

Reaction of Thiols with formaldehyde in Presence of succinimide and Reduction of Phenyl Tetrazole Derivative with Hydrogen and Borohydraide

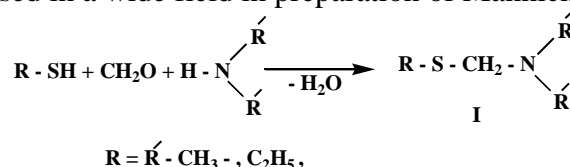
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Received 29, February, 2009

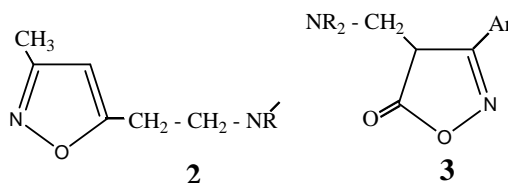
Accepted 10, January, 2010

Abstract:

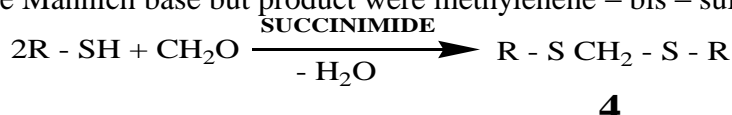
One of most the important compounds which have active hydrogen (substrate) is the thiols which used in a wide field in preparation of Mannich bases .



A large number of Mannich bases have been prepared as a biologically active compound (pharmaceutical, pesticides, bactericidal, fungicidal and tuberculostatic) and in order to correlate their structure and reactivity with their pharmacological activity such as .

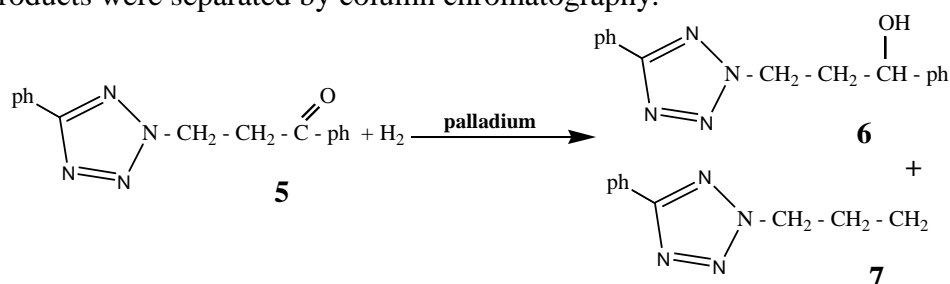


It has been reported that the reaction is easily proceeded by using primary and secondary amine beside formaldehyde. But when we tried the reaction of thiols as substrate and formaldehyde and succinimide instead of amine, the reaction did not proceed to give Mannich base but product were methylenene – bis – sulfide .



Mannich base can go farther reaction such as (addition, substitution, cleavage, polymerization, hydrogenation) to produce numerous number of compound so we tried to hydrogenate tetrazole derivative which gave different product which depended on type of hydrogen on reagent.

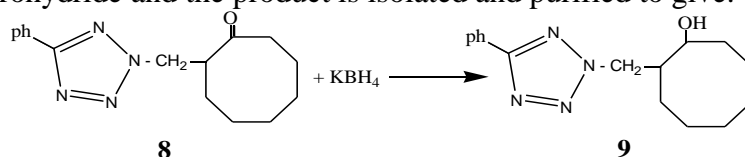
Reduction of 2 – ethyl benzoyl – phenyl tetrazole which performed with hydrogen gas in methanol solution in presence palladium on carbon as catalyst, the two products were separated by column chromatography.



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Reduction of 2-methyl-2-(2-cycloheptane)-5-phenyl tetrazole.

The methanolic solution the ketone was refluxed with equimolar amount of potassium borohydride and the product is isolated and purified to give.



and identified by C.H.N analysis and NMR spectra.

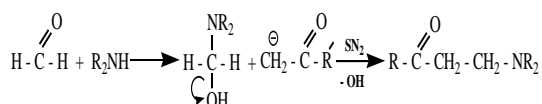
Key words: Phenyl Tetrazole, Reaction, formaldehyde, Thiols, succinimid

Introduction:

Mechanism of Mannich reaction :

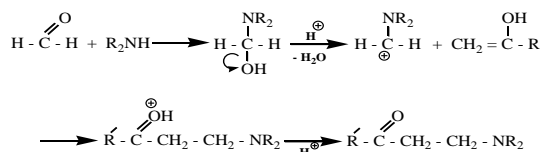
The mechanism of Mannich reaction has been well investigated in different pH media, because the reaction can be carried out in basic or acidic

condition and the used substrate and the amine reactant decide what condition is preferred.



Base – catalyzed reaction:

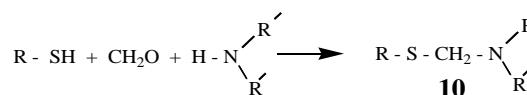
The base – catalyzed reaction appears to involve the reaction of a carbanion (derived from the active hydrogen compound) with the aminomethylol by an SN₂ mechanism. The rate increase at higher pH – value.



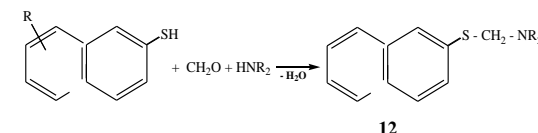
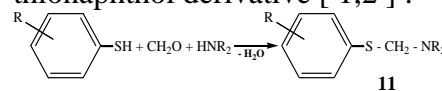
The reaction in acid media appears to involve the reaction of carbonium ion (derived from aminomethylol) with the active hydrogen compound. The rate is slower than for the reaction in basic media and is independent of pH at low pH values.

It has been reported than various thiophenols were used as the substrate in S – aminomethylation

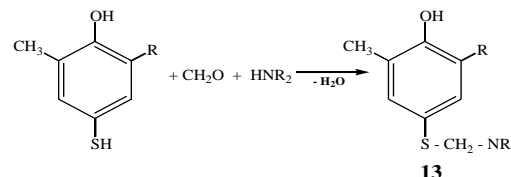
reaction carried out with ammonia and the primary or secondary and tertiary Mannich bases (10).



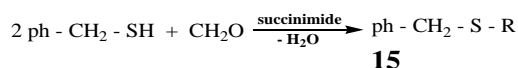
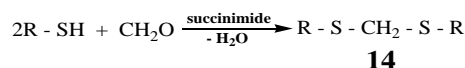
the most frequently used for the reaction were thiophenol and thionaphthol derivative [1,2] .



Similar results were obtained with thiols. The Mannich bases were usually prepared by refluxing a mixture of thiols with formaldehyde and secondary amines for 30 min. secondary amine and formaldehyde in methanol yielding Benzylthiols (methylene –N– dyaikyl) Thiol.[3,4] .



An attempted synthesis of Mannich bases from thiols, formaldehyde and secondary amine we found the reaction give methylene – bis – sulfide instead of Mannich bases.



The known procedure for ethylene – bis phenyl sulfide preparation involve reaction of methylene chloride with reaction of thiol and formaldehyde.

According to the literature strong acid of hydrochloric acid is recommended and the mechanism of the reaction with succinimide is different. Here also a primary Mannich base formed from the thiol, formaldehyde and succinimide can react with excess of the thiol yielding the methylene – bis – sulfide [5,6,7,8].

Material; and Methods

1- Preparation of methylene – bis – sulfide

General procedure for the reaction of thiols with formaldehyde in presence of succinimide. 0.08 mole of formaldehyde and 0.08 mole of succinimide or methylacetamide were suspended in 50 ml of appropriate thiols. The mixture refluxed for 10 hours, the excess of thiols was evaporated under reduced pressure to dryness. The residue was purified and recrystallized with hexane.

Results:

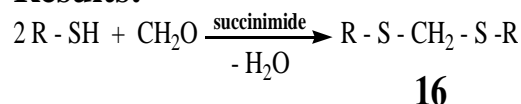


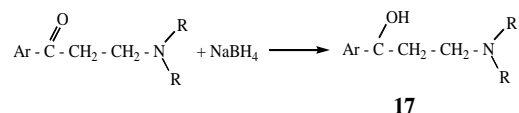
Table 1:Yield and properties to the synthesized methylene – bis – sulfide (16)

No.	Molecular formula	R	Yield	m.p* ^c		analysis		HNMR CoCl ₃ S(ppm)
						C	H	
1	C ₁₅ H ₁₆ S ₂	C ₆ H ₅ CH ₂ -	87	53	calc foun	69.23 69.16	6.15 6.31	3.39 (S, 2H) 3.66 (S4H) 7.26 – 7.3 (m, 10H)
2	C ₁₃ H ₁₂ S ₂	C ₆ H ₅ -	72	40	calc foun	67.24 67.46	5.10 5.26	4.34 (S, 2H) 7.23 (m, 10H)

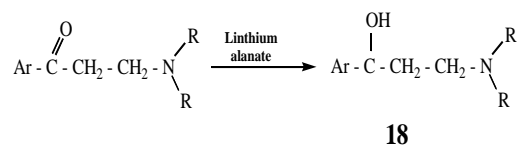
2- Reduction of 2 – ethylbenzoyl – S – phenyltetrazole:

3- It has been reported in literature that two types of product can be formed by reduction of ketonic Mannich bases with different types of reducing agent – besides the usual reagent (hydrogen and catalyst, zinc and acid) some novel reducing agent have been recently introduced including the chloride in an acidic medium, some borohydride and tri – butyltin hydride [9,10,11,12].

Excellent results were obtained by using sodium borohydride in alcohol as a reducing agent. Thus 2 – primary and secondary ethylaryl ketone were converted into the corresponding β – aminoalcohols by sodium borohydride (17).



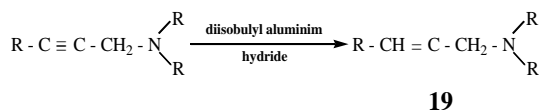
In some cases, 2 – aminoethylaryl ketone can be reduced to corresponding 1 – amino – 3 – arylpropanol by using Lithium alanate [10]. (18).



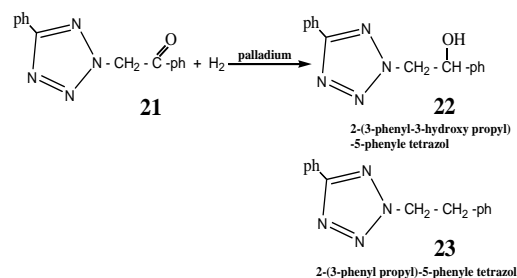
The same results was obtained by using acatalytic hydrogenation of the aminoethyl ketone. The reduction of acetylenic Mannich bases displays several interesting aspect. Thus the triple bond can be only partially hydrogenated with diisobutyl

aluminum hydride yielding allyamine [13,14,15].

If reduction of acetylenic Mannich bases methyl iodide carried out with a metal hydride an allen is produced (19).



The reduction of 2-ethylbenzoyl-5-phenyl tetrazole [16, 17] which performed in methanol solution in the presence of palladium on carbon as a catalyst. The mixture was shaken under 40 ps hydrogen pressure for 6 hrs. The resultant reaction mixture showed two product on TLC-plate. After separation by Colum chromatography the product were defined.



The two product were separated by Colum chrotography.

Elental analysis and NMR spectra for the two products of reduction of (21)

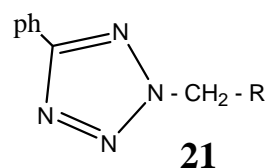


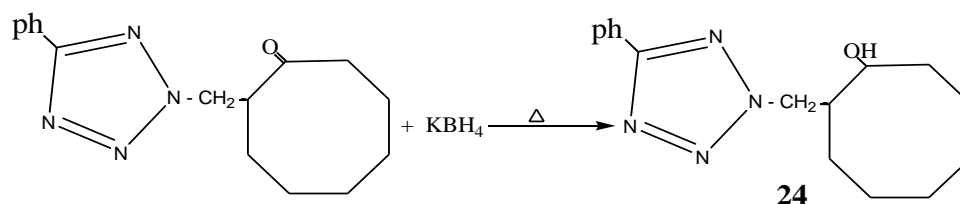
Table 1: Yield and properties the product methl [(2-y) cyclohexane]-5-phenyl tetrazole.

No.	Molecular formula	R		analysis			HNMR CoCl ₃ S(ppm)
				C	H	N	
1	C ₁₆ H ₁₆ N ₄ O		calc. foun.	68.57 68.12	5.71 5.43	20.00 19.65	1.9(S,1H). 2.46(dd,2H). 4.83 - 4.93 (m,1H). 7.2 - 7.47 (m,8H). 8.11 - 8.15 (m,2H).
2	C ₁₆ H ₁₆ N ₄		calc. foun.	67.24 67.46	5.10 5.26	21.21 21.01	2.37 - 2.42 (m,2H). 2.71 (t,2H) J=7.5 Hz 4.64 (t,2H) J=7.5 7.21 - 7.50 (m,8H). 8.17 - 8.19 (m,2H).

Reduction of 2-methyl (2-y 1-1 cycloheptanone) - 5 phenyltetrazole by potassium borohydride.

An attempted catalytic hydrogenation of 2-methyl (2-y) - 1 - cycloheptanone) - 5 phenyltetrazole. Under the same condition failed. Neither increase of the hydrogen pressure nor extension of the reaction

time did not give the positive result. In this case the borohydride reduction was method of choice. The methanolic Solution of the starting ketone was refluxed with equimolar amount of potassium borohydride for eight hours a typical work up the resulting alcohol was obtained.



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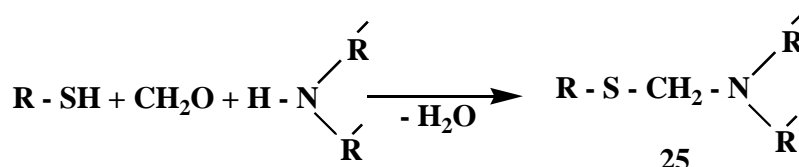
تفاعل الثايولات مع الفورملدهايد بوجود السكنتاميد واختزال مشتقات الفينيل تترازول مع الهيدروجين وهيدريد البورون

عبد الفارس حسين حاجم*

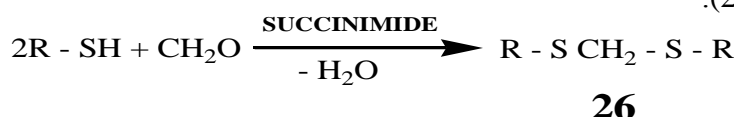
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الخلاصة:

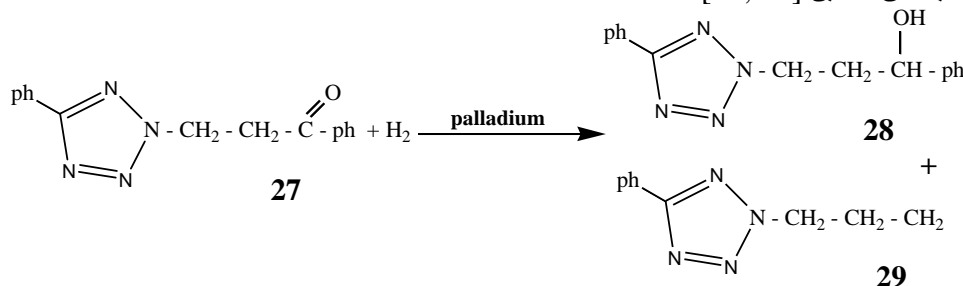
ان المواد التي تستعمل بوصفها اساسيات والتي تحتوي على هيدروجين فعال في تحضير (قاعدة مانخ) هي الثايولات وتستعمل بنجاح بوصفها مواداً اولية باضافة الفورملدهايد والامينات الاولية والثانوية ونشرت بحوث عديدة في الوقت الحاضر عن هذا الموضوع (25).



وفي بحثنا هذا عندما اردنا استعمال الثايول بوصفها مادة اساسية وباضافة السكنتاميد بدل الامينات واطافة الفورملدهايد لم نحصل على (قاعدة مانخ) وانما كان الناتج هو methylenene – bis – sulfide (26).



وتم تحضير مجموعة من هذه المشتقات والتأكد منها بإجراء التحاليل المختلفة. ان اهم ما تصف به (قاعدة مانخ) هي القابلية على التفاعلات المختلفة ومنها (الاضافة، الاستبدال، الكسر، الهدرجة والبلمرة) لاعطائها لمواد جديدة لا يمكن تحضيرها بالطرائق التقليدية. وقد تمت هدرجة مشتقات الفينيل تترازول في هذا البحث واعطت نتائج مختلفة باعتمادها على المادة المستعملة بالهدرجة (الهيدروجين مع عامل مساعد أو KBH_4 وقد فصلت المواد الناتجة ونقيت واخذت وعند القيام بهدرجة (27) ethyl benzoyl – phenyl tetrazole – 2 بواسطة الهيدروجين وبوجود عامل مساعد اعطت خليط من مادتين [29, 28].



وتم فصل المادتين بواسطة جهاز Colum chromatography باستخدام السلكاجيل والسلكوهكسان بوصفه مذيباً وتم اجراء التحاليل اللازمة.

وكذلك تمت هدرجة (30) 2 – methylcycloheptan – 1 – one – 5 – phenyltetrazole فشلت الهدرجة بواسطة الهيدروجين والعامل المساعد حتى في زيادة وقت التفاعل ولكن باستخدام مادة potassium borohydride تمت الهدرجة بسهولة وقد تم فصل الناتج والتأكد منه بواسطة التحاليل المختلفة.

