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ReviewArticle

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view Article
Medicinal Uses of Mannich Bases

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Introduction

The Mannich Reaction is used in the synthesis of natural products and pharmaceuticals. Therefore in this review we discuss the medicinal uses of Mannich bases with examples in the medicinal field. A large number of different bioactivities of Mannich bases are anticonvulsant, antimalarial, anticancer, analgesic and antimicrobial drugs. Also Mannich bases are used as prodrugs.

Application

The Mannich reaction is one of the most important C-C bond formation methods in organic synthesis **(Sharifi, *et. al* , 2001).** The Mannich-reaction is employed in the organic synthesis of natural compounds like, for instance, peptides, nucleotides, antibiotics and alkaloids. Other application are in agrochemicals such as plant growth regulators, paint and other polymer chemistry, catalysts and crosslinking and is used in the synthesis of medicinal compounds **(Dimmock, 1997)**.

Key word: Mannich reaction, medicinal uses, prodrugs

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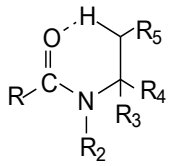
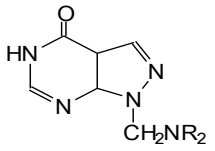
Prodrug uses

The Mannich bases are used as potential prodrugs of NH-acidic compounds. Interamolcular hydrogen bonding between the amine proton and the carbonyl oxygen hinders the solvation of the polar group of molecule and the solubility of drugs increases **(Guarino, and Stella 2004; Jezierska and Panket, 2007).**



Dissolution rate for drugs Allopurinol (**1**), Carbamazepine (**2**) and Rolitetracycline (**3**), was improved using N-Mannich bases derivatization **(Guarino, and Stella, 2004).**



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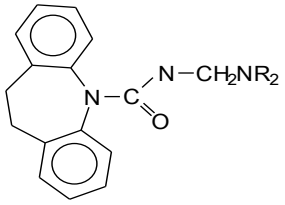

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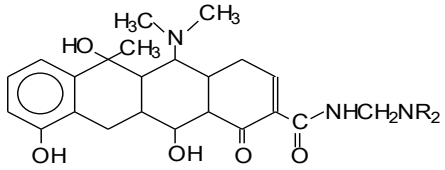

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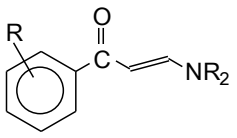
Anticancer activity

A series of mono Mannich bases derived from acetophenone like 1-aryl-5-dimethylamino-1-penten-3-one hydrochloride (**4**), and 1-aryl-3-diethylamino-1-propane hydrochloride (**5**), and corresponding bis-Mannich bases (**6**) were synthesized as an anti-cancer agent **(Dimmock. et-al 1998; Gul, *et. al* , 2000).**



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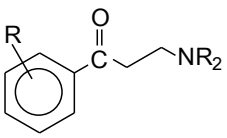

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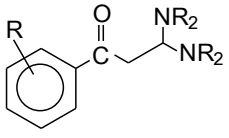

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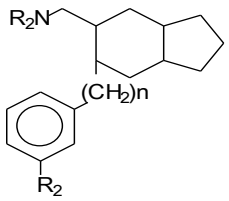
Analgesic activity

β-amino ketones like α-alkyl-β-dimethylaminopropiophenone **(Daruwala, *et. al* , 1974),** β-amino ketones derived from l-(N-p-hydroxyethyl-4-piperidyl)-3-(4-piperidyl) propane **(Varma and Obles, 1968),** a series of 6(alkylamino)methylhexahydro-5-arylmethanoindan-5-ols(**7**) alkyl-4,7-methanoindan-5-ols(**8**)Tramadol(**9**), **(Aboul-enein 1993)** a series of 3-{1-[4'-carbethoxy-4'-(R-) phenyl]-piperidino-propiophenones (**10**), **(Janssen, *et. al* , 1959)** exhibited slight analgesic effect.



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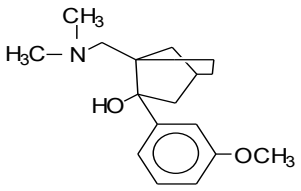

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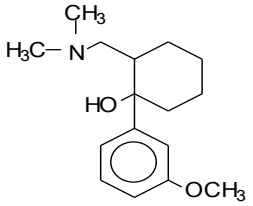

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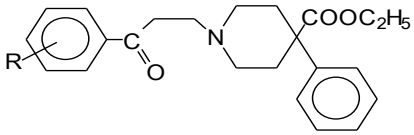

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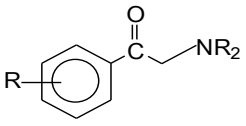
Anticonvulsant activity

Mono-Mannich bases 3-amino-1-aryl-propanone (**11**) , N,N'-bis(3-amino-1-aryl- propylidene) hydrazine **(Gul, etal, 2002), (12**) and 3-hydroxy-6-methyl-2-aminomethyl 4H-pyran (**13**), **(Aytemir, 2007),** were synthesized as anticonvulsant agent.



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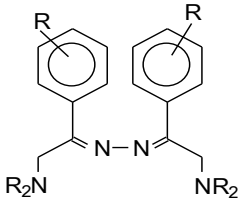

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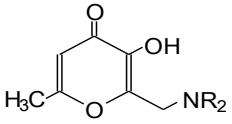

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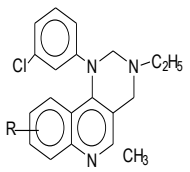
Antimalarial

1-(3-chloropheny1)-3,9-dimethyl-3-ethyltetrahydropyrimido[5,4c]quinoline (**14**), **(Nasr, *et. al*, 1978),** novel artemisinin derivatives bearing Mannich base (**15**) **(Li, *et. al*, 2003),** new series of 4-aminoquinoline Mannich base derivatives (**16**) **(Raynes, etal, 1999)** and series of 4-

[(7-chloro-4-quinolinyl)amino]-2-[(di-ethylamino)methyl]-6-alkylphenols (**17**) **(Kesten, etal, 1987)** were synthesized as anti-malaria agents.



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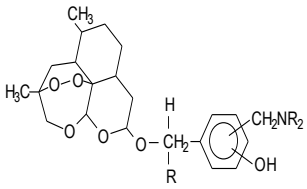

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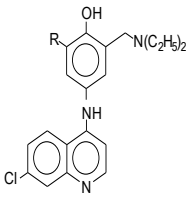

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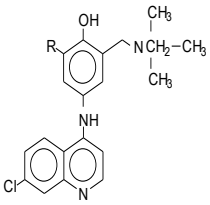

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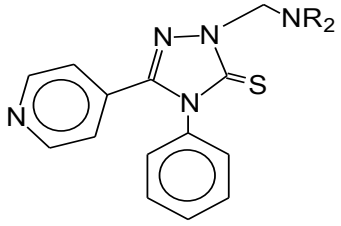
Antimicrobial

Mannich base derivatives of 4-phenyl-5-pyridin-4-yl-4H-1,2,4-triazole-3-thiol (**18**) **(Bayrak, etal, 2008),** alkoxymethyl-dimethyl{2-hydroxy-5-[(4-X-phenyl)azo]benzyl}ammonium chlorides, (**19**) **(Pernak, and Kmiecik, 1999)** were synthesized as antimicrobial agents.



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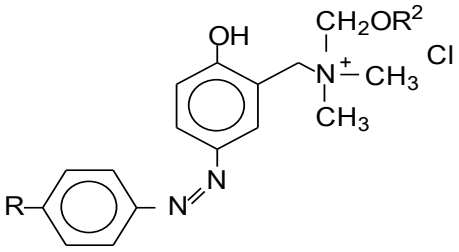

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Conclusion

In this work we reviewed the medicinal uses of Mannich bases and we summarized the biological activities of the Mannich bases in medicinal field with examples.

References

1. **Aboul-enein. M. N., El-Azzouny. A. A., Aballah. N. A., Moharam. S. Werner. W, Eid. A. and Makhluf. A. A**., *Journal of IslamiAcademy of Sciences*, **6**, 99, (1993).
2. **Aytemir. M. D. and Çalış. U**. *Hacettepe University Journal of the Faculty of Pharmacy,* **27**, 1, (2007).
3. **Bayrak. H., Demirbas. A., Karaoglu. S. A. and Demirbas. N.**, *European*

Journalof Medicinal Chemistry xx, 10, (2008).

4. **Dimmock, J. R., Vashishtha, C. R., J.Quail, W., Pugazhenthi, U., Z and Zimpel, Sudom, A. M., Allen, T. M., Kao, G. Y., Balzarini. J., and De Clercq**; *J. Med. Chem.,***41**, 4012,(1998).
5. **Dimmok, J. R., Kumar, p., Quial, J. W., Pugazhenthi, U., Yng. J., Chen, M., Reid R. S., Allen, T. M., Kao, G. Y., Cole, S. P. C., Batist, G., Delia. T. J. Scovill. J. P. and Munslow. W. D.** *Journal of Medicinal Chemistry,* **19**, 344, 1976.
6. **Daruwala, A. B. Gearien, J. A., Dunn, W. J. Benoit, P. S. and Bauer, L.**; *Journal of Medicinal Chemistry,***17**, 819, (1974).
7. **Gul. H. I., Vepsalainen. J. Gul. M., Erciyas. E., Hanninen. O**.,*Pharmaceutica Acta Helvetiae*, **74**, 393, (2000).
8. **Gul, H. I., Calisb, U. and Vepsalainen, J**., Drug Res., **52**, 863, (2002).
9. **Verkade, J. M. M., Hemert, L. J. C., Quaedflieg, P. L. M. and Rutjes, F. J. T**., *Chem. Soc. Rev*., **37**, 29, (2008).
10. **Jezierska. A., and Panek, A. J**., *J. Chem. Theory Comput.***1**, (2007).
11. **Janssen. P. A. J. Jagneau. A. H. M., Demoen. P. J., Alfons. C. V. W., Raeymaekers. H. M., Wouters. M. J. W, Sanczuk. S, Hermans. B. F. and Loomans. J. M.***Journal of Medicinal and Pharmaceutical Chemistry*, **1**, 106, (1959).
12. **Kesten. S J., Johnson. J. and Werbel. L. M**., *J. Med. Chem.*, **30**, 906., (1987).
13. **Li. Y., Yang. Z., Zhang. H., Cao. B., Wang. F., Zhang. Y., Shi. Y., Yangb. J. and Wu, B**., *Bioorganic & Medicinal Chemistry***11**, 4363, (2003).
14. **Nasr, M., Nabih, I. and Burckhalter. J. H.** *Journal of Medicinal Chemistry,***21**, 295,(1978).
15. **Pernak. J., Mirskab. I., Kmiecika. R**. *Eur. J. Med. Chem.* 34, 765, (1999).
16. **Raynes. K. J., Stocks. P. A., Neill. P. M., Park. B. K. and Ward. S. T.**, *J. Med. Chem.,***42**, 2747, (1999).
17. **Sharifi A., Mirzaei, M. and Naimi-Jamal. M.**
18. **R**.,*Monatshefte für Chemie*. 132, 875, (2001).
19. **Varma, R. S. and Nobles, W. L**., *J. Org. Chem*., **195**, (1968).