MECHANOCHEMICAL SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF NOVEL 1,2,3-TRIAZOLYL 2-ARYL BENZOTHIAZOLE DERIVATIVES

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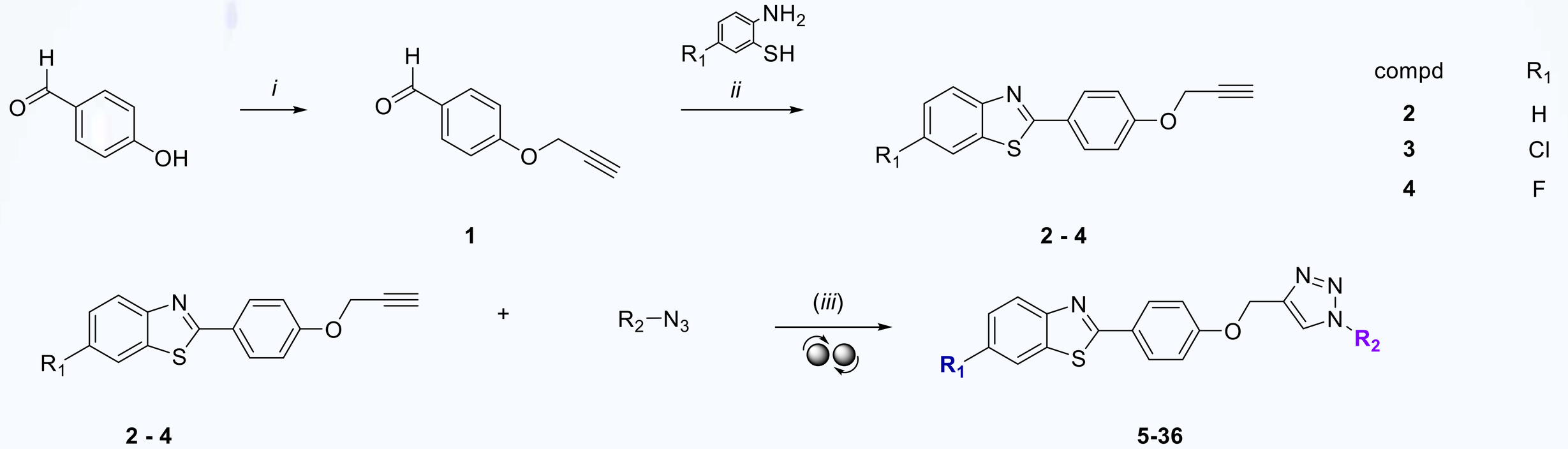
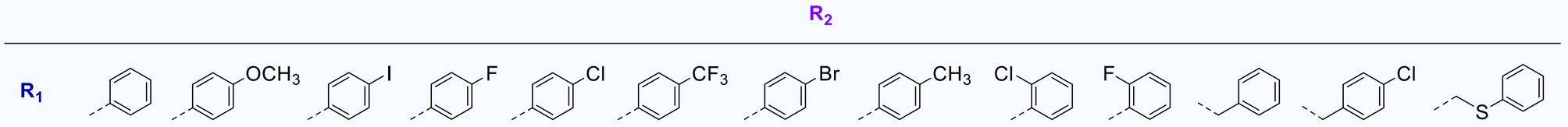
BACKGROUND:

Benzothiazole derivatives exhibit various biological activities such as antitumor, antimicrobial, antiviral and anti-inflammatory. [1] Among the azoles, 1,2,3- triazoles are biological active compounds and attract a lot of attention as pharmachophore. Besides, triazole ring represents an ideal linker due its physical and chemical properties and can interact with biological targets such as DNA and proteins. One of the most famous drug containing a triazole linker is Ribavirin which is used for antiviral treatment. Furthermore, 2-mercaptobenzothiazole and 1,2,3-triazole derivative demonstrated potent selective COX-2 inhibition comparable with the standard drug ibuprofen. [2] Nowadays, more attention is focused on the synthesis of new biologically active agents by ecofriendly methodologies such as microwave-assisted and mechanochemical syntheses.

SYNTHESIS:



SHEME 1. Reagents and conditions : (*i*) K_2CO_3/ethanol/600W/40°C/30min/propargyl bromide/600W/90°C/90min (ii) $Na_2S_2O_5$/DMF/reflux 2h (*iii*) corresponding 1-azidobenzene/ ethanol/ $Cu(OAc)_2$ / 1.5 h- 2 h/ 30 Hz



compd	5	6	7	8	9	10	11	12	13	14	15	16	17
H													
η/%	73,7	78,1	81,6	25,2	48,4	20,1	50,4	29,9	71,9	43	59,5	68,2	95

compd	18	19	30	21	22	23	24	25	26	27	28	29	30
F													
η/%	61,1	89,8	87,1	83,5	55,5	75,2	75,3	67,2	81	89,2	96,8	79,6	51,2

compd	31	32	33	34	35	36
Cl						
η/%	83,2	29	22	44,5	23,2	43,8

STRUCTURAL CHARACTERIZATION:

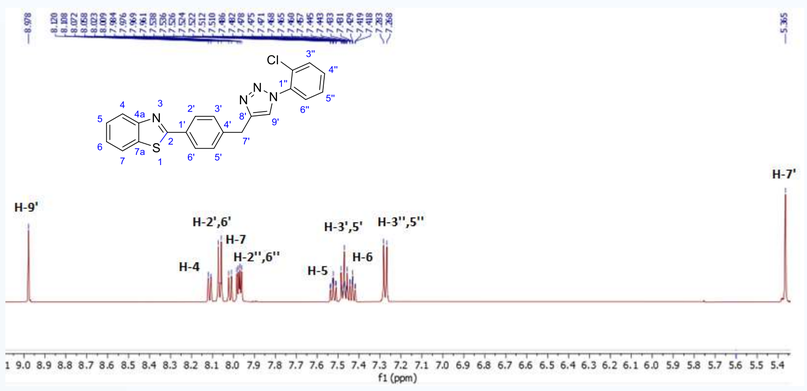


Figure 1. ^{1}H-NMR spectrum of compound **8**

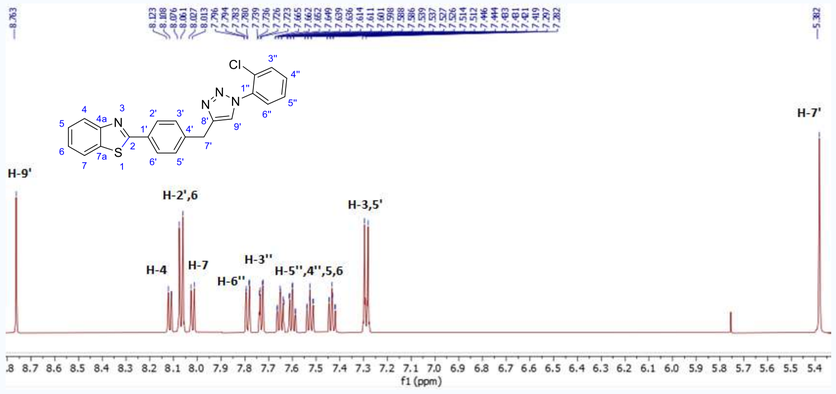


Figure 3. ^{1}H-NMR spectrum of compound **13**

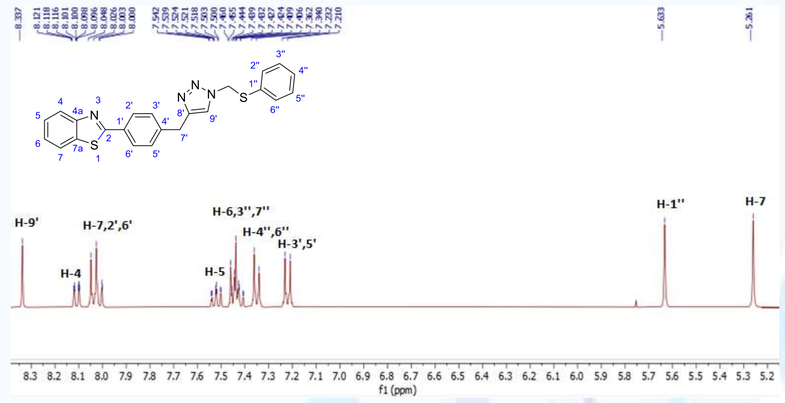


Figure 5. ^{1}H-NMR spectrum of compound **17**

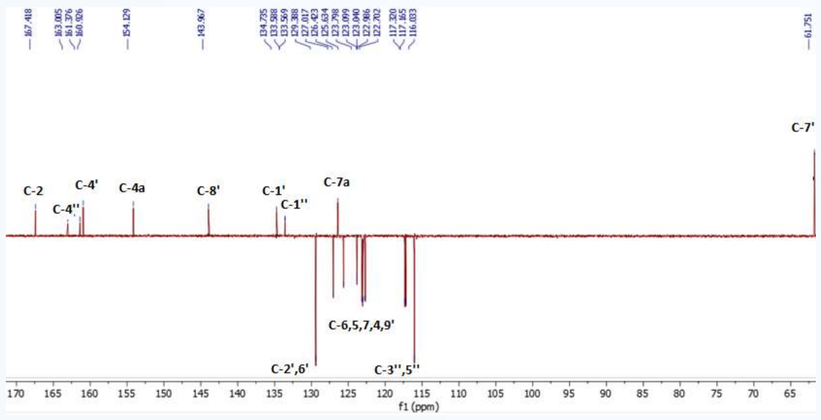


Figure 2. ^{13}C-NMR spectrum of compound **8**

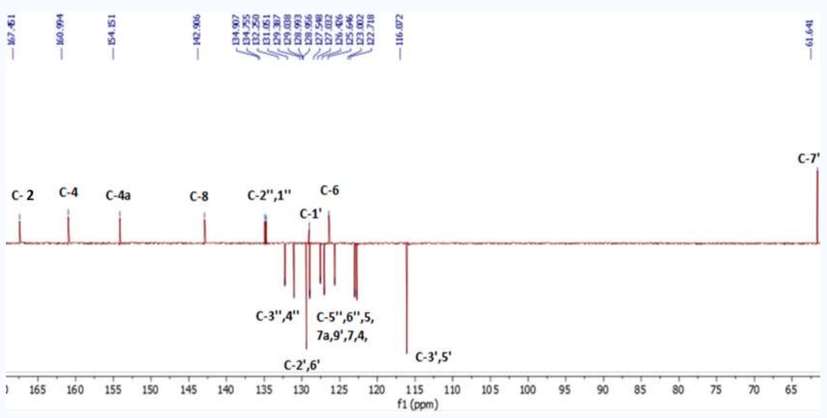


Figure 4. ^{13}C-NMR spectrum of compound **13**

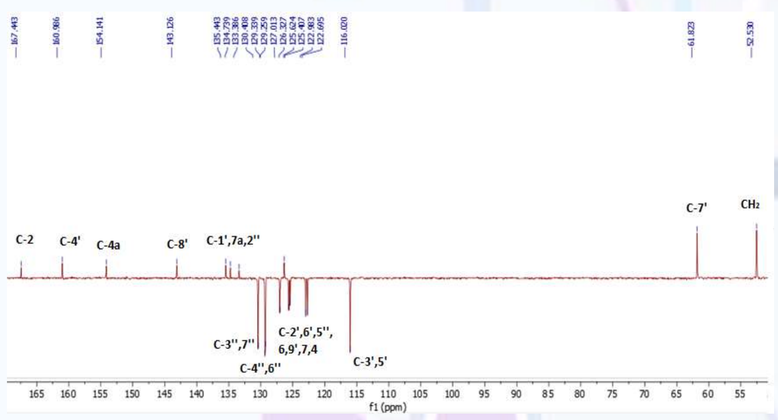


Figure 6. ^{13}C-NMR spectrum of compound **17**

REFERENCES:

[1] S.G. Agalave, S.R. Maujan, S. Vandana, Click Chemistry, Asian J. Chem. 6 (2011) 2696
[2] S. Shafi, M. Mahboob Alam, N. Mulakayala, C. Mulakayala, G. Vanaja, A.M. Kalle, M.S. Alam, Eur. J. Med. Chem. 49 (2012) 324

CONCLUSION:

***O*-propargylated benzaldehyde (1) was prepared by S_N2 reaction of 4-hydroxybenzaldehyde and propargyl bromide using K_2CO_3 as a base. Propargylated benzothiazole derivatives (2-4) were prepared by cyclization reaction of *O*-propargyl benzaldehyde and different substituted aminothiophenol in DMF using oxidizing agent $Na_2S_2O_5$). Target 1,2,3-triazolyl derivatives of benzothiazole (5-36) were prepared by mechanochemical Huisgen 1,3-dipolar cycloaddition reaction. Structures of all newly prepared benzothiazole derivatives were confirmed by ^{1}H and ^{13}C-NMR spectroscopy.**

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