NEW HYBRID QUATERNARY SALTS WITH SULFANYLAMIDE/BENZIMIDAZOLE SKELETON

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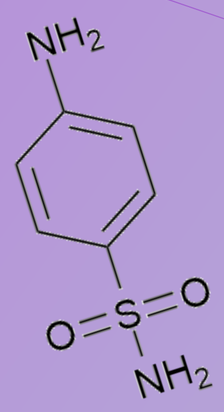
Introduction



Sulfanylamides and sulfanilamide derivatives are invaluable scaffolds in drug design and although they have been extensively studied over the years, they still remain of major interest in organic chemistry. On the other way, the chemistry of hybrid compounds containing both imidazole/benzimidazole and sulfanylamide fragments have attracted particular interest due to their biological profile.[1]

Aim of the work

Considering the above, our main objective was to synthesize and characterize novel hybrid quaternary salts with sulfanylamide/benzimidazole skeleton adopting a general and straightforward strategy, involving three steps: *N*-acylation, *N*-alkylation and quaternization.

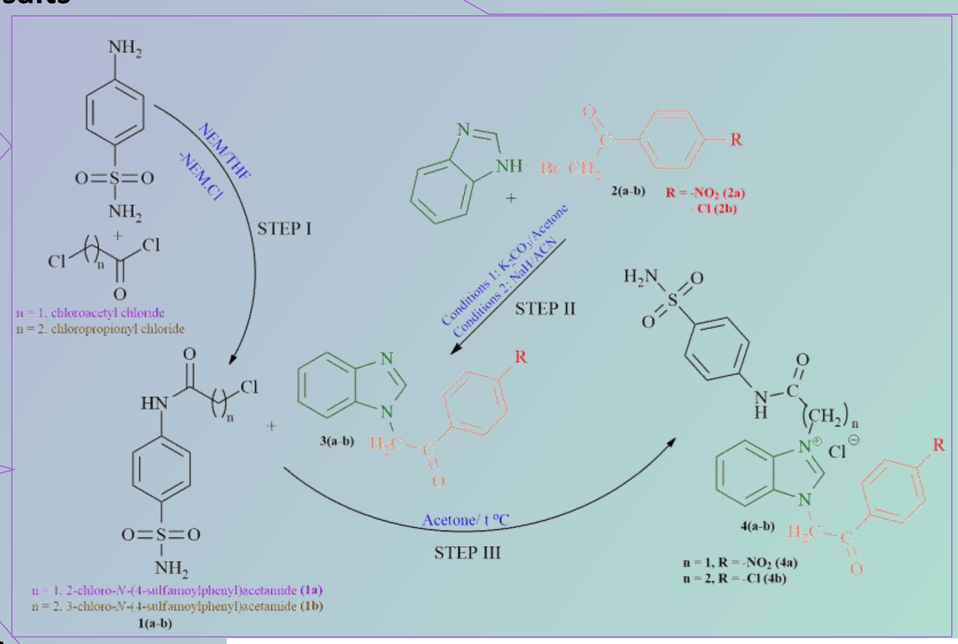
Experimental

I) N-acylation* of 4-aminobenzensulfonamide with α-chloroacetyl chloride or α-chloropropionyl chloride, giving the corresponding acylated compounds *(1a-b);

II) N-alkylation of benzimidazole using K_2CO_3 or NaH as bases and bromoacetophenones differently substituted at the para position;

III) N^3-quaternization of the benzimidazole derivatives (2a-b) previously obtained, using the acylated sulfonamides;

Scheme 1:
Syntesis of quaternary salts

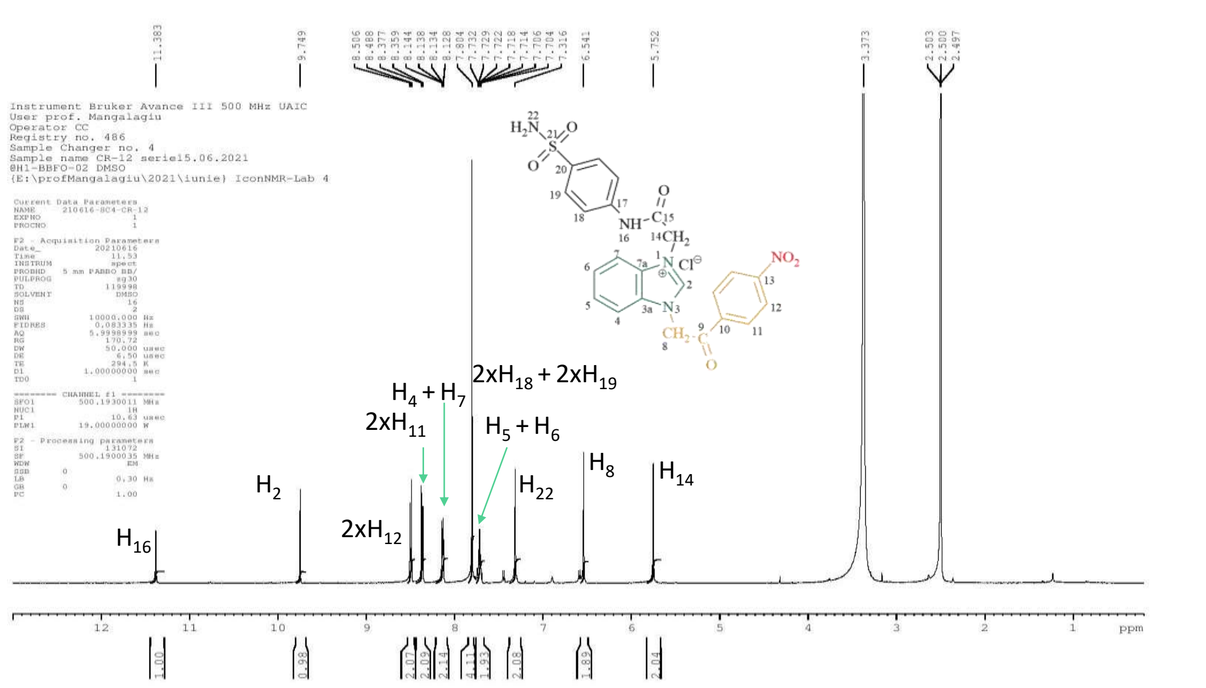


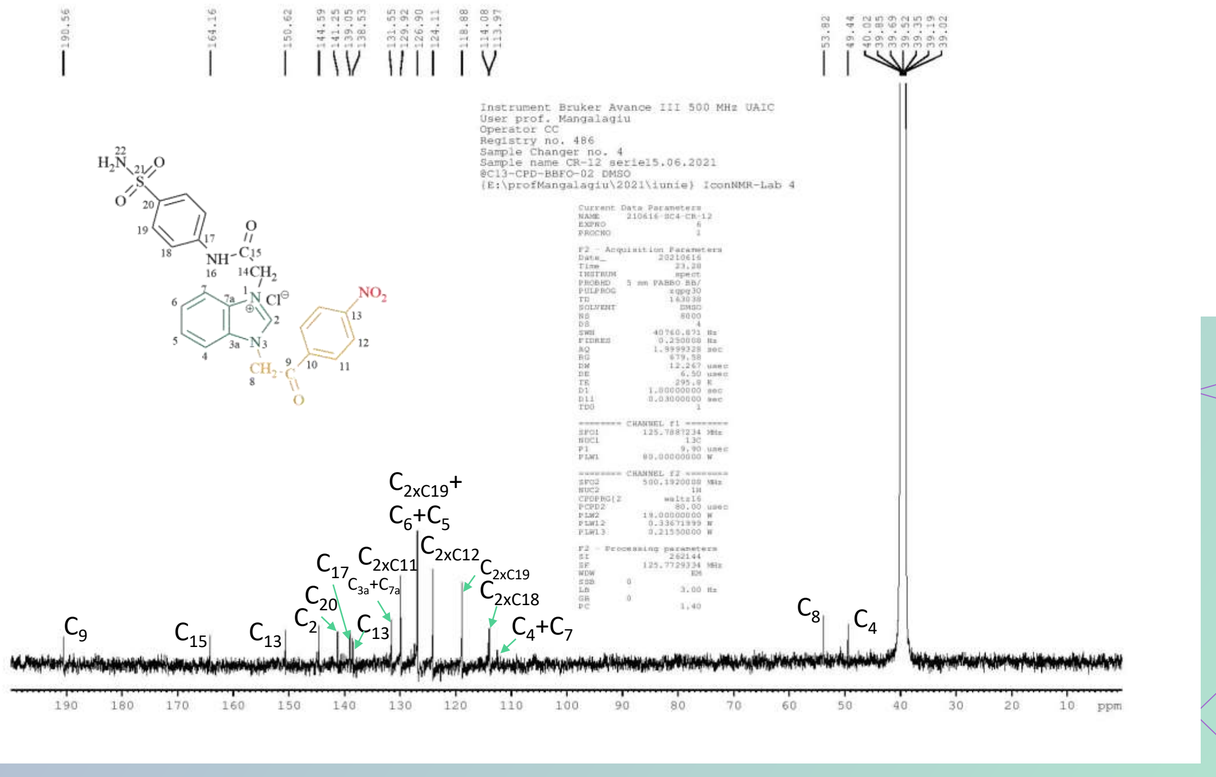
Quaternary salts when R is:	Yield (%)
4a	48
4b	25

Results and discussion

The obtained quaternary salts *(4a-b)* and some of the precursors *(2b)* are new compounds, which are not mentioned in the literature.[2,3]

The structure of newly compounds were proved using Nuclear Magnetic Resonance (NMR) experiments (^{1}H, ^{13}C, 2D-correlation). The NMR apparatus (Bruker Avance III 500 spectrometer) is equipped with a 5 mm PABBO detection probe, operating at 500.1 MHz for ^{1}H and 125 MHz for ^{13}C.





Conclusions

The hybrid sulfanylamide/benzimidazole quaternary salts *(4a-b)* were obtained using three steps procedure, by adapting the literature available protocols.[2,3] Quaternary salts were obtained in moderate to good yields (between 20% and 50%).

The newly synthesized quaternary salts are key intermediates that will be used in 3+2 dipolar cycloaddition reactions, using various dipolarophiles (symmetrically or asymmetrically substituted).

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References

1. Cowman, A.F., Healer, J., Marapana, D., Marsh, K. (2016), Malaria: Biology and Disease in „Cell", vol. 167, (p. 610-624), Elsevier.

2. Turken, H., Durgun, H., et all. Carbonic anhydrase inhibitors. Novel sulfanilamide/acetazolamide derivates obtained by the tail approach and their interaction with the cytosolic isosystem I and II, and the tumor-associated isozyme IX. Bioorg. Med. Chem. Lett. (2005), 15, 367-372.
DOI: 10.1016/j.bmcl.2004.10.070

3. Vargas-Oviedo, D., Butassi, E., Zacchino, S., Portilla, J. Eco-friendly synthesis and antifugal evolution of N-substitued benzimidazoles. Monatshefte für Chemie - Chemical Monthly (2020), 151, 575-588.
DOI: https://doi.org/10.1007/s00706-020-02575-9

4. Mantu, D., Antoci, V.; Moldoveanu, C., Zbancioc, Ghe., Mangalagiu, I.I. Hybrid imidazole (benzimidazole)/ pyridine (quinoline) derivatives and evaluation of their anticancer and antimycobacterial activity. J. Enzym. Inhib. Med. Chem. (2016), 31(sup 2), 96-103.
DOI: https://doi.org/10.1080/14756366.2016.1190711