Synthesis, silico and Antibacterial Activity Studies of 2-((substituted phenyl) amino)methyl)-5-ethyl-4-((5-(4-nitrophenyl)furfural-2-yl)methylene)amino)-2,4-dihydro-3H-1,2,4-triazole-3-thiones)) Hybrids

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Abstract : A series of 2-((substituted phenyl)amino)methyl)-5-ethyl-4-((5-(4-nitrophenyl)furfural-2-yl)methylene)amino)-2,4-dihydro-3H-1,2,4-triazole-3-thiones)) were synthesised and tested for antimicrobial activity. According to the findings, compounds with a fluorine substituent at the para position had a significant antibacterial effect against B.substilis and A.aerogenes. The structure of newly synthesised compounds was determined using spectral data. C=N stretching was observed in IR spectra at 1710 Cm^{-1} and NH stretching was observed at 1589 Cm^{-1}, whereas these Chiral carbons appeared as a doublet in NMR spectra.

Keywords : Triazole, furfural and schiff's bases

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Introduction

Mannich bases, beta-amino ketones carrying compounds, are the end products of Mannich reaction [1, 2]. Mannich reaction is a nucleophilic addition reaction which involves the condensation of a compound with active hydrogen(s) with an amine (primary or secondary) and formaldehyde (any aldehyde) .[3] Mannich bases also act as important pharmacophores or bioactive leads which are further used for synthesis of various potential agents of high medicinal value which possess aminoalkyl chain. The examples of clinically useful Mannich bases which consist of aminoalkyl chain are cocaine, fluoxetine, atropine, ethacrynic acid, trihexyphenidyl, procyclidine, ranitidine, biperiden [4–6], and so forth. Mannich bases are known to play a vital role in the development of synthetic pharmaceutical chemistry. The literature studies revealed that Mannich bases are very reactive and can be easily converted to other compounds, for example, reduced to form physiologically active amino alcohols [7]. Mannich bases are known to possess potent activities like anti-inflammatory [8, 9], anticancer [10, 11], antifilarial [8], antibacterial [12, 13], antifungal [13, 14], anticonvulsant [15], anthelmintic [16], antitubercular [17, 18], analgesic [19], anti-HIV [17], antimalarial [20], antipsychotic [21], antiviral [22] activities and so forth. Along with biological activities Mannich bases are also known for their uses in detergent additives [23], resins, polymers, surface active agents [24], and so forth. Prodrugs of Mannich bases of various active compounds have been prepared to overcome the limitations [25]. Mannich bases (optically pure chiral) of 2-naphthol are employed for catalysis (ligand accelerated and metal mediated) of the enantioselective carbon-carbon bond formation. Mannich bases and their derivatives are intermediates for the synthesis of bioactive molecules [26, 27]. Mannich reaction is widely used for the construction of nitrogen containing compounds [28]. Mannich bases have gained importance due to their application in antibacterial activity [29] and other applications are in agrochemicals such as plant growth regulators.

Materials and methods

Melting points of final products were measured on a Shimadzu-Gallenkamp apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DX instrument (Billerica, USA) (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR); $CDCl_3$ and DMSO-d_6 were used as solvent; chemical shifts are quoted in δ (ppm) from tetramethylsilane. Mass spectra were measured on a GCMS-QP1000EX (EI, 70 eV) mass spectrometer. Starting materials were obtained from Aldrich (Mumbai, India) and used directly

Procedure

Synthesis of 3-methyl -4-amino-5-mercapto-1,2,4-triazole (1):

A mixture of thiocarbohydrazide (0.094 mole, 10g) in glacial acetic acid (60ml) was refluxed for 4 hours. Within an hour of refluxing a solid mass started separating out. It was collected by filtration and recrystallized from hot water.[28]

Synthesis of 5- substituted -2-furfural derivatives (2):

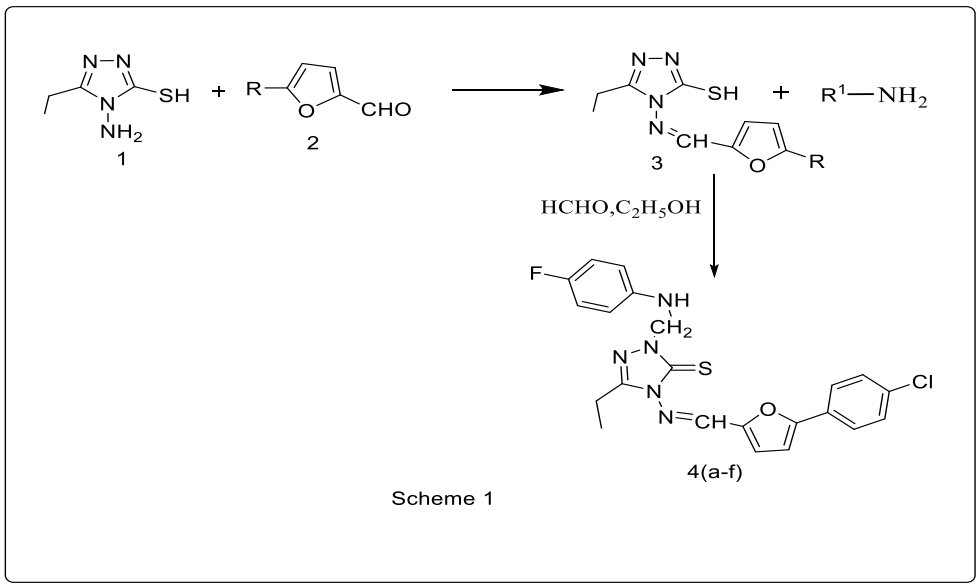
To a warm solution of halo-substituted aniline (0.1mole, 9.3ml) in 15% hydrochloric acid (60ml), water (90ml) was added. The mixture heated until it is clear, cooled to 0 0C, and diazotized with a 30% solution of sodium nitrite (24ml). To the filtered solution water (50ml) and furfuraldehyde (11.2ml,0.1mol) were added. An aqueous solution of cupric chloride (0.018mole,2.55g) was added drop wise and the mixture stirred for four hours at 20- 30 ^{0}C and kept overnight. The solid that separated was collected by filtration and purified by steam distillation in the presence of sodium carbonate solution to give 5-substituted -2-furfural moiety and derivatives were synthesised by changing the substituents[29]

Synthesis of Schiff Bases (3) :

Schiff bases were prepared by the refluxing mercapto triazoles(0.1mole,13g) with 5-substituted 2-furfuraldehyde (0.1mole) in the presence of catalytic amount of concentrated sulphuric acid(1ml) in ethanol medium(20ml) for 4hrs.Then reaction mixture was poured to Ice cold Water , Solid that was Separated was collected by filtration and it is recrystallized by ethanol and derivatives were synthesised by changing the substituents.[30]

Synthesis of Mannich Bases (4a-f):

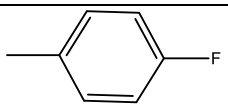
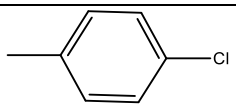
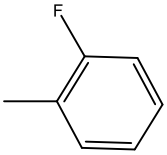
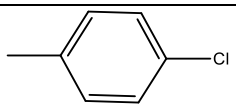
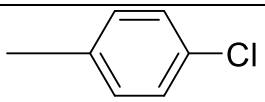
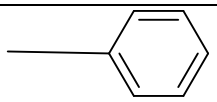
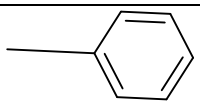
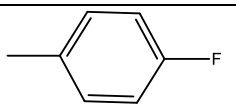
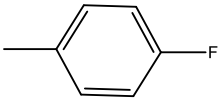
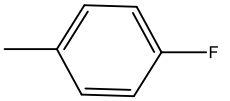
Mannich bases were prepared by the reaction of Schiff's bases(0.05mole), formaldehyde (40%) and a suitable primary or secondary amine (0.05mole) in ethanol medium (30ml) stirred for 5hrs and Solid obtained was filtered and recrystallized from ethanol and derivatives were synthesised by same procedure by changing the substituents at different Position. [31]

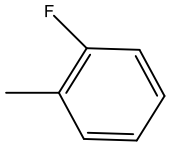
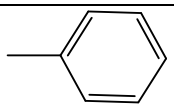


Scheme 1

Table 1

Characterisation data of4-(((5-(substitutedphenyl)furan-2-yl)methylene)amino)-5-ethyl-2-(((substituted phenyl)amino)methyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione

Compound Number	R	R^1	Color and Crystal Form	Melting point
4a			Yellow Crystals	126^0C
4b			Yellow Crystals	135^0c
4c			Yellow Flakes	156^0C
4d			Yellow Flakes	163^0C
4e			Yellow Micro Needles	106^0C

4f			**Orange Crystals**	**103^{0}C**

Spectral data of synthesised Compounds

Compound 4a :

^{1}H NMR: δ 1.11 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.62 (2H, s), 6.62 (1H, d, *J* = 3.5 Hz), 6.80-7.03 (4H, 6.87 (d, *J* = 8.4, 1.6, 0.5 Hz), 6.97 (d, *J* = 8.4, 1.9, 0.5 Hz)), 7.11 (1H, d, *J* = 3.5 Hz), 7.59-7.76 (4H, 7.65 (d, *J* = 8.7, 1.5, 0.5 Hz), 7.69 (d, *J* = 8.7, 1.5, 0.5 Hz)), 8.59 (1H, s).

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 112.6 (1C, s), 115.6 (2C, s), 118.2 (2C, s), 127.4 (2C, s), 128.7 (2C, s), 129.1 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 138.7 (1C, s), 149.1 (1C, s), 150.1 (1C, s), 155.2 (1C, s), 162.5 (1C, s), 177.4 (1C, s).

IR (KBr, cm^{-1}): 1726(νC= N), 1587(ν NH), 1552(νC = C), 1022(νCN–C).

Compound 4b:

^{1}H NMR: δ 1.11 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.58 (2H, s), 6.62 (1H, d, *J* = 3.5 Hz), 6.81-7.16 (5H, 6.87 (d, *J* = 7.8, 1.7, 0.5 Hz), 6.95 (d, *J* = 8.1, 1.1, 0.5 Hz), 6.97 (d, *J* = 8.1, 7.5, 1.7 Hz), 7.01 (d, *J* = 7.8, 7.5, 1.1 Hz), 7.11 (d, *J* = 3.5 Hz)), 7.59-7.76 (4H, 7.65 (d, *J* = 8.7, 1.5, 0.5 Hz), 7.69 (d, *J* = 8.7, 1.5, 0.5 Hz)), 8.59 (1H, s).

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 111.8 (1C, s), 112.6 (1C, s), 121.2 (1C, s), 126.0 (1C, s), 127.4 (2C, s), 128.2 (1C, s), 128.7 (2C, s), 129.1 (1C, s), 129.3 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 149.1 (1C, s), 150.1 (1C, s), 151.1 (1C, s), 155.2 (1C, s), 177.4 (1C, s).

IR (KBr, cm^{-1}): 1716(ν C= N), 1584(ν NH), 1551(ν C = C), 1021(ν CN–C).

Compound 4c:

^{1}H NMR: δ 1.10 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.62 (2H, s), 6.60-6.79 (3H, 6.65 (d, *J* = 3.5 Hz), 6.72 (d, *J* = 8.3, 1.6, 0.5 Hz)), 7.13 (1H, d, *J* = 3.5 Hz), 7.28-7.49 (5H, 7.35 (t, *J* = 7.2, 1.9, 1.3 Hz), 7.42 (d, *J* = 7.8, 7.2, 1.2, 0.4 Hz), 7.43 (d, *J* = 8.3, 1.7, 0.5 Hz)), 7.88 (2H, d, *J* = 7.8, 1.5, 0.4 Hz), 8.54 (1H, s).

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 112.6 (1C, s), 120.5 (2C, s), 125.7 (2C, s), 127.8 (1C, s), 128.4 (2C, s), 128.9 (2C, s), 129.1 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 138.7 (1C, s), 149.1 (1C, s), 150.1 (1C, s), 155.2 (1C, s), 177.4 (1C, s).

IR (KBr, cm^{-1}): 1716(ν C= N), 1584(ν NH), 1551(ν C = C), 1021(ν CN–C).

Compound 4d:

^{1}H NMR: δ 1.11 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.66 (2H, s), 6.57 (1H, d, *J* = 3.5 Hz), 6.88 (1H, t, *J* = 8.1, 1.2 Hz), 6.98-7.32 (7H, 7.04 (d, *J* = 8.3, 1.2, 0.5 Hz), 7.11 (d, *J* = 3.5 Hz), 7.15 (d, *J* = 8.8, 1.3, 0.5 Hz), 7.24 (d, *J* = 8.3, 8.1, 1.4, 0.5 Hz)), 7.64 (2H, d, *J* = 8.8, 1.5, 0.5 Hz), 8.59 (1H, s).

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 112.6 (1C, s), 115.4 (2C, s), 119.9 (2C, s), 124.9 (2C, s), 127.8 (1C, s), 128.2 (2C, s), 129.1 (1C, s), 133.7 (1C, s), 138.7 (1C, s), 149.1 (1C, s), 150.1 (1C, s), 155.2 (1C, s), 162.5 (1C, s), 177.4 (1C, s).

IR(KBr,Cm^{-1}): 1699(ν C= N),1502(ν NH),1534(ν C = C),1011(ν CN–C).

Compound 4e:

^{1}H NMR: δ 1.11 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.62 (2H, s), 6.57 (1H, d, *J* = 3.5 Hz), 6.80-7.03 (4H, 6.87 (d, *J* = 8.4, 1.6, 0.5 Hz), 6.97 (d, *J* = 8.4, 1.9, 0.5 Hz)), 7.05-7.22 (3H, 7.11 (d, *J* = 3.5 Hz), 7.15 (d, *J* = 8.8, 1.3, 0.5 Hz)), 7.64 (2H, d, *J* = 8.8, 1.5, 0.5 Hz), 8.59 (1H, s)

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 112.6 (1C, s), 115.4 (2C, s), 115.6 (2C, s), 118.2 (2C, s), 124.9 (2C, s), 129.1 (1C, s), 133.7 (1C, s), 138.7 (1C, s), 149.1 (1C, s), 150.1 (1C, s), 155.2 (1C, s), 162.4-162.6 (2C, 162.5 (s), 162.5 (s)), 177.4 (1C, s).

IR (KBr, cm^{-1}): 1713(νC= N), 1582(ν NH), 1553(νC = C), 1024(νCN–C).

Compound 4f

^{1}H NMR: δ 1.11 (3H, t, *J* = 7.3 Hz), 2.45 (2H, q, *J* = 7.3 Hz), 4.58 (2H, s), 6.65 (1H, d, *J* = 3.5 Hz), 6.81-7.18 (5H, 6.87 (d, *J* = 7.8, 1.7, 0.5 Hz), 6.95 (d, *J* = 8.1, 1.1, 0.5 Hz), 6.97 (d, *J* = 8.1, 7.5, 1.7 Hz), 7.01 (d, *J* = 7.8, 7.5, 1.1 Hz), 7.13 (d, *J* = 3.5 Hz)), 7.28-7.49 (3H, 7.35 (t, *J* = 7.2, 1.9, 1.3 Hz), 7.42 (d, *J* = 7.8, 7.2, 1.2, 0.4 Hz)), 7.88 (2H, d, *J* = 7.8, 1.5, 0.4 Hz), 8.54 (1H, s).

^{13}C NMR: δ 11.4 (1C, s), 18.7 (1C, s), 57.6 (1C, s), 107.9 (1C, s), 111.8 (1C, s), 112.6 (1C, s), 121.2 (1C, s), 125.7 (2C, s), 126.0 (1C, s), 127.8 (1C, s), 128.2 (1C,

s), 128.4 (2C, s), 129.1 (1C, s), 129.3 (1C, s), 133.7 (1C, s), 149.1 (1C, s), 150.1 (1C, s), 151.1 (1C, s), 155.2 (1C, s), 177.4 (1C, s).

IR (KBr, cm^{-1}): 1718(ν C= N), 1585(ν NH), 1558(ν C = C), 1026(ν CN–C).

Biological Activity

All as of late set up blends were thought about for antibacterial action in contrast to B.Subtilis and A.aerogenes by using plate scattering technique[23] The circles of each obsession were placed in three-overlap on supplement agar medium developed with new bacterial social orders independently. The agonizing was finished at 37^0c for 24 hrs.

Compound Number	**Minimum Inhibitory concentration Mg/disk (diameter of Zone of inhibition in mm)**	
	B.s	**A.nor**
4a	5(10.2)	5(9.7)
4b	<5(7.4)	5(8.2)
4c	5(11.4)	10(10.2)
4d	10(9.2)	<5(7.1)
4e	<5(7.8)	5(9.1)
4f	5(9.1)	5(8.6)

Screening impact showed that Compound Containing Fluorine at para position showed more dynamic than other comparative mixtures tried against B.Substilis and A.aerogenes.

Result and discussion

A series of 4-(((5-(substitutedphenyl)furan-2-yl)methylene)amino)-5-ethyl-2-(((substituted phenyl)amino)methyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione were synthesised and they screened for antibacterial movement against B.Subtilis and A.aerogenes by utilizing plate dispersion method. Hence we found that compounds containing fluorine at para position showed significant activity than other substituents.

References:

1. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, John Wiley & Sons, New York, NY, USA, 3rd edition, 1985.
2. V. J. Belinelo, G. T. Reis, G. M. Stefani, D. L. Ferreira-Alves, and D. Piló-Veloso, "Synthesis of 6*α*,7*β*-dihydroxyvouacapan-17*β*-oic acid derivatives. Part IV: mannich base derivatives and its activities on the electrically stimulated guinea-pig ileum preparation," *Journal of the Brazilian Chemical Society*, vol. 13, no. 6, pp. 830–837, 2002.
3. S. Joshi, N. Khosla, and P. Tiwari, "In vitro study of some medicinally important Mannich bases derived from anti-tubercular agent," *Bioorganic & Medicinal Chemistry*, vol. 12, no. 3, pp. 571–576, 2004.
4. L. Racane, V. T. Kulenovic, L. F. Jakic, D. W. Boykin, and G. K. Zamola, "Synthesis of bis -substituted amidino-benzothiazoles as potential anti-HIV agents," *Heterocycles*, vol. 55, pp. 2085–2098, 2001.
5. E. Kashiyama, I. Hutchinson, M.-S. Chua et al., "Antitumor benzothiazoles. 8.1 Synthesis, metabolic formation, and biological properties of the *C*- and *N*-oxidation products of antitumor 2-(4- aminophenyl)-benzothiazoles," *Journal of Medicinal Chemistry*, vol. 42, no. 20, pp. 4172–4184, 1999.
6. S. R. Bhusare, R. P. Pawar, and Y. B. Vibhute, "Synthesis and antibacterial activity of some new 2-(substituted phenyl sulfonamido)-6-substituted benzothiazoles," *Indian Journal of Heterocyclic Chemistry*, vol. 11, no. 1, pp. 79–80, 2001.
7. N. Raman, S. Esthar, and C. Thangaraja, "A new Mannich base and its transition metal (II) complexes—synthesis, structural characterization and electrochemical study," *Journal of Chemical Sciences*, vol. 116, no. 4, pp. 209–213, 2004.

8. B. Kalluraya, R. M. Chimbalkar, and J. C. Hegde, "Anticonvulsant activity of nicotinyl\isonicotinyl substituted 1,2,4-triazol-5-thione Mannich bases," *Indian Journal of Heterocyclic Chemistry*, vol. 15, no. 1, pp. 15–18, 2005.

9. M. Köksal, N. Gökhan, E. Küpeli, E. Yesilada, and H. Erdogan, "Analgesic and antiinflammatory activities of some new Mannich bases of 5-nitro-2-benzoxazolinones," *Archives of Pharmacal Research*, vol. 30, no. 4, pp. 419–424, 2007.

10. Y. Ivanova, G. Momekov, O. Petrov, M. Karaivanova, and V. Kalcheva, "Cytotoxic Mannich bases of 6-(3-aryl-2-propenoyl)-2(3*H*)-benzoxazolones," *European Journal of Medicinal Chemistry*, vol. 42, no. 11-12, pp. 1382–1387, 2007.

11. H. I. Gul, J. Vepsalainen, M. Gul, E. Erciyas, and O. Hanninen, "Cytotoxic activities of mono and bis Mannich bases derived from acetophenone against Renca and Jurkat cells," *Pharmaceutica Acta Helvetiae*, vol. 74, no. 4, pp. 393–398, 2000.

12. M. Ashok, B. S. Holla, and B. Poojary, "Convenient one pot synthesis and antimicrobial evaluation of some new Mannich bases carrying 4-methylthiobenzyl moiety," *European Journal of Medicinal Chemistry*, vol. 42, no. 8, pp. 1095–1101, 2007.

13. S. N. Pandeya, D. Sriram, G. Nath, and E. De Clercq, "Synthesis, antibacterial, antifungal and anti-HIV activities of norfloxacin Mannich bases," *European Journal of Medicinal Chemistry*, vol. 35, no. 2, pp. 249–255, 2000.

14. B. N. Singh, S. K. Shukla, and M. Singh, "Synthesis and biological activity of sulphadiazine Schiff's bases of isatin and their N-mannich bases," *Asian Journal of Chemistry*, vol. 19, no. 7, pp. 5013–5018, 2007.

15. S. C. Vashishtha, G. A. Zello, K. H. Nienaber et al., "Cytotoxic and anticonvulsant aryloxyaryl Mannich bases and related compounds," *European Journal of Medicinal Chemistry*, vol. 39, no. 1, pp. 27–35, 2004.

16. E. Bennet-Jenkins and C. Bryant, "Novel sources of anthelmintics," *International Journal for Parasitology*, vol. 26, no. 8-9, pp. 937–947, 1996.

17. D. Sriram, D. Banerjee, and P. Yogeeswari, "Efavirenz Mannich bases: synthesis, anti-HIV and antitubercular activities," *Journal of Enzyme Inhibition and Medicinal Chemistry*, vol. 24, no. 1, pp. 1–5, 2009.

18. J. S. Mulla, A. Y. Khan, S. I. Panchamukhi, M. A. Khazi, M. B. Kalashetti, and I. M. Khazi, "Synthesis and antitubercular activity of Mannich bases of imidazo [2,1-b] [1,3,4] thiadiazoles," *Indian Journal of Novel Drug Delivery*, vol. 3, no. 4, pp. 289–295, 2011.

19. W. Malinka, P. Świątek, B. Filipek, J. Sapa, A. Jezierska, and A. Koll, "Synthesis, analgesic activity and computational study of new isothiazolopyridines of Mannich base type," *Farmaco*, vol. 60, no. 11-12, pp. 961–968, 2005.

20. G. B. Barlin and C. Jiravinya, "Potential antimalarials . X. Di- Mannich Bases of 4-(7'-Trifluoromethyl-1',5'-naphthyridin-4'-ylamino)phenol and N-(4'-Diethylamino-1'-methylbutyl)-7-trifluoromethyl-1,5-naphthyridin-4-amine," *Australian Journal of Chemistry*, vol. 43, no. 7, pp. 1175–1181, 1990.

21. M. K. Scott, G. E. Martin, D. L. DiStefano et al., "Pyrrole mannich bases as potential antipsychotic agents," *Journal of Medicinal Chemistry*, vol. 35, no. 3, pp. 552–558, 1992.

22. M. L. Edwards, H. W. Ritter, D. M. Stemerick, and K. T. Stewart, "Mannich bases of 4-phenyl-3-buten-2-one: a new class of antiherpes agent," *Journal of Medicinal Chemistry*, vol. 26, no. 3, pp. 431–436, 1983.

23. R. E. Karll and R. J. Lee, "Process and compositions," US Patent no. 4,384,138, 1983.

24. F. P. Otto, US Patent, US 3 649 229, 1972.

25. J. R. Dimmock and P. Kumar, "Anticancer and cytotoxic properties of Mannich bases," *Current Medicinal Chemistry*, vol. 4, no. 1, pp. 1–22, 1997.

26. J.-X. Ji, L.-Q. Qiu, C. Wing Yip, and A. S. C. Chan, "A convenient, one-step synthesis of optically active tertiary aminonaphthol and its applications in the highly enantioselective alkenylations of aldehydes," *The Journal of Organic Chemistry*, vol. 68, no. 4, pp. 1589–1590, 2003.

27. P.-J. J. Huang, D. Youssef, T. S. Cameron, and A. Jha, "Microwave-assisted synthesis of novel 2-naphthol bis-Mannich Bases," *Arkivoc*, vol. 2008, no. 16, pp. 165–177, 2008.

28. M. Arend, B. Westermann, and N. Risch, "Modern variants of the Mannich reaction," *Angewandte Chemie—International Edition*, vol. 37, no. 8, pp. 1045–1070, 1998.

29. B. S. Holla, M. K. Shivananda, M. S. Shenoy, and G. Antony, "Studies on arylfuran derivatives. Part VII. Synthesis and characterization of some Mannich

bases carrying halophenylfuryl moieties as promising antibacterial agents," *Farmaco*, vol. 53, no. 8-9, pp. 531–535, 1998

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