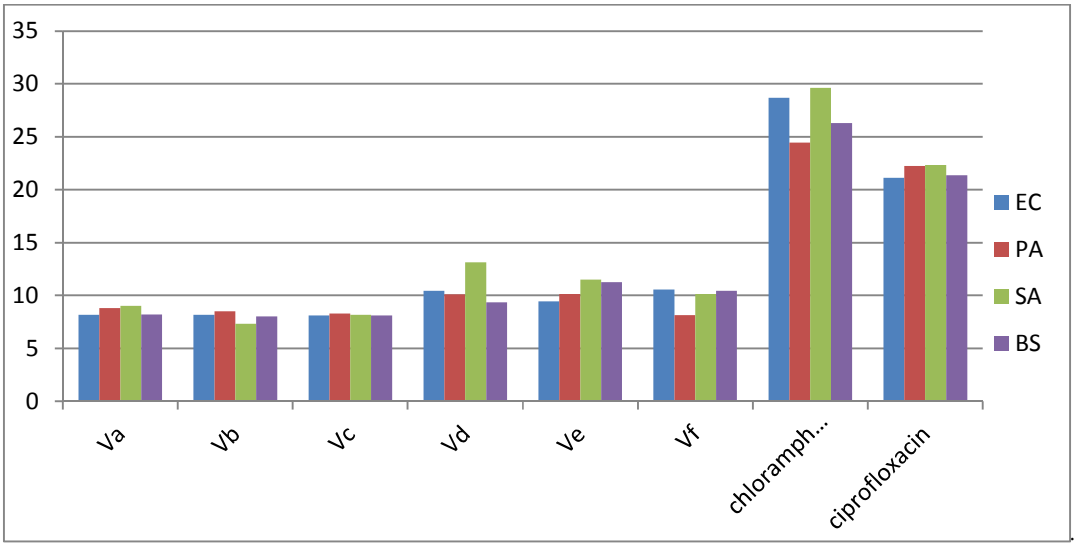
Table-2 Antimicrobial activity of compounds

Sr. No.	Compounds	EC	PA	SA	BS
1	IVa	9.61	10.12	13.81	13.23
2	IVb	8.4	9.23	13.21	12.36
3	IVc	8.5	7.11	8.46	8.56
4	IVd	11.23	9.12	10.14	10.23
5	IVe	12.14	11.01	9.89	10.11
6	IVf	8.5	8.12	9.75	9.89
7	Va	8.2	8.8	9.01	8.23
8	Vb	8.2	8.5	7.33	8.01
9	Vc	8.1	8.3	8.2	8.1
10	Vd	10.45	10.11	13.14	9.37
11	Ve	9.45	10.12	11.52	11.24
12	Vf	10.56	8.13	10.12	10.45
13	VIb	8.5	8.2	8.3	8.1
14	VIe	8.2	8.3	8.5	8.9
15	chloramphenicol	28.67	24.44	29.63	26.30
16	ciprofloxacin	21.11	22.23	22.33	21.34

Graph-1: comparative antimicrobial activity of compounds (Iva-f)



Graph-1: comparative antimicrobial activity of compounds (va-f)



CONCLUSION

In the above research work we conclude that, the diazido Derivatives are synthesized good yield. The Procedure can be employed for further synthesis of various heterocyclic system. The compounds were shows good to mild Anti microbial activity.

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