

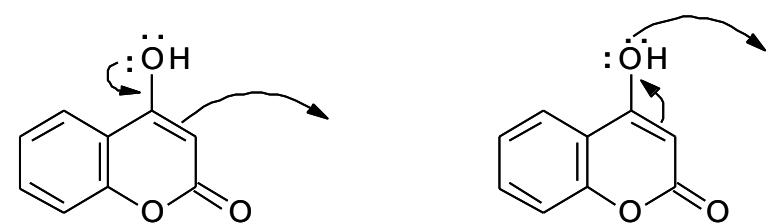
Aligning 4-Hydroxycoumarins into β -chains, 3-Substituted 7-dimethylamino-4-hydroxycoumarins

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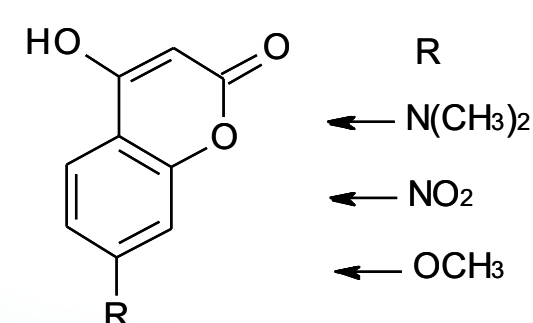
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INTRODUCTION

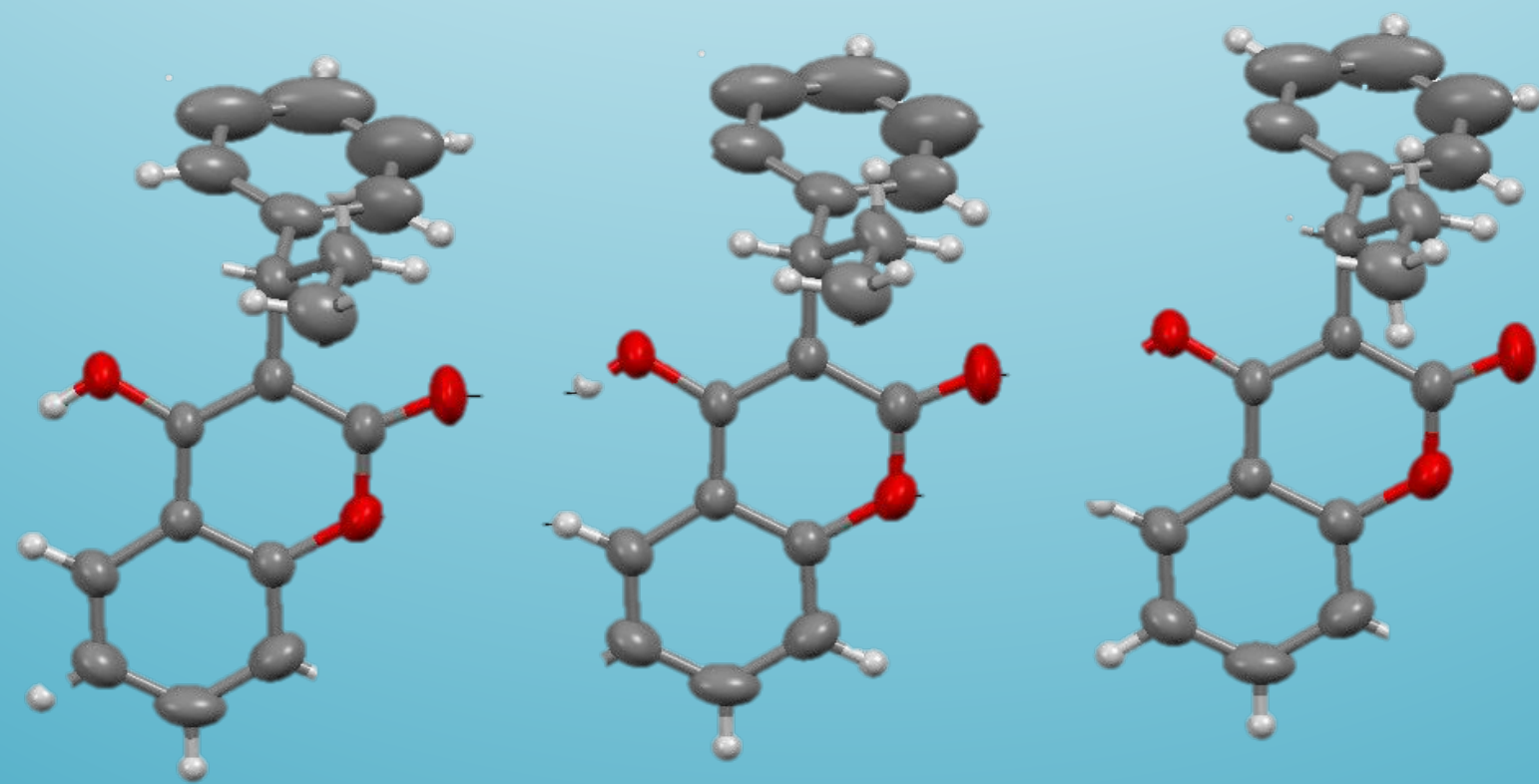
- The tautomeric properties of 4-hydroxycoumarin allow for it to react as an oxygen or a carbon nucleophile, and its chemistry is largely defined by these options



- Prepare 7-substituted derivatives of 4-hydroxycoumarin and to explore several literature methods of 3-substitution. The derivatives chosen are dimethylamino, nitro and methoxy as these are poor Hydrogen-bond donors or acceptors.



- Hydrogen-bonded assemblies allows for adjacent alignment of the β -enolones forming a 717 pm repeat unit in the crystalline environment. Such an arrangement is disturbed by Hydrogen-bonding donors and acceptors substituted at the 3-position. Non-polar 3-substituents apparently accommodate this Hydrogen-bonding scheme. Because of the alignment, it seems possible 7-substituents may be accommodated, again, if they are not Hydrogen-bond competitors. This area of chemistry has not been explored.

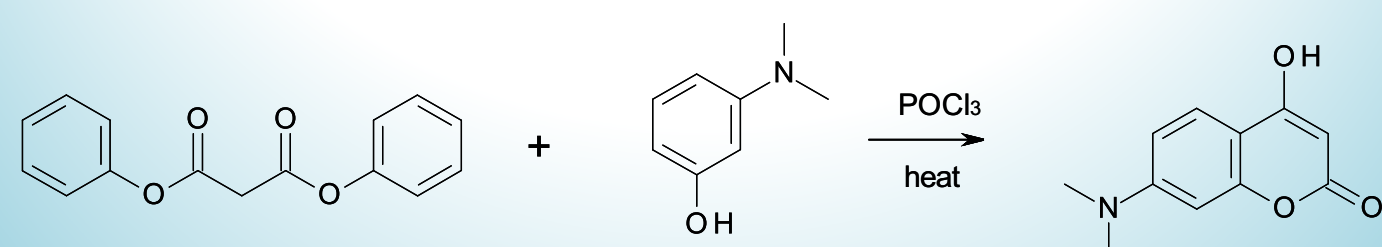


Hypothesis

- Inspection of the phenprocoumon system shows that substitution at the 7-position may not introduce bulky elements which might otherwise disrupt the formation of the β -chains. Other possibilities might be 7-methoxy or 7-nitro groups.

Making 7-dimethylamino-4-hydroxycoumarin

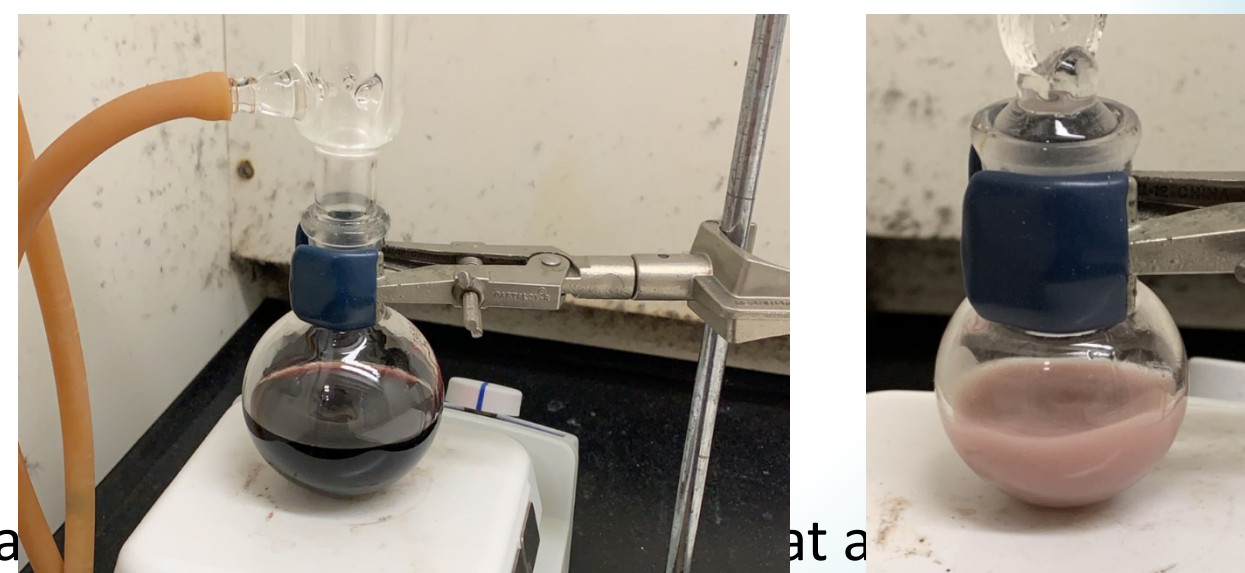
- Of the several literature methods, the most direct is to form this compound from diphenyl malonate and 3-dimethylaminophenol with POCl₃.



PREPARATION OF 7-DIMETHYLAMINO-4-HYDROXYCOUMARIN:

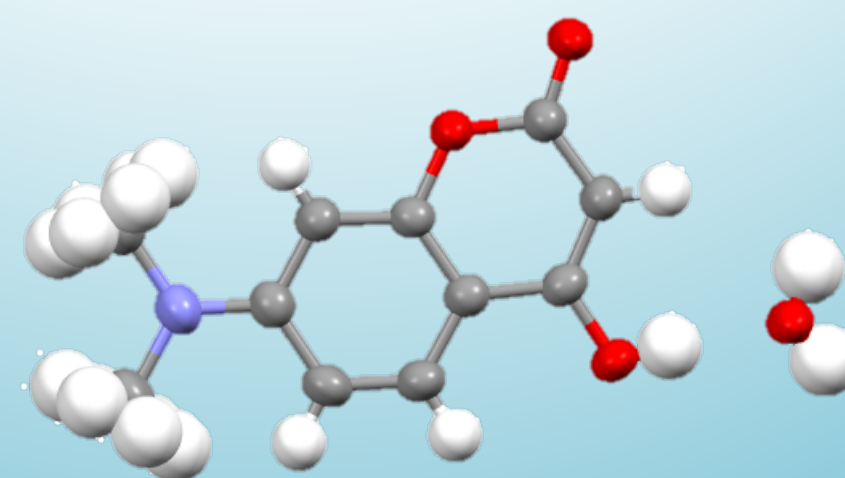
Gray precipitate formed
1.647 g, 73.7%. produced

TLC on product indicated
that the product is a relatively
polar compound with the illumina



Compound identity was confirmed by proton and carbon NMR. It forms deep green crystals from dimethylsulfoxide solution., and occurs as a hydrate. The structure was determined.

CELL IS MONOCLINIC, SPACE
GROUP P2(1)/c.

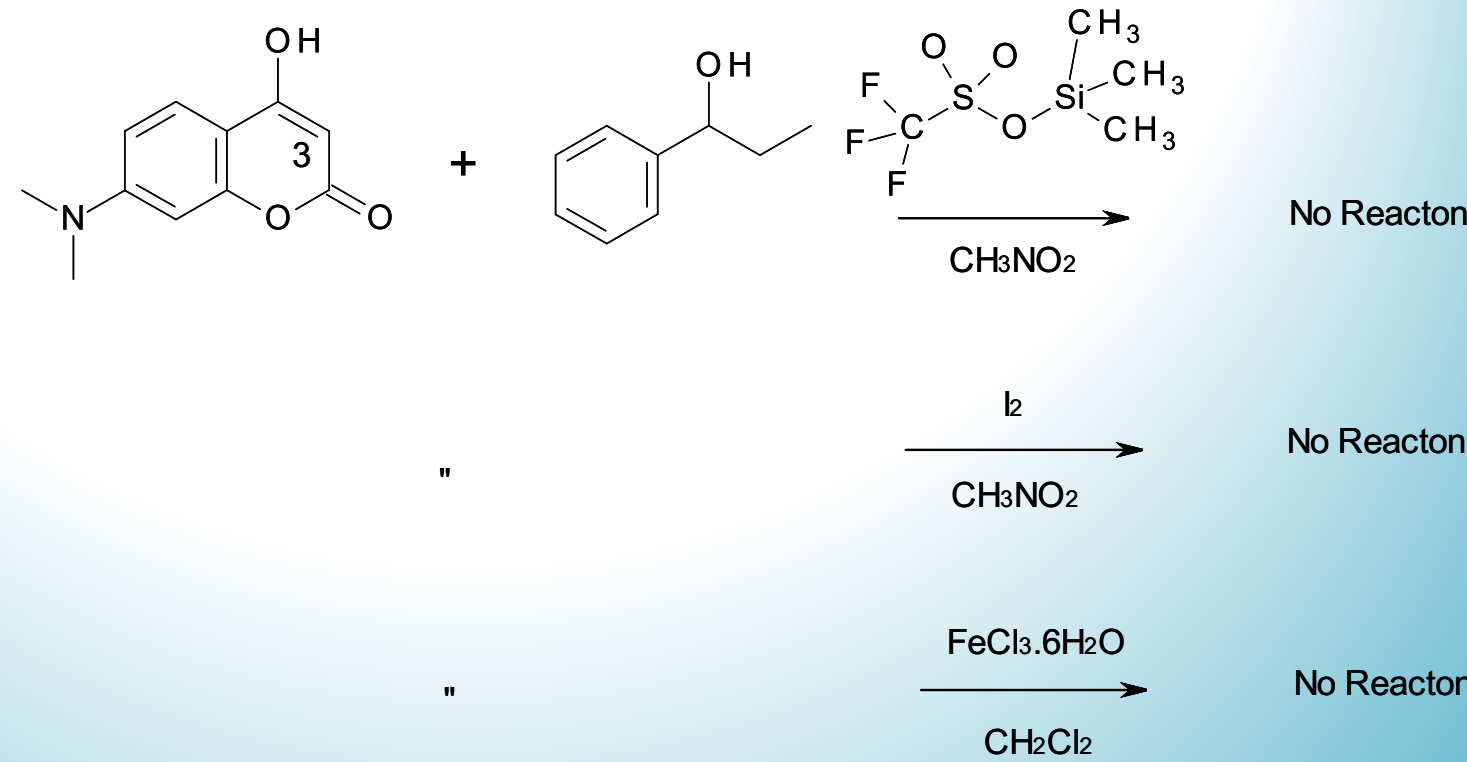


Attempts to substitute at 3-position:

Reaction with 1-phenyl-1-propanol was pursued by several preciously reported useful **methods**.

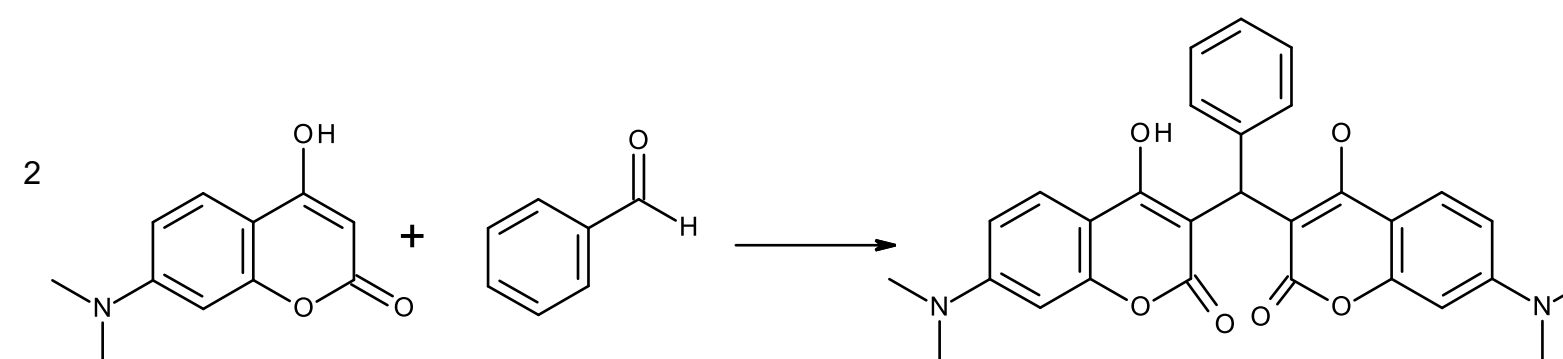
Failures

In each case, only
unreacted starting
materials were
recovered.

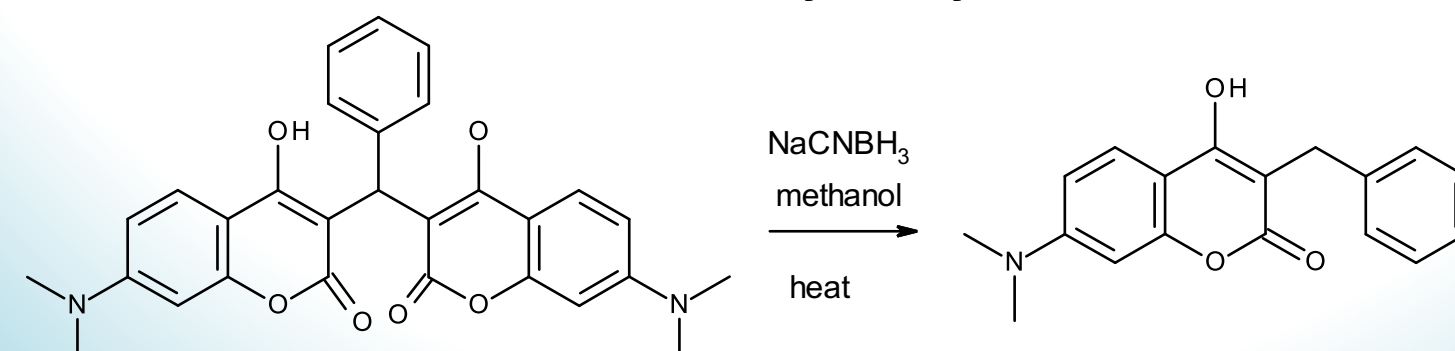


Condensation with benzaldehyde:

Benzaldehyde is known to react with 4-hydroxycoumarins to form very insoluble (substituted) dicoumarols. There are many examples.



Reaction of 7-dimethylamino-4-hydroxycoumarin with benzaldehyde gave the dicoumarol as a very insoluble yellow solid. A method is known to reductively cleave dicoumarols to 3-substituted 4-hydroxycoumarins.

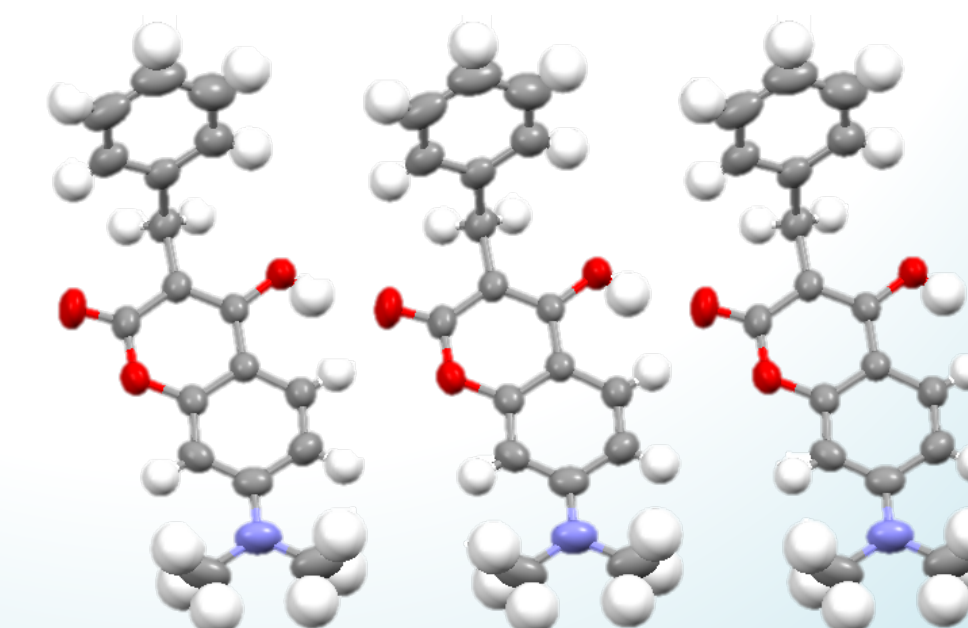


In this way, 3-benzyl-4-hydroxycoumarin was prepared as a colorless solid. Its crystal structure shows β -chain formation.

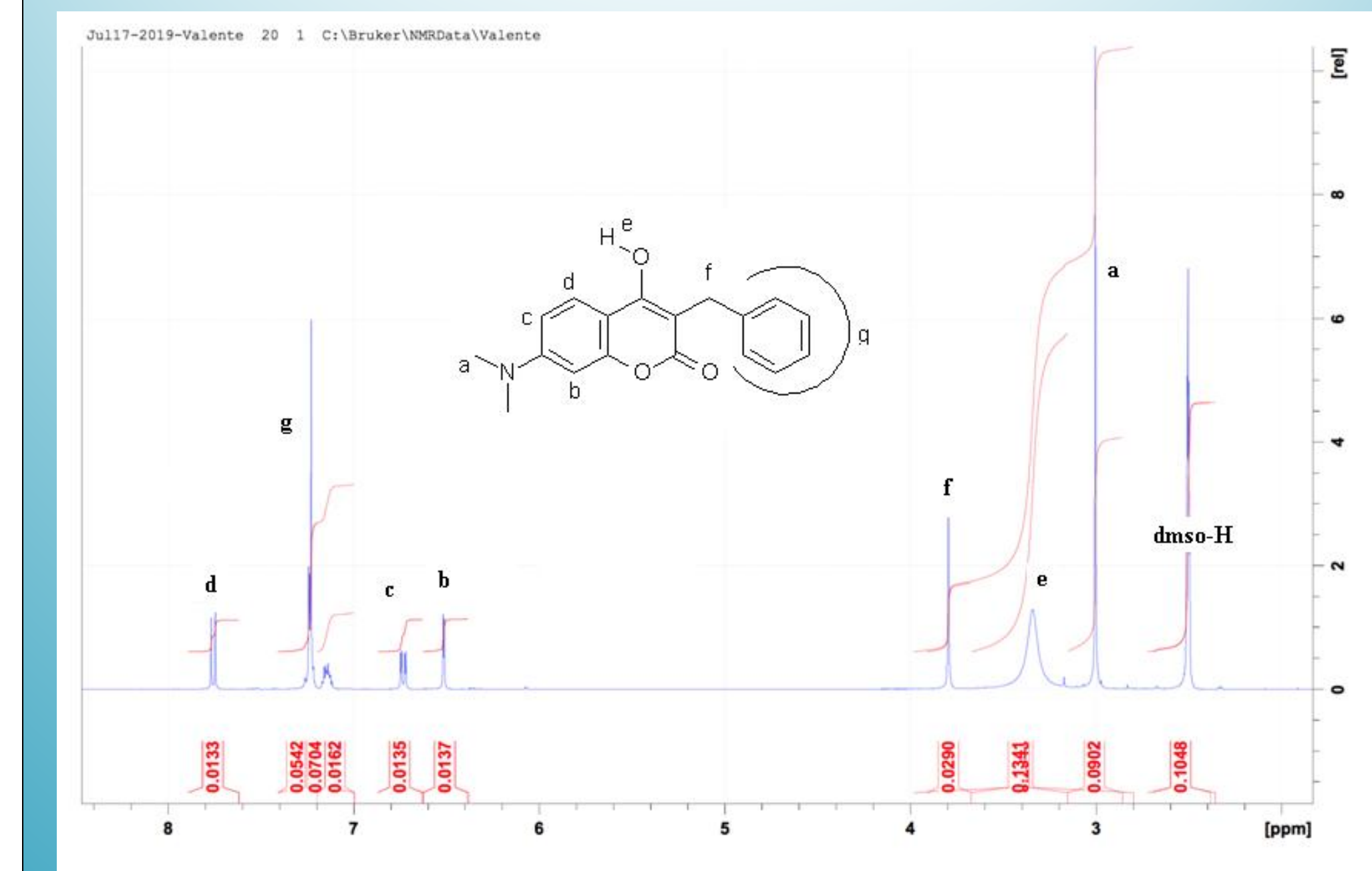
STRUCTURE OF 3-BENZYL-7-DIMETHYLAMINO-4-

HYDROXYCOUMARIN

CELL IS TRICLINIC,
SPACE GROUP P-1



NMR SPECTROSCOPY



CONCLUSION

Phenprocoumon

- 7-Dimethylamino-4-hydroxycoumarin was prepared in pure form and characterized by proton and carbon NMR, and the structure of its hydrate was determined.
- Nucleophilic addition of this substance to 1-phenyl-1-propanol was not an effective method to substitute the coumarin ring on the 3-position
- Using a route through the dicoumarol was successful in making 3-benzyl-7-dimethylamino-4-hydroxycoumarin
- The benzyl substituted analog did produce well-aligned β -chains
- These results suggest that acidic conditions may inhibit desired reaction to the 7-dimethylamino phenprocoumon.
- Other methods may yet prove effective in taking advantage of the nucleophilic properties of 7-dimethylamino-4-hydroxycoumarin.

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