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Original Research Article

Synthesis, characterization and antibacterial activities of new substituted (1,3)oxazepine 1,5-diones

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ABSTRACT

Novel Imine were prepared via the reaction of (p-chloro and p-methyl)aniline with (p-nitro and p-methoxy) benzaldehyde and later engaged in a condensation reaction with 2-O-Acetylmalic anhydride in a dioxane as a solvent. The resulting products were found to be 1,3-oxazepine-1,5-diones and their derivatives. FT-IR, 1HNMR and C.H.N. spectra were used to confirm the structures of products. The antibacterial properties of these compounds were also examined.

Keywords:seven-member, antibacterial activities, 1,3-oxazepine, Imine (Schiff's Bases)

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Introduction:

Oxazepine has a seven-member unsaturated non-homologous ring containing two heteroatoms, oxygen and nitrogen, and five carbon atoms. [1] One sort of pericyclic reaction used to make 1,3-oxazepine was the cycloaddition process. [2] Several studies have found that imported Oxazepine compounds exhibit a wide range of biological actions, including antibacterial [3], antifungal [4], antitumor [5], anti-influenza [6], antianxiety[7], antipsychotic[8], anticonvulsant[9], anticancer [10], They also have anticorrosion properties[11]. The target of this research is to create novel (1,3) oxazepine 1,5-diones molecules, characterize them, The antibacterial properties of these compounds were also examined.

Material and Methods

The use of all chemicals was done without additional purification and they were all bought from Sigma-Aldrich. The infrared spectra were captured using a Tensor 27 Bruker, Germany spectrometer (spectral range: 4000-600 cm-1). The 1H NMR spectra were captured using DMSO-d6 as the solvent on a Bruker Ultershield 400 MHz NMR spectrometer in Germany. The C.H.N analyses were performed by Euro Ea Elemental Analyser.

Procedure for prepare of Schiff's Bases A_1-A_4

A solution of p-methylaniline or p-chloro aniline (0.01 mol) in Ethanol absolute (15 mL) was added to 50 mL round bottom flask containing appropriate aldehyde (0.01 mol) . Refluxing the mixture for three hours, After filtering, the precipitate was re-crystallized from ethanol. Table 1 provides a list of some of the physical characteristics of compounds prepared

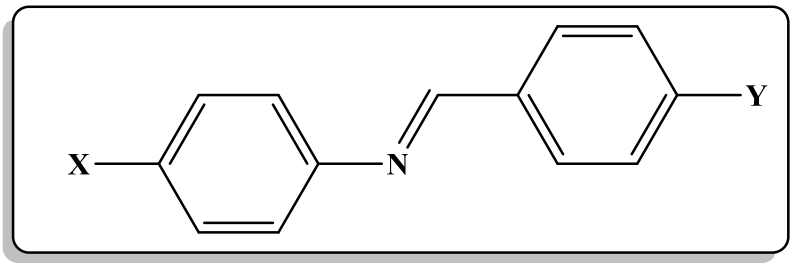


Table (1): Some of the Physical properties of compounds A1-A4

Com. Symb.	Yields					Colour
	Formula	X	Y	Mol.Wt.	%	
A_1	$C_{14}H_{12}ClNO$	Cl	OCH_3	245.71	74	white
A_2	$C_{13}H_9ClN_2O_2$	Cl	NO_2	260.68	83	Yellow
A_3	$C_{15}H_{15}NO$	CH_3	OCH_3	225.29	71	white
A_4	$C_{14}H_{12}N_2O_2$	CH_3	NO_2	240.26	79	Yellow

Procedure for prepare of 1,5-Disubstituted oxazepine

In a condenser-equipped, 100-ml round-bottom flask that has been thoroughly dried, a mixture of equivalent amount (0.001mole) of Schiff's bases A(1-4) and (0.001mole) of 2-O-Acetylmalic Anhydride in anhydrous Benzene (30 ml) was refluxed for (4 hr.). In an ice bath, the reaction mixture was allowed to cool. separated out some compounds as solid product during cooling, and some other as a Gummy. The product was washed in distilled water. and later dried and recrystallized from benzene. The chemical formula, Molar mass, yield %, melting points and colours, are given in table (2).

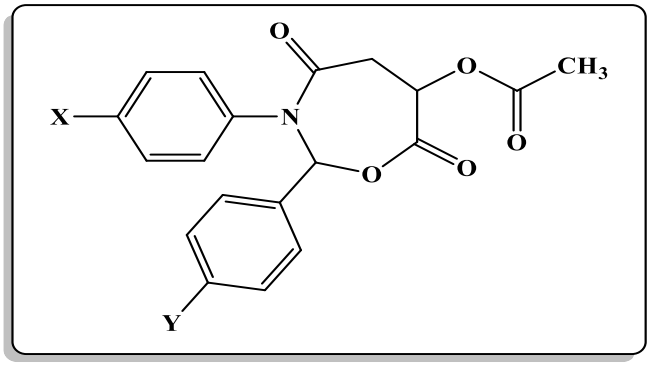
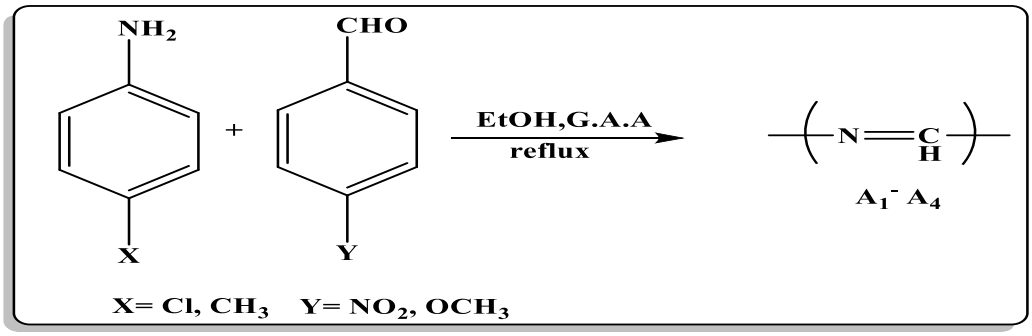


Table (2): The structural formula, yield, colors of compounds

Symb.	Yields					M.P. ^{O}C	Colour
	Formula	X	Y	Molar mass	%		
B_1	$C_{20}H_{18}ClNO_6$	Cl	OCH_3	403.28	76	Gummy	Brown
B_2	$C_{19}H_{15}ClN_2O_7$	Cl	NO_2	418.79	59	Gummy	Brown
B_3	$C_{21}H_{21}NO_6$	CH_3	OCH_3	383.40	78	Gummy	Brown
B_4	$C_{20}H_{18}N_2O_7$	CH_3	NO_2	398.37	68	Gummy	Brown

Results and Discussion

The reaction of anhydride derivatives as an electrophilic reagent with imines (Schiff's bases) as mild nucleophilic reagents is described in this paper. Schiff's bases were prepared using an acid catalyzed thermal condensation reaction with p-methylaniline or p-chloroaniline and an appropriate aldehyde, according to a well-known procedure.

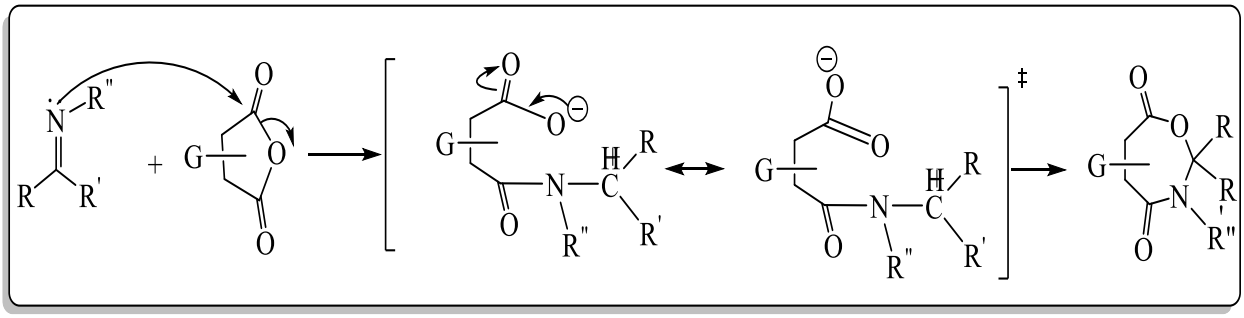


The mechanism of imine synthesis has been fully explained in the literature [12-13]. The structures of imine were confirmed by their FT-IR spectra which showed the disappearance and appearance of the characteristic absorption frequencies (bands) of the principal functional groups. According to the FT-IR spectra, the distinctive absorption frequencies of both (C=O) at (1720-1740) cm-1 and (-NH2) at (3300-3500) cm^{-1} vanished, of the primary amine and the aldehyde, respectively. and the occurrence of the stretching absorption bands of the azomethine group (C=N) at (1619-1625) cm^{-1}, in addition to the appearance of stretching absorption of the other groups in the structure of each individual compounds table (3).

Table (3): FT-IR data of imine compounds [A_1-A_4]

Comp.	υ C-H ar. st.	υ C=N st.	υ C=C st.		υ C-N st.	δ(C-H) Bending	Other cm^{-1}
A_1	3018	1619	1567	1477	1090	726, 838	2962 C-H al. st.
A_2	3099	1624	1597	1487	1008	713, 823	1371 C-NO_2 sy. 1340 C-NO_2 as.
A_3	3077	1621	1595	1504	1022	724, 835	2971 C-H al. st
A_4	3078	1625	1596	1514	1005	711, 836	1376 C-NO_2 sy. 1339 C-NO_2 as.

By mixing equivalent amounts of anhydride derivatives in anhydrous Benzene and refluxing under dry conditions, the reaction of anhydride derivatives with a variety of Schiff's bases was studied. The reaction's plausible reaction mechanism was described as follows:



In this work, the (2+5) polar cycloaddition reaction of Schiff's Bases as mild nucleophile to 2-O-Acetylmalic Anhydride as electrophile in anhydrous Benzene is reported. The structures of the synthesized oxazepine were confirmed by the FT-IR spectra which showed the disappearance and appearance of the characteristic absorption frequencies (bands) of the principal functional

groups. The FT-IR spectra showed the disappearance of the characteristic absorption frequencies of azomethine group (C=N) at (1619-1625) cm^{-1}, and the appearance of the stretching absorption bands of (C=O lactone) at (1750-1765) cm^{-1}, (C=O lactame) at (1673-1711) cm^{-1}in addition to the appearance of stretching absorption of the other groups in the structure of each individual compounds Figure 1 and Figure 2 : IR spectrum of compound B_1, . ^{1}HNMR spectra confirm the structures of synthesized compounds. Figure 3 and Figure 4: ^{1}H NMR spectrum of B_{1-4} .[14-16]

Table (4): FT-IR data of 1,3-oxazepines derivatives

Comp.	υ C-H ar. st.	υ C=O lactone	υ C=O lactame	υ C=C ar. st.		υ C-N st.	δ(C-H) Bending	Other cm^{-1}
B_1	2998	1750	1673	1572	1522	1090	739, 858	2962 C-H al.st.
B_2	3104	1761	1680	1596	1517	1010	739, 851	1400 C-NO_2 sy. 1341 C-NO_2 as.
B_3	3075	1765	1709	1591	1515	1018	718, 837	2992 C-H al. st.
B_4	3021	1759	1711	1600	1518	1008	739, 842	1400 C-NO_2 sy. 1344 C-NO_2 as.

Table (5): Chemical Shift δ (ppm) and (C.H.N.)analysis of 1,3-oxazepines derivatives

Comp.	Formula	M.Wt (g/mole)	Chemical Shift δ ppm	C.H.N % Calculated (Found)		
				C%	H%	N%
B_1	$C_{20}H_{18}ClNO_6$	403.82	(1Hs) δ=8.07 (N-C-H), (8Hm)δ=7.09-7.64 (-C-$H_{arom.}$), (1Hm)δ= 5.59-5.60 (O-C-H) (3H s) δ= 4.07 (OCH_3) (2H d) δ= 2.94-2.97 ($CH_{2\ ring7}$) (3H s) δ= 1.72 (O=C-CH_3)	59.49 (58.87)	4.49 (4.27)	3.47 (2.84)
B_2	$C_{19}H_{15}ClN_2O_7$	418.79	(1Hs) δ=8.15 (N-C-H), (8Hm)δ=6.88-7.58 (-C-$H_{arom.}$), (1Hm)δ= 5.19-5.21 (O-C-H) (2H d) δ= 3.66-3.68 ($CH_{2\ ring7}$) (3H s) δ= 2.11 (O=C-CH_3)	54.49 (53.76)	3.61 (2.93)	6.69 (5.59)
B_3	$C_{21}H_{21}NO_6$	383.40	(1Hs) δ=8.18 (N-C-H), (8Hm)δ=6.92-7.18 (-C-$H_{arom.}$), (1Hm)δ= 6.11-6.14 (O-C-H) (3H s) δ= 4.03 (OCH_3) (2H d) δ= 3.27-3.29 ($CH_{2\ ring7}$) (6Hs)δ=2.68(O=C-CH_3),(Ar-CH_3)	65.79 (63.79)	5.52 (4.93)	3.65 (3.09)
B_4	$C_{20}H_{18}N_2O_7$	398.37	(1Hs) δ=7.98 (N-C-H), (8Hm)δ=7.09-7.77 (-C-$H_{arom.}$), (1Hm)δ= 5.56-5.60 (O-C-H) (2H d) δ= 2.92-2.95 ($CH_{2\ ring7}$) (6Hs)δ=2.68(O=C-CH_3),(Ar-CH_3)	60.30 (60.79)	4.55 (3.93)	7.03 (6.89)

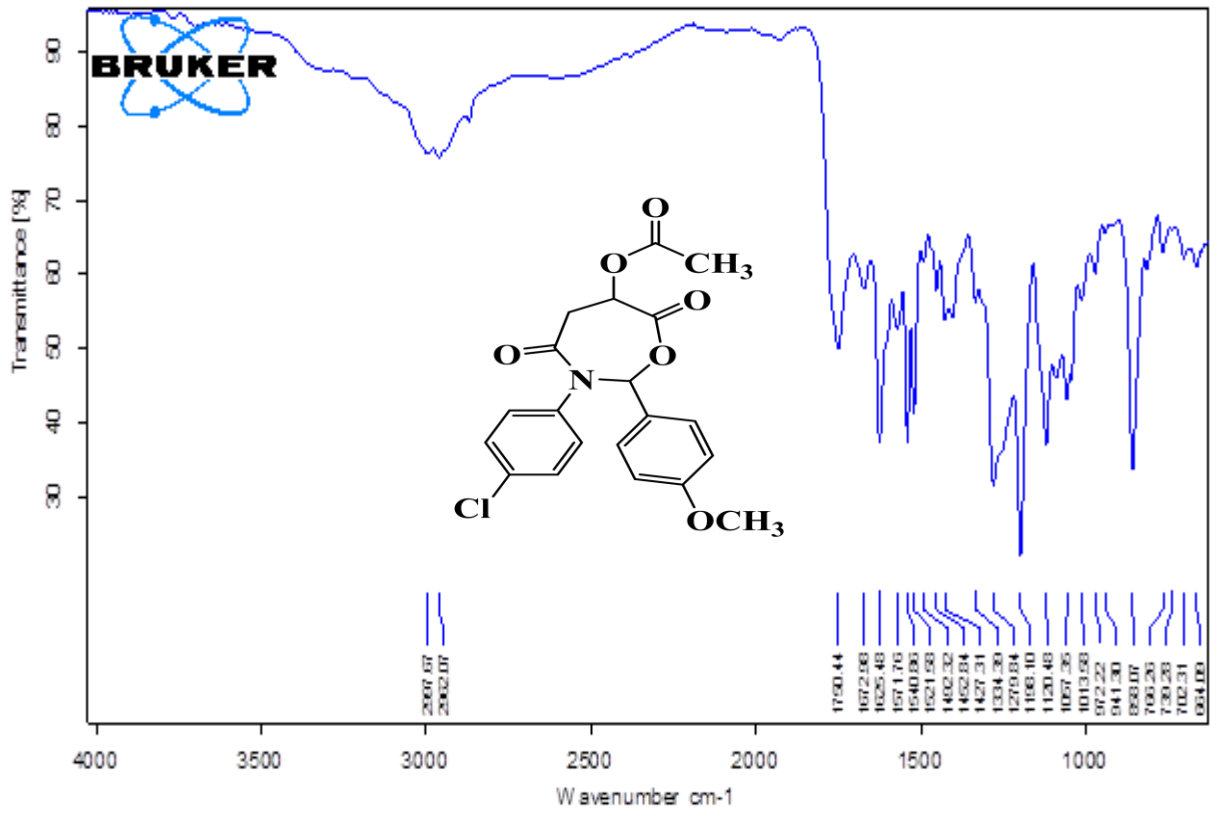


Figure 2: IR spectrum of compound B_1.

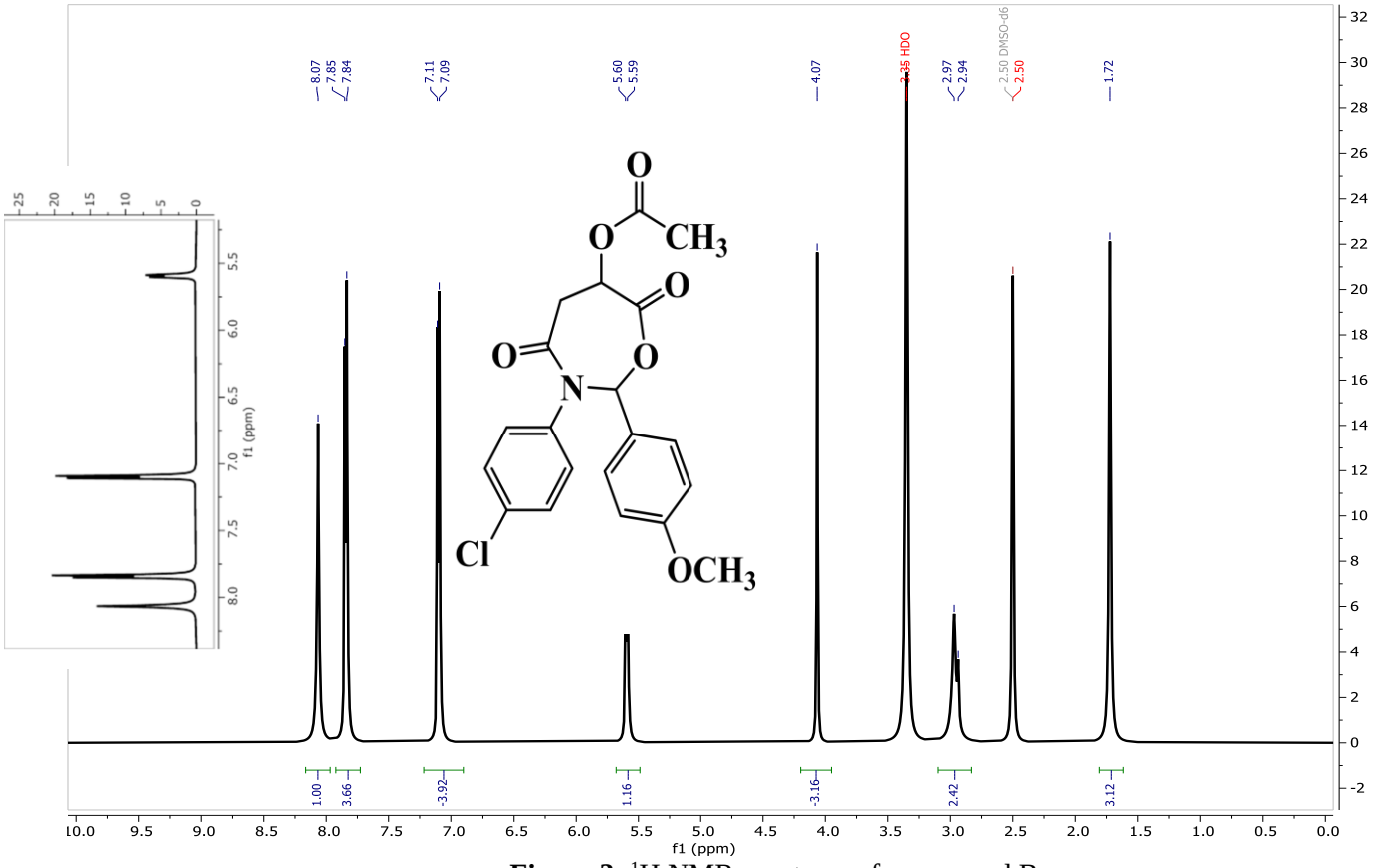


Figure 3: ^{1}H NMR spectrum of compound B_1.

Biological Activity against Bacteria

The heterocyclic derivatives of 1,3-oxazepines have been shown to have antibacterial action against a variety of bacteria, including E. coli, S. aureus, and P. aregenosa. utilizing nutritional agar medium and the well diffusion method. Each substance was suspended in aqueous solutions at various concentrations (10–100 mg/mL), Solvent blanks were used in all assays against each test organism, and the results are represented as MICs (minimal inhibitory concentrations). The experimental biological data is shown in Table 6.

Table 6: Antibacterial activity data of the heterocyclic derivatives of 1,3-oxazepines

Comp.	E. coli	S. aureus	P. aregenosa
B_1	22	21	22
B_2	23	21	19
B_3	17	19	20
B_4	20	20	18
Antibiotics	---------	---------	---------
Ampicillin	23	20	21
Vibromycin	24	22	20

Conclusions

In this work, the new substituted 1,3- oxazepine-4,7-dione derivatives were prepared successfully by using various substituted Schiff's bases . The 1,3-oxazepines has been evidenced by spectral analysis. The substances' antibacterial efficacy against several types of bacteria was assessed, and they shown similar activity to that of conventional medications.

References:

1. N. A. J A- Al-awwadi,. B. A. H. Alsaffee, M. M.Abdulridha, *African Journal of Pharmacy and Pharmacology* 10, 728 (2016).
2. W. F. Al-Hiti, M. A.Saeed, *International Journal of Humanities, Arts, Medicine and Science* 5, 65 (2017).
3. I.K. Jassim, A. M.Ali, Journal of Education and Scientific Studies-Chem Sci. 12,172 (2018).
4. R. F. Muslim, H. M. Tawfeeq, M. N. Owaid, O. H. Abid, *Acta. Pharm. Sci.* 56,39 (2018)
5. D.uni, C.Ranjitha, M.Rama, K. S. R.Pai, *International Journal of Innovative Research in Science, Engineering and Technology* 3, 15357 (2014)
6. A. O. H. El-Nezhawy, A. F. Eweas, I. A.Maghrabi, A. S. Edalo, S. F. Abdelwahab, *Arch. Pharm. Chem. Life Sci.* 348,786 (2015)
7. D. K. Mahapatra, R. S. Shirhare, S. D.Gupta, , *Asia J. Res. Pharm. Sci.* 8, 25 (2018)

8. F.Naporra, S.Gobleder, H.Wittmann, J.Spindler, M.Bodensteiner, G.Berhardt, H.Hubner, P.Gmeiner, S.Elz, A. Strasser, *Pharma Cological Research* 113,610 (2016)
9. M.Sahu, A. G.Nerka, H. U. Chikhale, S. D. Sawant, *Journal of Young Pharmacists* 7,21 (2015)
10. M.S.Al-Rawi, D.F.Hussei, A. F. Al-Taie, M.M. Al-Halbosiy, B. A. Hameed, *IOP Conf. Series: Journal of Physics: Conf. Series* 1003,1 (2018)
11. K.F. Hamak, H.H.Eissa, *International Journal of ChemTech Research* 5, 2924 (2013).
12. William, H. Brown, B.L. Iverson, E.V. Anslyn, C.S.F. "Organic Chemistry", 7th Ed., Wadsworth Cengage Learning. (2014)
13. J.Mcmurry, "Organic Chemistry", 9th Ed., CENGAGE Learning (2016).
14. L.D.S.Yadav, Organic Spectroscopy, Springer Science,Business Media Dordrech, Springer-Science. Business Media, B.V. (2005).
15. L.Donald Pavia, M.Gary Lampman, S.George, R. James Vyryan, *Introduction to spectroscopy, 4th Ed., Brooks\ cole cengage Learning*, 16,104 (2009).
16. M. Robert Silverstein, X. Francis Webster, J. David Kiemle, *spectrometric Identification of Organic compounds, 7th Ed, John- Wiley & Sons, INC.*, 72,126 (2005).

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