Synthesis and structural characterization of novel 1,2,3-triazole derivatives of benzo[*d*]oxazole-2-thiol

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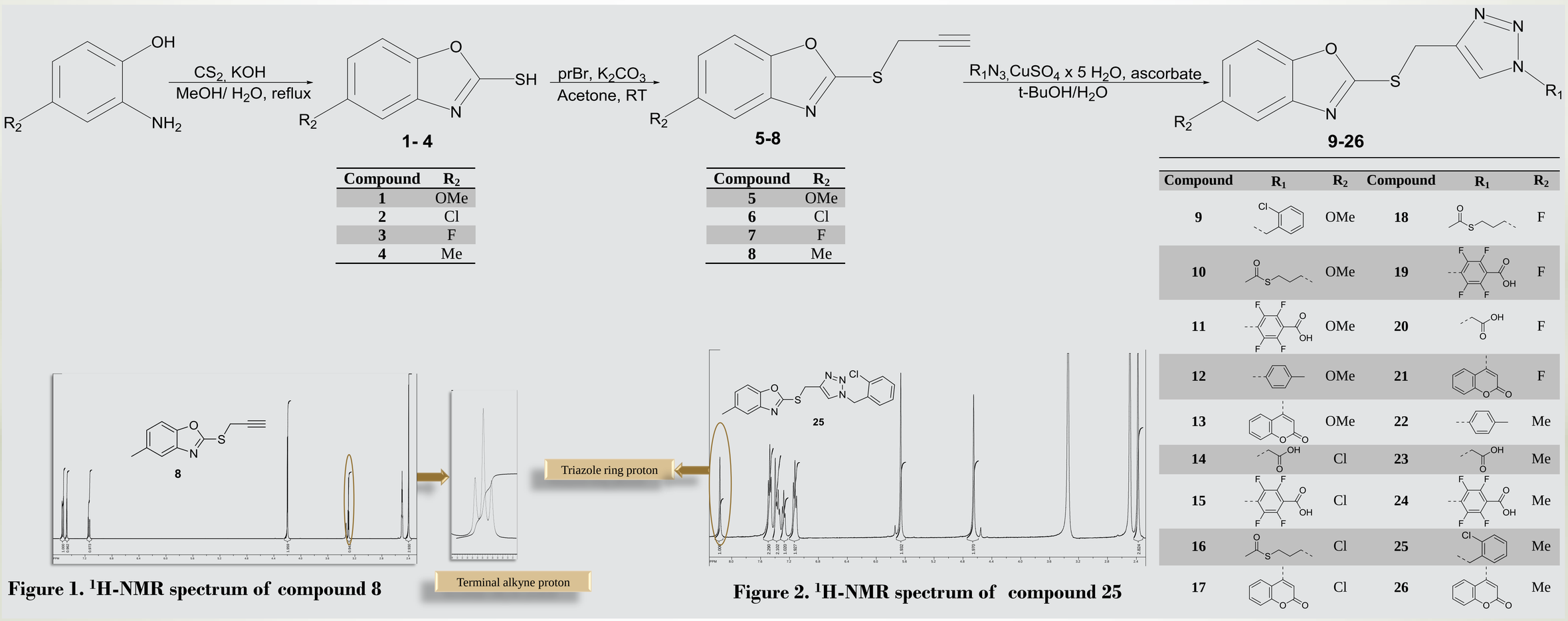
Background

Treatment of malignant diseases is among the most demanding challenges in modern medicine. Despite significant progress in diagnosing and treating of malignant diseases in the last few decades, there is still a lot of space for improvement. Modern chemotherapy is mostly not selective and attention is focused on the development of new, potent and selective antitumor agents. Benzoxazoles represent an important class of heterocyclic compounds that exhibit remarkable pharmacological activities such as anticancer, antiviral, antibacterial and antifungal. Furthermore, some benzoxazole derivatives are used as fluorescent bleaching agents and functional materials.[1-2]
In order to evaluate their antitumor activity, novel derivatives of benzo[*d*]oxazole-2-thiol containing 1,2,3-triazole ring as a linker were synthesized. Propargylated 2-thiobenzoxazole was prepared by cyclization reaction of 2-aminophenol using carbon disulfide, followed by *N*-alkylation reaction with propargyl bromide as an alkylating reagent. 1,2,3-triazole derivatives of benzo[*d*]oxazole-2-thiol were prepared by utilizing the copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC) of 2-propargylated benzoxazoles with corresponding azides. Structures of synthesized 1,2,3-triazolyl derivatives of benzo[*d*]oxazole-2-thiol were confirmed by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry as well.

Results

- Propargylated derivatives of benzo[*d*]oxazole-2-thiol (5-8) were prepared by cyclization reaction of 4-substituted-2-aminophenol using carbon disulfide, followed by alkylation reaction with propargyl bromide as an alkylating reagent.
- Benzo[*d*]oxazole-2-thiol derivatives with 1,2,3-triazole moiety (9-26) were synthesized by Cu(I) catalyzed click reaction of propargylated derivatives of benzo[*d*]oxazole-2-thiol with corresponding azides (Scheme 1).



Compound	R_2
1	OMe
2	Cl
3	F
4	Me

Compound	R_2
5	OMe
6	Cl
7	F
8	Me

Compound	R_1	R_2	Compound	R_1	R_2
9		OMe	18		F
10		OMe	19		F
11		OMe	20		F
12		OMe	21		F
13		OMe	22		Me
14		Cl	23		Me
15		Cl	24		Me
16		Cl	25		Me
17		Cl	26		Me

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

Figure 2. ^{1}H-NMR spectrum of compound 25

Scheme 1. Synthesis of 1,2,3-triazole derivatives of benzo[*d*]oxazole-2-thiol

- Formation of the triazole ring is confirmed by the disappereance of the triplet at ~3,2 ppm of the terminal alkyne proton in ^{1}H-NMR spectra of propargylated benzoxazole derivatives (5-8) (Figure 1.) and the appereance of the singlet of the triazole ring proton at ~ 9 ppm in ^{1}H-NMR spectra of compounds 9-26 (Figure 2.).

Conclusion

- In order to evaluate their antitumor activity, novel 1,2,3-triazole derivatives of benzo[*d*]oxazole-2-thiol (9-26) were synthesized by Cu(I) catalyzed click reaction of propargylated benzo[*d*]oxazole-2-thiol derivatives (5-8) with corresponding azides.
- Structures of the synthesized compounds were confirmed by ^{1}H and ^{13}C-NMR spectroscopy and mass spectrometry as well.

References

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