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Synthesis, Reaction and Theoretical Study of 3-Formylchromones

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Abstract: Synthesis and theoretical study of five new 2-oxopyranochromone-3-carbaldehydes, and their reactions with 2,4-dinitrophenylhydrazine and 2-benzothiazolylhydrazine were investigated.

Keywords: 2-Oxopyranochromone-3-carbaldehydes, Vilsmeier-Haack reaction, AM1 method.

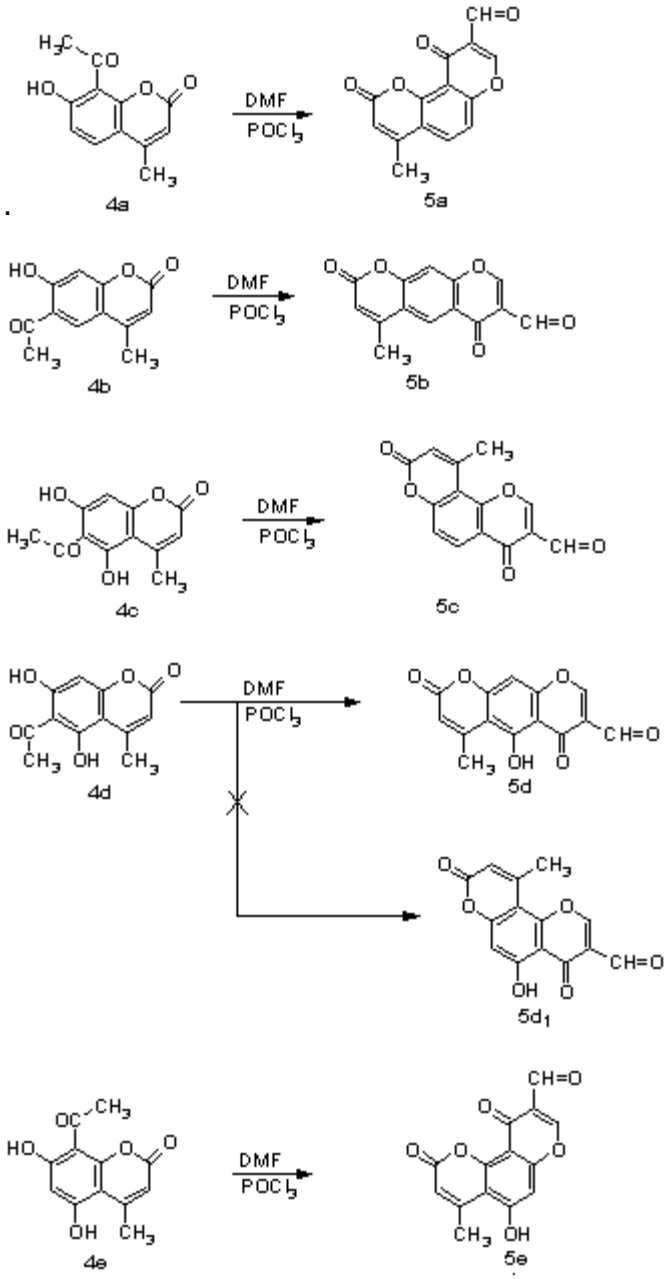
Introduction

Thanks to their biological activity, chromone derivatives are the subject of the considerable pharmaceutical and chemical interest. 3-Formylchromones occupy a unique position from three reasons .They are carrying a significant biological activity [1,2], they have comfortable preparation by Vilsmeier-Haack reaction in very good yields [3] and they are attractive intermediates.

This work is in connection with our program of the synthesis, theoretical , spectral and antimycobacterial study of 3-formylchromone derivatives [4 -10].

Results and Discussion

We developed the optimal method of synthesis of 3-formylchromone **5a - 5e** with condensed 2-oxopyrane ring. The synthetic strategy of 3-formylchromones has to be based on building of 2-benzopyrone skeleton. The key step in the synthesis was the preparation of a suitable acetyl derivatives **4a-4e** from which requested 3-formyl- chromones were obtained by Vilsmeier-Haack formylation in 80 - 90 % yields. The synthesis of **5a - 5e** is depicted in scheme. Acetylderivative **4d** produced only aldehyde **5d**, in any case could not to be prepared isomer $\mathbf{5d_1}$.



The infrared spectra were registered in nujol suspension . The stretching vibration of the carbonyl groups of the aldehydes **5** were observed as intensive bands in three very well distinguishable regions. Bands in 1637 - 1655 cm^{-1} belonging to v(CO) of -pyrone ring, v(CO) aldehyde groups were found in the region at 1693 - 1904 cm^{-1}, v(CO) -pyrone ring can be observed in the region at 1724 - 1760 cm^{-1}

The ^{1}H NMR spectra of prepared compounds confirmed their structure. The signals of protons have displayed chemical shifts and multiplicities corresponding to their surroundings.^{1}H -NMR -spectra of the prepared compounds are shown in experimental part.

Conclusion

The semiempirical AM1 molecular orbital calculations have been used to the study of optimal geometries. The information about conformational properties and the substituent effects on electronic structure of prepared aldehydes **5** were obtained.

. From calculation results were found a significant effect of -pyrone-carbonyl group at formyl group. The activity was recorded on both characteristics of the formyl bond. The polarization was magnified and

multiplicity was diminished . Owing to -pyrone-carbonyl group effect there were found remarkable changes in increasing of positive charge at formyl carbon (0.241), proton acidity (0.170) and negative charge of oxygen (- 0.309). On the other hand effect of formyl group on structure -pyrone ring was by much less effective. There were observation slightly increasing of polarization and smooth lowering of bond order (1.682) at double bond C-2 - C-3.

The little effect of benzene ring was noticed at formyl- and -pyrone carbonyl groups and at mutual bond of both rings. The substituents caused also only slight changes on the study systems.

The calculation of the dependence of the total energy values on the formyl group rotation have shown an advantage of the both planar arrangements . S-cis conformer was prefered. The deviation of formyl groups from planar structure in s-cis conformer was nearly to 0.5and s-trans conformer deviated about 10. The difference of total energy of both conformers was in the range 22 - 26 $kJmol^{-1}$.

Experimental

^{1}HNMR spectra were measured on spectrometers Tesla BS 487 (80 MHz) and Bruker AM 300 (300,13 MHz) in solution of DMSO-d6, using HDMSO as internal standard. The infrared spectra were recorded on Specord IR 75 spectrometer in paraffine oil. Melting points were determined on a Kofler block. The reaction course was monitored by thin-layer chromatography (ethyl ethanoate + cyclohexane).

The purity and structures of the prepared compounds were monitored by IR, ^{1}HNMR spectroscopy as well as their elemental analyses

The synthesis of acetophenones **4a - 4e** are described in [11-13].

Synthesis of 3-formylchromones **5**

General procedure

$POCl_3$ (0,49 mol) was added droppwise to dimethylformamide (DMF) (121 ml) with stirring at 30-35 C, after the addition, the mixture was stirred at 50C for 1 h. Then the solution of 2-hydroxy- acetophenone derivatives **4** (0.12 mol) in least amount of DMF was added droppwise with stirring to the above mixture. After that the mixture was stirred at 45-55^{o}C for 2 hours, kept over the night at room temperature and slowly poured over mixture ice and water(200 g).Product was stirred for 6 hours, then filtered off and recrystallized from ethanole

The following compounds were prepared by general pocedure:

8-Methyl-4,6-dioxo-4H,6H-pyrano[3,2-g]chromone-3-carbaldehyde (**5a**)

M.p. 310 - 312 deg.C.

^{1}H-NMR (DMSO): 10.12(1H,s,CHO), 8.86(1H,s,H-2), 8.18(1H,d,H-10), 7.67(1H,d,H-9), 6.53(1H,s,H-7)

Anal. calc. for $C_{14}H_8O_5$ (256.2): C 65.62, H 3.13; found: C 65.33, H 3.12 .

6-Methyl-4,6-dioxo-4H,8H-pyrano[3,2-g]chromone-3-carbaldehyde (**5b**)

M.p. 255 - 260 deg.C.

^{1}H-NMR (DMSO): 10.12(1H,s,CHO),8.97(1H,s,H-2), 8.39(1H,s,H-5), 7.87(1H,s,H-10), 6.56(1H,s,H-7), 2.54(3H,s,CH)

Anal. calc. for $C_{14}H_8O_5$ (256.2): C 65.62, H 3.13; found: C 65.48, H 3.01 .

10-Methyl-4,8-dioxo-4H,8H-pyrano[2,3-h]chromone-3-carbaldehyde (**5c**)

M.p. 233 - 234 deg.C.

^{1}H-NMR (DMSO): 10.14(1H,s,CHO), 9.02(1H,s,H-2), 8.31(1H,d,H-5), 7.58(1H,d,H-6), 6.57(1H,s,H-9), 2.74(3H,s,CH)

Anal. calc. for $C_{14}H_8O_5$ (256.2): C 65.62, H 3.13; found: C 65.32, H 3.07 .

6-Methyl-5-hydroxy4,8-dioxo-4H,8H-pyrano[3,2-g]chromone-3-carbaldehyde (**5d**)

M.p. 273 - 274 deg.C.

^{1}H-NMR (DMSO) : 10.05(1H,s,CHO), 8.63(1H,s,h-2), 8.12(1H,s,H-10), 6.78(1H,s,H-7), 6.26(1H,s,OH), 2.54(3H,s,CH)

Anal. calc. for $C_{14}H_8O_6$ (272.2): C 61.79, H 2.94; found: C 61.62, H 2.99 .

8-Methyl-9-hydroxy4,6-dioxo-4H,6H-pyrano[2,3-f]chromone-3-carbaldehyde (**5e**)

M.p. 290 - 293 deg.C.

^{1}H-NMR (DMSO) : 10.07(1H,s,CHO), 9.06(1H,s,H-2), 7.30(1H,s,H-10), 6.31(1H,s,H-7), 2.62(3H,s,CH)

Anal. calc. for $C_{14}H_8O_6$ (272.2): C 61.79, H 2.94; found: C 61.77, H 2.92 .

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Comments

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