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SYNTHESIS OF NEW DERIVATIVES OF 4,5-DIHYDRO-1*H*-BENZO[*G*]INDOL

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***Abstract**: Various enamines were synthesized by the reaction of 2-propargyl-α-tetralone with amines in the benzene media. The triple bond of the propargyl group in the side chain of the synthesized enamines is activated by the BF_3•OEt_2 catalyst to make nucleophilic addition of amines to the triple bond easier. An intermediate is obtained as a result of cyclization. In the course of the subsequent reaction, the intermediate is isomerized to form new derivatives of 4,5-dihydro-1H-benzo[g] indole.*

Keywords: *pyrrole, indoles, tetralone, enamine, 2-propargyl-α-tetralone*
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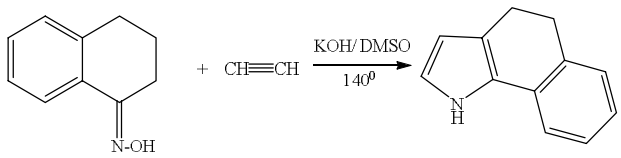
It should be noted that many biologically active natural products containing pyrrole and its derivatives are widely spread in the nature. For example, 2-acetyl pyrrole has been found in cocoa, coffee and tobacco leaf. Other natural molecules such as hemoglobin, chlorophyll, porphines and some natural dyes are made on the basis of pyrrole scaffold [1].

One of the most important condensed derivatives of pyrroles are 4,5-dihydrobenzo[*g*]indoles. These compounds are important building blocks in the synthesis of phthalocyanines, naphthalocyanine, special conductors, red line optical materials, infrared dye compounds and other specially formed compounds [2-4].

Also, some derivatives of 4,5-dihydrobenzo[*g*] indole have antimicrobial, antivirus and inhibitory properties [5, 6].

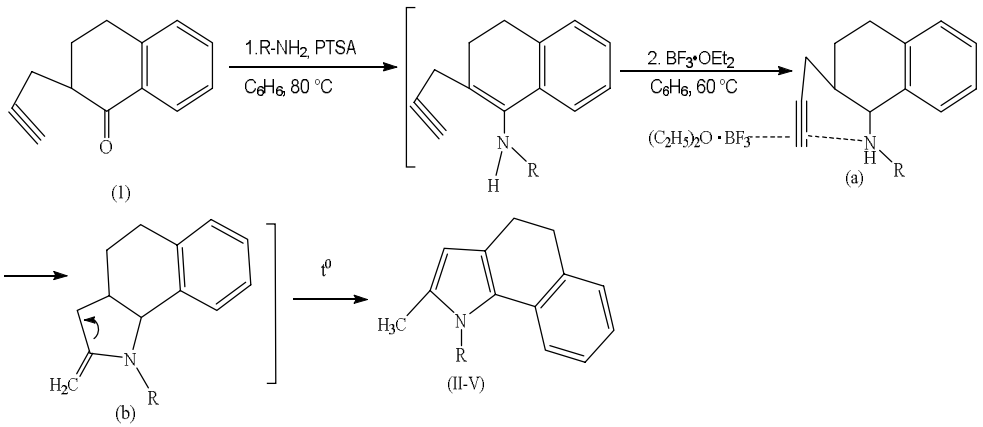
There are some works in the literature dealing with the synthesis of dihydrobenzo[*g*] indoles. For example, Makata et al. synthesized some derivatives of 4,5-dihydro[*g*]indole in 40-45% yield from the reaction between 2-acetyl-1-tetralone and glycine ethyl ester hydrochloride under reflux condition at a temperature of 140°C [7] in the dimethylsulfoxide atmosphere.

Trofimov and others synthesized 4,5-dhydrobenzo[*g*]indole and its *N*-vinyl derivative in 71 % yield by the reaction of α-tetralone oxime and acetylene in super-basic media at 140°C [1].



Here in presented research work is devoted to obtaining new *N*-derivatives of 4,5-dihydrobenzo[*g*]indoles based on the reaction of 2-propargyl *α*-tetralone with various amines in the presence of BF_3•OEt_2 catalyst.

As can be seen from the scheme given above, the first step of synthesis is the enamine formation [8] which is followed by C≡C bond activation through catalytic influence of BF_3•OEt_2 that makes the nucleophilic attack of nitrogen possible. Thus, intra-molecularly cyclized intermediate (b), at the next stage, isomerizes and forms the final products by means of heating. As a result, *N*-based 4,5-dihydrobenzo[*g*]indoles (II-V) were synthesized in 55-60% yields in a single pot fashion.



Note that chemical structures of synthesized new products were characterized by NMR spectroscopy (Fig. 1-2) CH_3 protons of 1-benzyl-2-methyl-4,5-dhydro-1*H*-benzo[*g*] indole compound were observed at 2.06 ppm as a singlet while protons of -CH_2 - CH_2 - fragment as triplets at 2.55-2.61 (t, *J*=8,2, 2H, CH_2), and 2.74-2.79 (t, *J*=8,2, 2H, CH_2) ppm. The - CH_2N - fragment of benzylic protons appeared at 5.25 (s, 2H, *N*-CH_2) ppm, and that of =CH proton of the pyrrole at 5.82 (s, 1H, =CH) ppm. The all 9 aromatic protons resonated between 6.85-7.29 (m, 9H, Ar-H) ppm as multiplets.

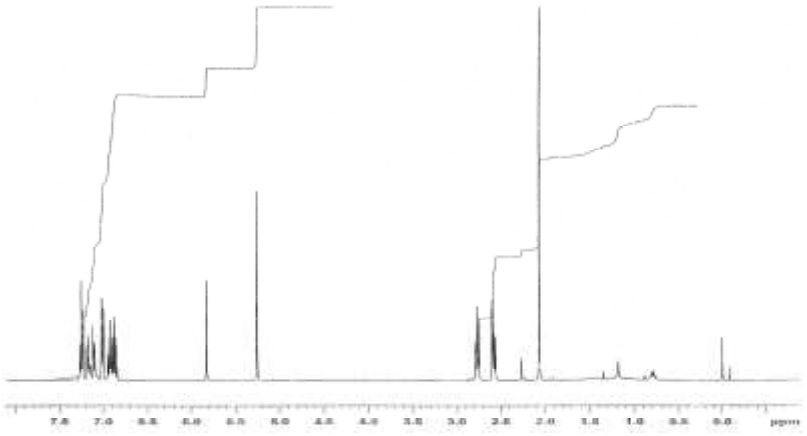


Fig.1. ^{1}H NMR spectra of 1-benzyl-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (II).

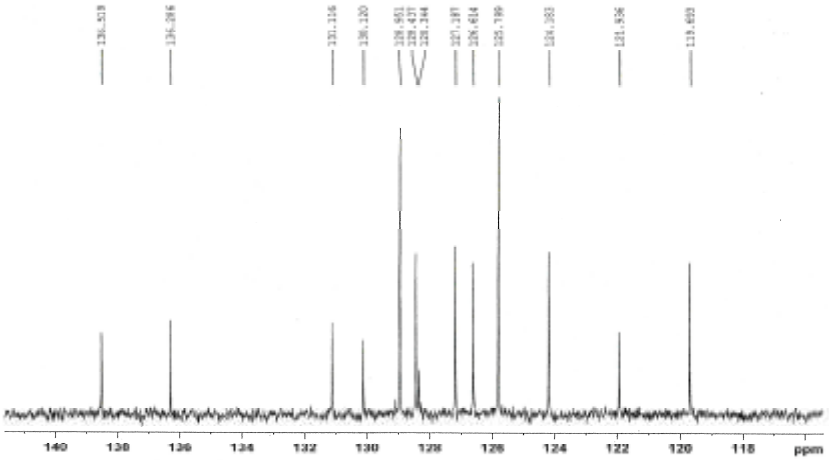


Fig.2. ^{13}C NMR spectra of 1-benzyl-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (II).

The ^{13}C NMR spectra of 1-benzyl-2-methyl-4,5-dhydro-1*H*-benzo[*g*]indole is:

(100 MHz, at DMSO): δ, 12.31 ($\underline{C}H_3$), 22.54 ($\underline{C}H_2$), 31.39 ($\underline{C}H_2$), 48.51 (N - $\underline{C}H_2$), 106.10 (N - $\underline{C}$H), 119.69 ($\underline{C}$H - Ar), 121.94 ($\underline{C}$ - Ar), 125.80 (2$\underline{C}$ - Ar), 126.61 ($\underline{C}$H - Ar), 127.19 ($\underline{C}$H - Ar),128.34 ($\underline{C}$ - Ar), 128.43 ($\underline{C}$H - Ar), 128.95 (2$\underline{C}$H - Ar), 130.12 ($\underline{C}$ - Ar), 131.12 ($\underline{C}$ - Ar), 136.27 (N - $\underline{C}$), 138.50 (N - $\underline{C}$).

The detailed NMR analysis of 4,5-dihydrobenzo[*g*] indoles is presented in the experimental part.

Experimental part

The ^{1}H and ^{13}C NMR spectra of the synthesized compounds were taken in the Brucker DPX400 ($CDCl_3$). IR spectroscopic measurements were studied on a Perkin Elmer 1600 FTIR. The purity of the compounds were analyzed by UB light (λ = 254nm) on a thin layer and their H-NMR spectra. Starting compounds were synthesized by well-known literature procedures [9, 10].

The synthesis of 1-benzyl-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (II).

1.84 g (0.01 mol) 2-propargyl-1-tetralone, 1.6 g (0.015 mol) benzylamine and some crystal of PTSA were added to a round bottomed flask equipped with Dean Stark apparatus with 30 ml dry benzene stirred for 8 hours at 80 °C, then 5 drop BF_3•OEt_2 was added and stirring contunied for 6 hours. Finally, the reaction mixture was allowed to get cooled at a room temperature, then extracted with diethyl ether and washed with water. Organic phase was dried on $MgSO_4$. Benzene was evaporated and the products obtained as yellow crystals. Melting point is 138-140 ˚C.

Compounds **III-V** were synthesized by the same method.

The synthesis of 1-phenyl-2-methyl-4,5-dihydro-1*H*-benzo[g]indole (III).

55% yield. Melting Point is 142-144˚C. ^{1}H NMR (400 MHz, DMSO, d^6): –CH_3 fragment were detected at 2.10 (s, 3H, CH_3), –CH_2–CH_2– fragment at 2.60-2.65 (t. *J*=8.2, 2H, CH_2), 2.75-2.80 (t. *J*=8.2, 2H, CH_2), = CH proton of of the pyrroles circle at 5.85 (s.1H, =CH) and 9 protons of aromatic circle at 6.88-7.20 (m, 9H, Ar) ppm as multiplets.

^{13}C – NMR (100 MHz, DMSO, d^6): δ 12.35, 22.50, 31.60, 107.45(N-$\underline{C}$), 120.10, 121.85, 124.70, 125.80, 126.90, 127.20, 128.40, 128.95, 128.99, 130.15, 131.15, 136.40 (N-$\underline{C}$), 149.00 (N-$\underline{C}$).

The synthesis of 1-(R-α-phenylethyl)-2-methyl-4,5-dihydro-1*H*-benzo[g]indole (IV).

50% yield. Saturated liquid [α]= + 18,2° (0.55, CH_3OH), ^{1}H NMR (400 MHz, DMSO, d^6) 1.55 (d, J=7.10, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.55-2.64 (t, J=8.25, 2H, CH_2), 2.70-2.78 (t, J=8,25, 2H, CH_2), 5.40 (q, J=7.10, 1H, CH-CH_3), 6.55-7.10 (m, 9H, Ar).

^{13}C-NMR (100 MHz, DMSO, d^6): 12.20, 12.55, 22.35, 31.50, 51.20, 105.90, 120.20, 121.90, 124.60, 125.70, 125.90, 127.10, 128.35, 128.90, 129.04, 130.10, 131.20, 136.35 (N-$\underline{C}$),149.40 (N-$\underline{C}$).

The synthesis of 1-propynil-2-methyl-4,5-dihydro-1*H*-benzo[g]indole (V).

50% yield. Saturated yellow liquid. ^{1}H NMR (400 MHz, DMSO,d6). 2.10 (s, 3H, CH_3), 2.40 (t, J=2.60 Hz, 1H, ≡CH), 2.50-2.80 (m, 4H, CH_2–CH_2), 4.62 (d, J-2.60 Hz, 2H, CH_2), 6.50-7.05 (m. 9H, Ar).

^{13}C- NMR (100 MHz, DMSO, d6): 12.30, 22.45, 31.40, 36.45, 48.50, 73.50, 79.40, 106.11, 120.12, 121.90, 125.70, 126.35, 127.20, 128.90, 136.30.

References

1. Trofimov B.A., Mikhaleva A.I., Schmidt E.Yu., Sobenina L.N.. Chemistry of Pyrrole. Moscow: Nauka Publ., 2012, p. 383.
2. Ono N., Hironaga H., Ono K., Kaneko S., Murashima T., Ueda T., Sukamura Ch.T., Ogawa T. A new synthesis of pyrroles and porphyrines fused with aromatic rings. *J.Chem.Soc. Perkin Trans*. 1995, no. 1, pp. 417-426.

3. Clagg K., Hou H., Weinstein A. B., Russell D., Stahl S. S., Koenig S. G. Synthesis of Indole-2-carboxylate Derivatives via Palladium-Catalyzed Aerobic Amination of Aryl C–H Bonds. *Organic Letters.* 2016, vol. 18(15), pp. 3586–3589.
4. Tarkuc S., Sahmetlioglu E., Tanyeli C., M.Akhmedov I., Toppare L. Electrochromic properties of poly (1-(phenyl)-2,5-di(2-thienyl)-1H-pyrrole-co-3,4-ethylendioxy thiophene) and its application in electrochromic devices. *Optical Material.* 2008, vol. 30, pp. 1489-1494.
5. Islam M.S., Baraqat A., Majid A.A., Ali M. Catalytic asymmetric synthesis of indole derivatives as novel α-qlusidose inhibitors in vitro. *Biorganic chemistry*. 2018, vol. 79, pp. 350-354.
6. Anekal D., Biradar J.S. Synthesis, characterization and antimikrobal aktivites of 2-substituted-3-phenyl-1H-indoles. *J*. Chem. Pharm. *Res*., 2013, vol. 5(*1*), pp. 75-85.
7. Mataka Sh., Takahashi K., Tusuda Y., Tashiro M. Preparation of ethyl 3,5-disubstituted pyrrole-2-carboxylates from 1,3-diketone and ethyl glycinate hydroxloride. *Synthesis.* 1982, pp. 157-159.
8. Demir A.S., Akhmedov I.M., Sesenoglu O. Synthesis of 1,2,3,5-tetrasubstituted pyrrole derivatives from 2-(2-bromallyl)-1,3-dicarbonyl compounds. *Tetrahedron.* 2002, vol. 58, p. 9793.
9. Arcadi A., Guiseppe S.D., Marinelli F., Rossi E. Conversion of homochiral amines and α-aminoesters to their chiral 1,2,3,4- pyrrole derivatives via gold-catalysed amination reactions of 2-propynyl-1,3-dicarbonyl compounds. *Tetrahedron: Asymmetry.* 2001, vol. 12, pp. 2715-2720.
10. Arcadi A., Guiseppe S.D., Marinelli F., Rossi E. Cold-catalized sequential amination/anulation reactions of 2- propynyl- 1,3-dicarbonyl compounds. *Synth.Catal.* 2004, vol. 345, no. 5, pp. 443-446.

4,5-DİHİDRO-1H-BENZO[G]İNDOLUN YENİ TÖRƏMƏLƏRİNİN SİNTEZİ

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Benzol mühitində 2-propargil-α-tetralonun aminlərlə qarşılıqlı təsirindən müxtəlif enaminlər sintez edilmişdir. Sintez edilən enaminlərin yan zəncirindəki propargil qrupunun üçqat rabitəsi $BF_3{\cdot}O(C_2H_5)_2$ katalizatoru ilə aktivləşdiyindən amin qrupunun üçqat rabitəyə nukleofil həmləsi asanlaşır. Nəticədə tsiklləşmə baş verərək aralıq məhsul alınır. Reaksiyanın sonrakı gedişi zamanı aralıq məhsul izomerləşərək 4,5-dihidro-1H-benzo[g]indolun yeni törəmələri əmələ gətirir.

Açar sözlər: *pirrol, indol, tetralon, enamin.*

СИНТЕЗ НОВЫХ ПРОИЗВОДНЫХ 4,5-ДИГИДРО-1Н-БЕНЗО[G]ИНДОЛА

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Различные енамины были синтезированы по реакции 2-пропаргил-α-тетралона с аминами в бензольных средах. Тройная связь пропаргильной группы в боковой цепи синтезированных енаминов, которая облегчает нуклеофильное присоединение аминов к тройной связи, активируется катализатором BF3 • OEt2. В результате циклизации получается промежуточный продукт. В ходе последующей реакции промежуточное соединение изомеризуется с образованием новых производных 4,5-дигидро-1Н-бензо[g]индола.

Ключевые слова: *пиррол, индол, тетралон, енамин, 2-пропаргил-α-тетралон*