

## MICHAEL ADDITIONS OF BENZOINS VERSUS MICHAEL-STETTER ADDITIONS<sup>1</sup> OF ALDEHYDES

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Summary: Triethylamine catalyzed Michael additions of benzoin to chalcone can prevail over the expected Michael-Stetter additions when certain thiazolium ion conjugate bases -prepared in situ from the pertinent thiazolium salts and triethylamine- are used as catalysts.

A recent report<sup>2</sup> on the use of acyloin anions as addends in Michael condensations, prompts us to describe our own results in this and related fields.

Thiazolium ion conjugate bases are catalysts for the benzoin condensation<sup>3</sup> as well as for the addition of aldehydes to activated double bonds<sup>1</sup> (Michael-Stetter additions). In a typical example of this relatively new and synthetically useful reaction, using as catalyst the conjugate base of 3-benzyl-4-methyl-5-(2-hydroxyethyl)thiazolium ion -prepared in situ from the corresponding thiazolium chloride (Ia) and triethylamine- furfural adds to chalcone to give 1-(2-furyl)-2,4-diphenyl-1,4-butanedione (II), in 85% yield<sup>4,5</sup>.

However, we find now that when the thiazolium salt employed is either (Id)<sup>6</sup> or (Ie)<sup>6</sup>, the compound directly isolated from the reaction mixture (15-20% yields) is no longer diketone (II) but 2-hydroxy-1,2-di(2-furyl)-3,5-diphenyl-1,5-pentanedione, m.p. 143-5° (IIIa)<sup>7</sup>. The presence of small amounts of diketone (II) in the reaction mixtures can be established by spectral means.

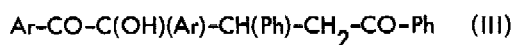
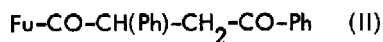
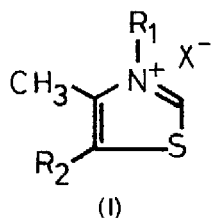
Formation of hydroxy-diketone (IIIa) could be understood after we had found that, under the

catalytic action of triethylamine, furoin adds to chalcone (in ethanol solution) to give that compound (18% yield). We can hypothesize that not all thiazolium ion conjugate bases have identical catalytic characteristics and that the conjugate bases of 3-(1-phenylethyl)- and 3-(1-benzylethyl)-4-methylthiazolium ions are good benzoin condensation catalysts but particularly poor Michael-Stetter condensation catalysts, with this hypothesis, we can explain that the expected addition of furfural to chalcone be superceded by the triethylamine catalyzed addition to chalcone of the furoin which is being formed simultaneously.

As can be seen from the results collected in the Table, other thiazolium salts show an intermediate behaviour between those described above. There appears that with regard to good Michael-Stetter condensation catalytic activity, branching in the N-substituent is a negative feature while the presence of a 5-(2-hydroxyethyl) substituent is a positive one.

TABLE

	<u>Thiazolium salt (I)</u>			<u>Yield of (II)/%</u>	<u>Yield of (IIIa)/%</u>
	$R_1$	$R_2$	X		
a)	Ph-CH <sub>2</sub>	HOCH <sub>2</sub> -CH <sub>2</sub>	Cl	84	---
b)	Ph-CH <sub>2</sub>	H	Cl	56	3
c) <sup>8</sup>	Ph-CH-CH <sub>3</sub>	HOCH <sub>2</sub> -CH <sub>2</sub>	Br	26	10
d)	Ph-CH-CH <sub>3</sub>	H	I	---	20
e)	Ph-CH <sub>2</sub> -CH-CH <sub>3</sub>	H	Cl	---	15

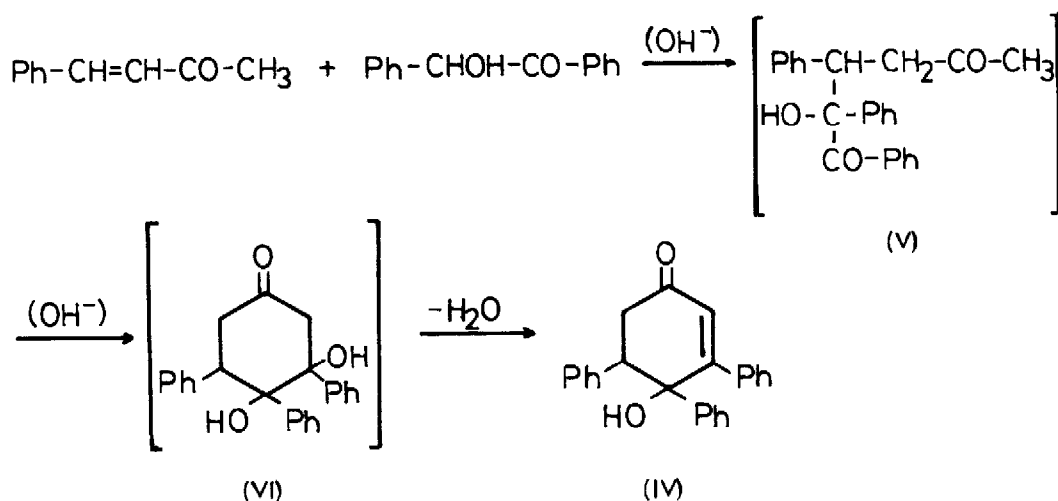


a) Ar = Fu

b) Ar = Ph



There are few reports on the use of acyloins and benzoin as addends in Michael condensations<sup>2,9</sup>. After our initial finding, we have confirmed that benzoin behaves as furon and adds to chalcone (ethanol solution; triethylamine or KOH as the base) to give 2-hydroxy-1,2,3,5-tetraphenyl-1,5-pentanedione (IIIb)<sup>7</sup> in 19% yield (KOH). We have found, too, that benzoin reacts with benzalacetone to give 3,4,5-triphenyl-4-hydroxy-2-cyclohexenone (IV), in 50% yield. The sequence of events which take place can be visualized as follows



Cyclohexenone (IV) was obtained long ago<sup>10</sup> by cyanide catalyzed reaction between benzoin and acetone. The interplay of Michael, (retro)benzoin and aldol condensations, the three of them catalyzed by cyanide ion, explains nicely Smith results, for which the following rationale can be postulated: i) Partial reversion of benzoin to benzaldehyde, ii) Aldol condensation between acetone and benzaldehyde to give benzalacetone, iii) Michael addition of benzoin to benzalacetone, followed by the sequence of events depicted above.

In view of the established possibility of using a chiral basic catalyst to prepare optically active Michael addition products<sup>11</sup>, we have studied the addition of furon to chalcone, with brucine as the basic catalyst. The resulting hydroxy-diketone (IIIa) (45% yield), which has two chiral centers, was resolved by column chromatography in samples of different optical activity: one of them had a negative specific rotation,  $[\alpha]_{\text{D}}^{20} = -3.4^\circ$ , and another, a positive one,  $[\alpha]_{\text{D}}^{20} = 4.7^\circ$ .

Substituent effects on the catalytic activities of thiazolium ions, synthetic extensions of the use of benzoin and acylouins as addends in Michael condensations, and the scope of Michael additions of benzoin are being actively explored.

#### REFERENCES AND NOTES

- 1.- In view of the very considerable work done by Stetter and coworkers on the addition of aldehydes to activated double bonds, under the catalytic action of cyanide ion or of a conjugate base of a thiazolium ion, we name Michael-Stetter condensations this type of reactions. For a review, see Hermann Stetter, Angew. Chem. Int. Ed. Engl., 1976, 15, 639.
- 2.- Tapio Hase, Synthesis, 1980, 36
- 3.- R. Breslow, J. Am. Chem. Soc., 1958, 80, 3719
- 4.- In all our experiments, thiazolium salt, triethylamine, furfural and chalcone were used in a molar ratio of 1.6:20:20 Dry ethanol was used as solvent (8.5 cm<sup>3</sup> for mmol of thiazolium salt). The solutions were refluxed for about 20 hours.
- 5.- 93% in the original reference: Hermann Stetter und Manfred Schreckenber, Chem. Ber., 1974, 107, 2453.
- 6.- J.C. Sheehan, Takeshi Hara, J. Org. Chem., 1974, 39, 1196. Racemic amines were used in the present work.
- 7.- N.m.r., i.r., m.s., as well as elemental analysis were in agreement with the proposed constitution Stereochemistry remains undefined (two pairs of diastereomers are possible).
- 8.- This salt was prepared by reaction between 4-methyl-5-(2-hydroxyethyl)thiazole and 1-bromo-1-phenylethane.
- 9.- a) Jacob Szmuskovicz and Harry Born, J. Am. Chem. Soc., 1953, 75, 3350, b) Jean Colonge et Pierre Brison, Bull. Soc. chim. Fr., 1962, 96, c) Jean Colonge et Pierre Brison, Bull. Soc. chim. Fr., 1962, 98.
- 10.- A. Smith, Ber., 1893, 26, 65.
- 11.- Cf. K. Hermann and Hans Wynberg, J. Org. Chem., 1979, 44, 2238.

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