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СИНТЕЗ НЕКОТОРЫХ НЕПРЕДЕЛЬНЫХ ПРОИЗВОДНЫХ БЕНЗОТРИАЗОЛА В УСЛОВИЯХ РЕАКЦИИ ВИТТИНГА

Аннотация: *Олефиновые производные бензотриазола синтезированы в условиях реакции Уиттинга. Оптимизация условий соответствующей реакции была получена: основная среда этоксида натрия при комнатной температуре в течение 2 часов. Синтезированные соединения были очищены хроматографией, затем идентифицированы с помощью спектроскопии. Наибольший выход полученных изомеров был транс.*

Ключевые слова: *бензотриазол, реакция Уиттинга, соли фосфония, ароматические альдегиды*

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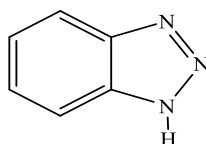
SYNTHESIS OF SOME UNSATURATED DERIVATIVES OF BENZOTRIAZOLE IN WITTING REACTION CONDITIONS

Annotation: *Olefin derivatives of benzotriazole have been synthesized in Witting Reaction conditions. Optimizing the conditions of the corresponding reaction has been obtained those are a base medium of sodium etoxide at room temperature for 2hours. The synthesized compounds have been purified by chromatography then have been identified by spectroscopies. The most yield of the produced isomers was trans.*

Key words: *benzotriazole, Witting Reaction, phosphonium salts, aromatic aldehydes.*

1. Introduction:

Benzotriazole is an important heterocyclic compound figure (1), many factors made benzotriazole a synthetic catalyst of great importance in the reactions of organic-synthesis, this importance appeared when the scientist Alan Katertsky and his group (in 1987) studied the preparation and properties of heterocyclic compounds [1,2].



m p =95-98°C

pKa=8

MW=119

Figure. 1 chemical structure of benzotriazole.

Where benzotriazole plays the role of a nucleophilic and an electrophilic depending on the substrate with which it reacts, it is also an important reactant in dozens of organic reactions as it reacts easily and can be removed from the organic compound easily / good leaving group /.

Benzotriazole is a Versatile Synthetic Auxiliary that it **easy enters** into other molecules in several ways, including: condensation, and addition substitution reactions as it **easily enters** and leaves in nucleophilic substitution reactions [3, 4].

Therefore, benzotriazole was used in many of interactions to obtain some important compounds such as amino ketones, aldehydes, β -keto-esters and other products of addition and substitution, since benzotriazole is a good leaving group, especially compared to the cyanide and sulfo groups [4,5], Also one of the important addition reactions that benzotriazole enters. “ Michael addition “ that can reacted with enoles e enamate, amides, phenylsulfoxide, benzotriazole is stable , and exhibits desirable physical and innocuous biological properties and / **intermediate compound**

And benzotriazole can play a role as a donor or receiver of electrons depending on the nature of the exchanges with which it is connected and according to the nature of these exchanges, benzotriazole can be ionzaited as shown in figure (2) [6,7,8].

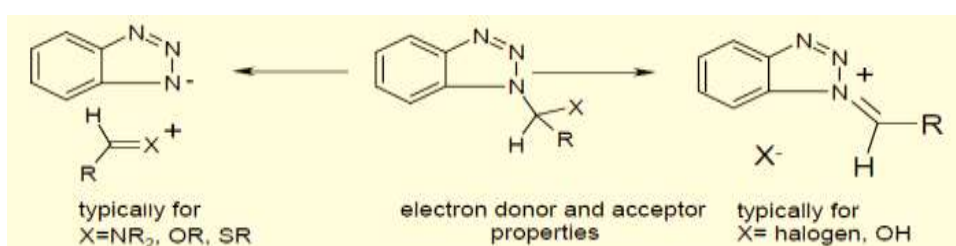


Figure. 2 types ionization of benzotriazole.

Then many products of benzotriazole were synthesized as: 1- stilbenes derivate, One of the important functions of stilbenes in plants is probably their role as phytoalexins in disease resistance , Much attention has been paid in the past few years to reports that stilbene (usually resveratrol and its derivatives in wine) can be beneficial to human health because it is an antioxidant, [9,10] or because it may be active in preventing coronary heart disease or even cancer [11], 2- cinanamic acid: (Synthesis of Ethyl trans-Cinnamate) , Which possesses desirable characteristics in the food, cosmetic and pharmaceutical industries [12]

The alkyl derivatives of benzotriazole (**1- Alkyl Benzotriazole**) are very important compounds because of their great effectiveness as herbicides, fungicides and insecticides. In addition, these compounds show great effectiveness as anti-inflammatory, anti-viral, and diuretics, and they also have great importance in organic synthesis reactions as raw materials for the preparation of new compounds Of which [12,13,14].

Some alkaline derivatives have been used in the fields of pharmaceutical chemistry and many syntheses, including the preparation of benzotriazole epoxides with great activity and activity, and then using these prepared epoxides in subsequent reactions [15], Many unsaturated compounds of benzotriazole containing the cyanide group have been prepared, which have shown great biological efficacy against many types of bacteria and viruses as well as have a toxic and deadly effect on the growth of some cancer cells [16,17].

2. EXPERIMENTAL:

2-1. Apparatus

- Spectra NMR proton and carbon device 400 MHz model Bruker by Switzerland company,
- spectrum infrared device model FT-IR-4100 from the Japanese company Jasco,

2-2. Reagents and materials

All chemical material and catalysts, from Sigma Aldrich and Merck

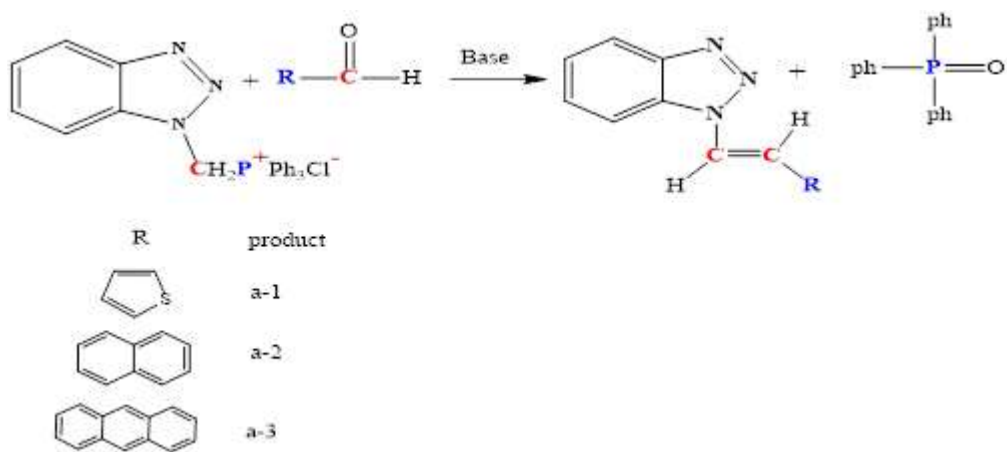
2-3. EXPERIMENTAL PROCEDURE:

The synthetic reactions were carried out in an inert atmosphere of nitrogen gas, where the reaction flask was equipped with a magnetic stirrer.

First, the phosphonium salt is added to the reaction flask and then the solvent is added, after the salt is completely dissolved, the base used is added by a slow drip, and then the aldehyde is added to the reaction medium drop wise through a drip funnel / ratio reactant : aldehyde : phosphonium 1:1) and the reaction continues for (3- 4) hours at room temperature, The reaction process was tested by thin layer chromatography using a mobile phase (60% ethyl acetate, 40% n-hexane), After the reaction had ended by 15ml of distilled water With shaking and extraction, we get two layers and proton solvents aqueous phase: contains the residual alkali organic phase: contains product and excess aldehyde, and phosphine oxide, When the reaction was ended the product was separated from the reaction medium with an extraction: water and dichloromethane (3 times), then the organic layers were combined with the evaporation of the solvents, and dried over MgSO₄ , The resulting compounds were purified using column chromatography using a mobile phase: n- hexane systems: ethyl acetate.

3. RESULTS AND DISCUSSION:

The olefin compounds of benzotriazole were synthesis by reacting the phosphonium salt benzotriazole with a number of aromatic aldehydes. Our study focused on the comparison of the reactions of homogeneous aromatic aldehydes / thiofen carbaldehyde / and heterogeneous aromatic aldehydes /anthra aldehyde/ and / naphtha aldehyde / by treating this aldehyde with phosphonium salt (PBT) according to the witting reaction, in order to obtain unsaturated compounds of benzotriazole scheme (1), The witting reaction is carried out with basic conditions, polar solvents, and temperature (0-25°C).



Scheme .1 Preparation of unsaturated compounds of benzotriazole.

It was found, - that the mechanism for forming unsaturated compounds of benzotriazole takes place in two steps, The first step: (acid-base reaction): A proton is removed from the phosphonium salt by the base to form the ylidyne reagent, which has high stability as it has two reassurances, the two compounds The second step: (reaction between ylidyne and aldehyde),the ylidyne carbon atom attacks the aldehyde carbon atom to form an intermediate compound, which in turn turns into another intermediate cyclic compound that is more stable to remove the phosphine oxide molecule to form the corresponding alkane [21,22,23].

Many factors affecting the synthesis of unsaturated compounds of benzotriazole were studied, including: temperature, solvent, reaction time, base used, ratios of reactants, and then the best conditions were chosen in terms of yield and ease of separation.

In this type of reactions, non-polar solvents cannot be used, while non-proton polar and proton polar solvents can be used. We made a comparison between some of these solvents in terms of their effect on the yield, reaction time and ease of removal from the reaction medium.

it is preferable to use non-proton polar solvents over /than / proton as it avoids proton slippery problems in the case of polar solvents, It is also possible to use proton solvents since many of them can be disposed of more easily, but care must be taken to add these as little as possible, especially in the case of strong foundations, As it is one the disadvantages of proton polar solvents is that the deprotonation of the solvent

competes with the de-protonation of the phosphonium salt, which leads to a significant decrease in the yield.

Therefore, it is often preferred for this type of reaction in polar non-proton solvents with the exception of tetrahydrofuran, being the phosphonium salt weakly dissolved in it compared with other non-proton solvents.

this reaction takes place under basic conditions, the influence of several bases on witting interactions has been studied, including: ETONa , MEONa , BuLi , NaOH, 25% Butyl-lithium is considered one of the very strong bases, but it is preferable not to use it with polar-proton solvents, as it has been observed that the yield is low compared with sodium etoxide, due to the possibility of competing with the deprotonation of the solvent with the deprotonation of the phosphonium salt.


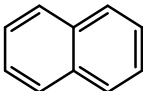
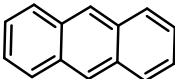
When using the sodium hydroxide solution, the yield was significantly reduced compared to the use of sodium etoxide because the alkaline aqueous medium, perhaps, encourages the hydrolysis processes. Also, the aqueous medium is not suitable for the dissolution of most aldehydes used in the synthesis.

Table .1 effect of base

ETOH , 2h , RT, ratio: (1:1)	
The Base	Ylide
NaOH	25
MeONa /MeOH	46
ETONa	79
BuLi	60

The best molar ratios for the reaction between aldehyde and phosphonium salt are: 1:1 compared to other ratios, where heat must be taken because there is no aldehyde in the reaction medium in an excess amount.

Table. 2 comparative synthetic compounds

Entry	Reaction time /h	Base	Y%	Solvents
	2	ETONa	77%	EtOH
	4	ETONa	59%	CH ₂ Cl ₂
	3	ETONa	79%	CH ₂ Cl ₂

4. CHARECTARIZATION:

(1-benzotriazol 2- carbatiofen) ethelen): dark brown precipitate, yield 77%, m. p= 90-91°C.

FT-IR:(KBr, cm⁻¹) :(C_{SP2}-H; 3105, 3066), (N=N; 1455), (C-N=C;1056)

(C-S;1166), (C=C.tiofen;1620,1648), (C=C(alken);1734), (C=C(Ar);1487), (C=C-H(bend,alkene);922), (C-H(bend, Ar);743) ,(C_{sp2}- N;1257)

¹H-NMR(δ:ppm,CDCl₃):,(olefin : 2H , d , 7,74-7,84) , Aromatic tiofen range , (1H ,d,7,22,),(1H,d,7,80) ,(1H,m, 7.08) (2H,d,7,30-7,40),(2H,dd,7.67-7,62), (1H,d,7,74)

¹³C-NMR(δ:ppm,CDCl₃), DEPT-135 :(C=C olefin: 125.32, 114.97) (CH,Ar: 120;124;124,7;127,6;127,9;128,35), (C,Ar: 146.26 , 138.35 , 130.95).

(b1-benzotriazole 2- naphtha) ethylene: oil brown product, Y=59%.

FT-IR(KBr,cm⁻¹): (C=C-H(alkene):3048), (C=C-H(aromatic): 2925) , (N=N: 1430) , (C-N: 1216) ,(N-N: 1169), (C=C(Ar): 1591-1509), (C=C (alkene): 1622), (C-H(bend, alkene): 886-1055), (C-H(bend,Ar) ,649)

¹H-NMR(δ:ppm,TMS=0ppm,CDCl₃): =C-H:1H,d:5,6) (1H,d ,6,91) 11H,Ar, m ,7,4-8.03)

¹³C-NMR(δ:ppm,CDCl₃), DEPT-135: (=CH, olefin, 132, 119), (C,Ar: 145, 132, 132.8, 133.6, 135.6) (CH,Ar:119, 112, 124, 126 , 126.9, 122, 128.08, 128.8)

(1-benzotriazole2-anthra)ethylene: yellow precipitate , m. p (131-134 °C), y = 79%.

FT-IR(KBr,cm⁻¹): (C=C-H(alkene): 3055), (C=C (alkene): 1590), (C=C-H(Ar): 2927) , (C=C(Ar): 1729), (N=N: 1438), (C-N: 1189), (N-N: 1121), (C=C-H(alkene,bend): 996 – 1072), (C=C(Ar bend): 697).

¹H-NMR(δ:ppm,TMS=0ppm,CDCl₃): (=C-H:1H , d , 5.6) , (=C-H :1H , d ,6.91) ,(14H , d , m , 7.4-8.32).

¹³C-NMR((δ:ppm, TMS=0ppm,CDCl₃), DEPT-135: (C,olefin, 132.7, 119.8) (CH,Ar: 119.2, 126.2, 128.8, 112.9, 125, 128.3, 121.6, 128.3, 125.4) (C,Ar: 145, 138.2, 133.1, 125.8, 131.3).

5. Conclusion:

The previous results show that aldehydes can be converted into corresponding olefins by interacting with a phosphonium salt called the Wittig Reagent to obtain unsaturated products of benzotriazole, as this reaction takes place in a basic medium and in the presence of polar solvents, as this type of reaction is a direct application of the Wittig reaction that The artificial interactions are important in important areas, and these experiments can also be used in research and academic laboratories for undergraduate students as a direct application to this interaction.

References:

- [1] Katritzky, A.R., Lan, X, Yang, J.Z, Denisk, 1998-O.V.Chem.Rev, V(98),P(409).
- [2] Claudio M.P. Pererira, Helio A. Stefani ,Karla P. Guzen & Aline T.G. Orafao, 2007- Improved Synthesis of Benzotriazoles and 1-Acylbenzotriazoles by Ultrasound Irradition. Letters in Organic Chemistry, V(4),P(43-46).
- [3] S. Nanjunda Swamy, Basappa, G. Sarala, B.S. Priya, a S.L. Gaon J. Shashidhara Prasadb & K.S. Rangappa, 2005- Microwave-assisted synthesis of N-alkylated benzotriazole derivatives: Antimicrobial studies, Bioorganic & Medicinal Chemistry, V (16), P(999–1004).
- [4] GONNET, Lori, et al. N-Acyl benzotriazole derivatives for the synthesis of dipeptides and tripeptides and peptide biotinylation by mechanochemistry. *ACS Sustainable Chemistry & Engineering*, 2017, 5.4: 2936-2941.

- [5] Antonio Carta, Paolo Sanna, Michele Palomba, Laura Vargiu, Massimiliano La Colla, & Roberta Loddo, 2002- Synthesis and antiproliferative activity of 3-aryl-2-(1H-benzotriazol-1-yl) acrylonitrile, *European Journal of Medicinal Chemistry*, V(37), P(891/900).
- [6] Alan R. Katritzky, Ruxiat Maimait, Anna Denisenko, & Sergey N. Denisenko, 2001 - Synthesis and reactions of benzotriazolyl epoxides, *ARKIVOC* (V) 68-78
- [7] Chavon R. Wilkerson, Katritzky, A.R.; Barczynski, P.; Ostercamp, D.L.; Yousuf, T.I. BENZOTRIAZOLE-MEDIATED SYNTHESIS OF *N*-ACYLBENZOTRIAZOLES AND 2*H*-AZIRINES, *J. Org. Chem.*, 1986 V (51), P(4037).
- [8] Alan R. Katritzky, and Olga Denisko. The magic of benzotriazole, *Chem.Rev.* 1998, V(98). N(409).
- [9] Chavon R. Wilkerson, Katritzky, A.R.; Barczynski, P.; Ostercamp, D.L.; Yousuf, T.I. BENZOTRIAZOLE-MEDIATED SYNTHESIS OF *N*-ACYLBENZOTRIAZOLES AND 2*H*-AZIRINES, *J. Org. Chem.*, 1986 V (51), P(4037).
- [10] Burckhalter, J.H., Stephens, V.C., L.A.R., Preparation of alkybenzotriazole, *J. Am. Chem. Soc.*, 1952, V(74), P(3868).
- [11] T. Solomoxis, *organic chemistry*, 1996. 6th edition P (1218).
- [12] M. Soleman, Florida U.S.A., Preparation derivative of benzotriazole 1983
- [13] AMMARE, Yibrah. Synthesis, Characterization and Antibacterial Evaluation of Piperidine Derived (E)-Cinnamate Analogues. 2019. PhD Thesis. Mekelle University.
- [14] Alan R. Katritzky, Wojciech Kuzmierkiewicz, and John V. Greenhill, An improved method for the *N*-alkylation of benzotriazole and 1,2,4-triazole, 1991, pp(369-373)
- [15] S.N. Swamy, Basappa, G. Sarala, B.S. Priya, S.L. Gaonkar, J. S. Prasad, and K.S. Rangappa, Microwave-assisted synthesis of *N*-alkylated benzotriazole derivatives:

Antimicrobial studies, *Bioorganic & Medicinal Chemistry Letters*, 2006, V (16) P (999–1004).

- [16] A.K. Nezhad, A.Zare, A.Parhami, M.N. Soltani Rad and G.R. Nejabat, Highly Regioselective N- Alkylation of Benzotriazole under Solvent-Free Condition, *J. Iran .chem.Soc.*, 2007, V(4),N(3), p(271- 278).
- [17] Alan R. Katritzky, Rexiat Maimait, Anna Denisenko, and Sergey N. Denisenko, Synthesis and reactions of benzotriazolyl epoxides, *ARKIVOC*, 2001, V(v)P(68-78).