A RING TRANSFORMATION OF 2-BENZOYL-1,4-BENZOTHIAZIN-3-ONE INTO 1,3-BENZOTHIAZOLE AND PYRAZOLE DERIVATIVES.

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Abstract
2-benzoyl-1,4-benzothiazin-3-one 1 under the liquid-solid phase transfer catalysis in the presence of an excess of methyl chloroacetate undergoes a ring transformation to lead to 1-methoxycarbonylmethyl 1,3-benzothiazol-2-one 2. Also the condensation of compound 1 with hydrazine hydrate in refluxing methanol in the presence of hydrochloric acid affords in particular the bipyrazolic compound 4. A possible mechanisms reactions have been proposed.

Introduction
In continuation of our previous works on the study of ring transformation of a various heterocyclic systems including 1,5-benzodiazepin-2-ones[1-12], 1,5-benzothiazepin-2-ones [13], 1,5-benzodiazepine-2,4-diones [14,15] and 1,2,4-triazolotriazepinones [16-17], we report in this current work the rearrangement of 2-benzoyl-1,4-benzothiazin-3-one under liquid-solid phase transfer catalysis (CTP) conditions during the alkylation reactions using an excess of methyl chloroacetate as an alkylating reagent, as well as under the action of hydrazine hydrate in refluxing methanol in the presence of hydrochloric acid.
1-Alkylation of 2-benzoyl-1,4-benzothiazin-3-one 1

2-benzoyl-1,4-benzothiazine-3-one 1 containing three nucleophilic sites: the lactamic nitrogen and oxygen atoms as well as the carbon atom at position 2 of the bicyclic compound reacted in alkylation reaction using methyl chloroacetate as alkylating reagent in liquid-solid phase transfer catalysis (PTC) conditions in the presence of potassium carbonate as base and tetra n-butylammonium bromide (TBAB) as catalyst in DMF for 24 hours at room temperature.

The reaction studied provided in 60% yield 2-(2-oxo-benzothiazolin-3-yl) ethanoate 2 (Scheme 1) after purification by a column chromatography on silica gel (eluant: CH₂Cl₂ / (C₂H₅)₂O; 9 / 1)

![Scheme 1](image)

The structure of the benzothiazolic compound 2 was elucidated using spectral data (¹HNMR, ¹³CNMR, IR) and confirmed by a single crystal X-ray diffraction study [¹⁸] (figure 1)
The $^1$HNMR spectra of compound 2 taken in CDCl$_3$ exhibits a signal at 3.79 ppm corresponding to the methoxy group, a signal at 4.72 ppm related to the methylene group linked to the lactamic nitrogen atom.

The $^{13}$C NMR spectra presents in particular a signal at 167.5 ppm related to the ester carbonyl group, a signal at 43.4 ppm corresponding to the methylene group and a signal at 203 ppm assigned to the carbonyl group in 2-position of the benzothiazole moiety.

A plausible mechanism reaction has been presented explaining the formation of 1-methoxycarbonylmethyl-1,3-benzothiazol-2-one 2. The alkylation reaction of compound 2 with methylchloroacetate provided the dialkylated 1,4-benzothiazin-3-one [A] which undergoes a transannular reaction involving the sulfur atom and the amide carbonyl group to lead the unstable tricyclic intermediate [B]. The latter, after the ring opening of the thirin moiety induced by the abstraction by potassium carbonate the acidic hydrogen atom of the methylene group gives the 2-hydroxy-benzothiazoline [C] which after the loss of the insatured ketone affords 1-methoxycarbonyl-1,3-benzothiazol-2-one 2 (Scheme 2).

Scheme 2: Plausible mechanism for the formation of methoxycarbonyl-1,3-benzothiazol-2-one 2

**2- Hydrazinolysis of 2-benzoyl-1,4-benzothiazin-3-one**

In a previous work, Baryala et al. [19] studied the action of hydrazine hydrate on 2-benzoyl-1,4-benzothiazin-3-one 1 in refluxing acid acetic for 3 hours. The authors isolated the pyrazolic compound 3 (Scheme 3).
Continuing our work in this area, we report the study of the hydrazinolysis reaction by modifying the reaction conditions. Thus, the condensation of 2-benzoyl-1,4-benzothiazin-3-one 1 with hydrazine hydrate in refluxing methanol in the presence of hydrochloric acid for 24 hours leads to 4-[(3-hydroxy-5-phenyl-1H-pyrazol-4-yl)-methyl]-5-phenyl-1H-pyrazol-3(2H)-one 4 next to 1,4-benzothiazine 5 and dithiodianiline 6 (Scheme 4).

The structure of compounds 5 and 6 have been determined using spectral data ($^1$H NMR, $^{13}$C NMR).

The structure of the bipyrazolic compound 4 has been elucidated using spectral data ($^1$HNMR, $^{13}$CNMR, Mass and IR) and confirmed by a single-crystal X-ray diffraction study \cite{20} (Figure 2).
The $^1$HNMR spectrum of compound 4 showed in particular a signal at 3.47 ppm corresponding to the methylene group, while the $^{13}$CNMR spectrum highlights in particular a signal at 15.9 ppm related to the methylene group and a signal at 162 ppm corresponding to the carbon atom bearing the hydroxyl group.

A plausible mechanism reactions explaining the formation of compounds 4, 5 and 6 have been proposed (Scheme 5).

Scheme 5: Probable mechanism reaction explaining the formation of the bipyrazolic compound 4

The initial step corresponds to the nucleophilic attack of hydrazine on the benzoylic carbonyl group of compound 1 leading to the pyrazolic compound 3 via the hydrazono intermediate [A] as previously reported by Baryala et al.[13]
Under the excess of hydrazine hydrate acting as a reducing reagent the compound 3 undergoes a cleavage of the C-S bond to afford \( o \)-aminothiophenol 7, which oxidizes to dithiodianiline 6 next to pyrazolone 8. The latter acted as a nucleophilic reagent on the carbonyl atom of the protonated methanol to give after the loss of a water molecule methylpyrazolone [B1] which can exist in the tautomeric form 4-methylidene-3-phenyl-pyrazolin-5-one [B2] acting as a Michael acceptor towards the nucleophilic pyrazolone 8 to afford the bipyrazolic intermediate [C] which loses an hydrogen molecule to give the target bipyrazolic compound 4b (Schema 5).

It is worthy to note that when the reaction was carried out in refluxing ethanol, it was possible to obtain 5-phenyl-1,2-dihydro pyrazol-3-one 8, confirming its role as a key intermediate in the formation of the bipyrazolic compound 4 in refluxing methanol showing that the results observed depend on the nature of the solvent used (Schema 6)

![Scheme 6: Condensation of an excess of hydrazine hydrate with 2-benzoyl-1,4-benzothiazin-3-one in refluxing ethanol](image)

Also, the heating of compound 1 in the presence of hydrazine hydrate in refluxing methanol afford 3-oxo-1,5-benzothiazine 5 in good yield (Scheme 9).

Finally 1,4-benzothiazin-3-one 5 was obtained from the unstable intermediate [D] coming from the nucleophile attack of hydrazine hydrate on the benzyol carbonyl of compound 1. The 1,4- benzothiazine intermediate [D] ejected later a benzylhydrazide molecule (Schema 7)

![Scheme 7: Plausible mechanism for the formation of 1,4-benzothiazin-3-one 5 and benzhydrazide.](image)
Conclusion
In this work we report a new rearrangement of 2-benzoyl-1,4-benzothiazin-3-one under alkylation and hydrazinolysis reactions.

Compound 1 with methylchloroacetate in liquid-solid phase transfer catalysis conditions affords a benzothiazolone derivative 2.

Furthermore a pyrazolylmethylpyrazolone derivative 4 was obtained during the reaction between 2-benzoyl-1,4-benzothiazin-3-one 1 in the presence of chlorhydric acid.

A plausible mechanism explaining the formation of compounds 2 and 4 have been proposed and discussed.

Experimental part
General: Melting points (m p) were determined on a BÜCH apparatus were uncorrected. Nuclear magnetic resonance spectra (^1H and ^13C) were recorded on a Bruker AVANCE at 300 MHz. The chemical shifts were reported as parts per million (ppm) relative to the internal TMS (Tetramethylsilane) reference. Infrared spectra were recorded on a Fourier Transform infrared spectrometer in potassium bromide. Electrospray ionization was used as ionization technique.

Synthetic procedure of 2-(2-oxo-benzothiazolin-3-yl) ethanoate 2
To a solution of 0,01 mole of 2-benzoyl-3-oxo-benzothiazine in 30 ml of DMF, were added 0,03 mole of methyl chloroacetate, 0,6g of K2CO3 and 20 mg of tetrabutylammonium bromide (TBAB). The reaction mixture was stirred at room temperature for 24 hours. After filtration, the solution was concentrated at reduced pressure. The residue obtained was chromatographed on silica gel column using as eluent: (CH2Cl2 / (C2H5)2O 9: 1).

Yield (60%), mp: 116-118 (ethanol)

^1H NMR (CDCl3; δppm) 3.79(s, 3H); 4.72(s, 2H); 7.20-7.50 (m, Har)

^13C NMR (CDCl3; δppm) 43.4(CH2); 52.9 (CH3); 122.5(CHar); 123.0(CHar); 123.7(CHar); 124.0(CHar); 136.0(Cq); 153.0(Cq); 167.5(Cq); 203.0(C2)

IR(νcm-1) 2922-2851 ν(C-H); 1733 ν(C-O); 1667 ν(C-O) (ester)

Action of hydrazine hydrate on 2-benzoyl-1,4-benzothiazin-3-one in the presence of hydrochloric acid in refluxing methanol
To a solution of 1g of 2-benzoyl-1,4-benzothiazine in 50 ml of methanol containing some drops of hydrochloric acid was added an excess of hydrazine hydrate. The reaction mixture
was refluxed for 24 hours. The precipitated compound 4 was filtered and washed with ether, then recrystallized from ethanol.

The filtrate was evaporated under reduced pressure. The oil obtained was chromatographed in silica gel column using \( \text{CH}_2\text{Cl}_2 / (\text{C}_2\text{H}_5)_2\text{O} \) as eluent. Compounds 5 and 6 were isolated respectively,

\( 4-\text{[3-hydroxy-5-phenyl-(1H)-pyrazol-4-yl)methyl]-5-phenyl-1,2-dihydropyraol-3-one} \) 4

**Yield** (15%), **mp**: 226-228 (ethanol)

\( ^1\text{H NMR} \) (DMSO\(_d_6\); \( \delta \) ppm): 3.47 (s, 2H, CH\(_2\)); 6.94-7.30 (m, Har)

\( ^{13}\text{C NMR} \) (DMSO\(_d_6\); \( \delta \) ppm): 15.9 (CH\(_2\)); 101.2 (C\(_q\)); 128.1 (CHar); 128.6 (CHar);
129.1 (CHar); 131.1 (C\(_q\)); 136.0 (C\(_q\)); 142.6 (C\(_q\)); 154.0 (C\(_q\)); 162.5 (C\(_q\))

\( 3\)-**oxo-1,4-benzothiazine** 5

**Yield** (65%), **mp**: 182-184 (ethanol)

\( ^1\text{H NMR} \) (CDCl\(_3\); \( \delta \) ppm): 3.43 (s, 2H); 6.92-7.31 (m, 4Har); 9.75 (s, 1H; NH)

\( ^{13}\text{C NMR} \) (CDCl\(_3\); \( \delta \) ppm): 29.9 (C2); 117.7 (CHar); 124.1 (CHar); 127.4 (CHar);
127.9 (CHar); 119.9 (C\(_q\)); 136.4 (C\(_q\)); 166.4 (C3)

**References**


