The Benzoin Condensation Catalysis By Bis(azolin-2-ylidene)s and Bis(azolidin-2-ylidene)s and its Interpretation Within the Context of Nucleophilic Carbene Chemistry

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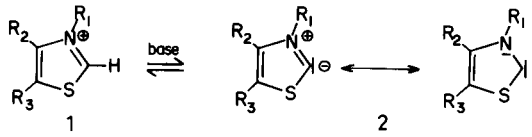
Received October 22,1985

The preparation of bis(thiazolin-2-ylidene)s by passing a methanol solution of the corresponding thiazolium salt through an ion exchange column (basic form) is reported and the use of these "dimers" as benzoin condensation catalysts is studied. The "dimers" show better catalytic activity than the corresponding thiazolium salt plus base. A general discussion of the benzoin condensation catalysis within the framework of nucleophilic carbene chemistry is carried out and as a result of it the important role played by the "dimers" is emphasized. Mechanistic suggestions related with this fact are put forward.

J. Heterocyclic Chem., **23**, 715 (1986).

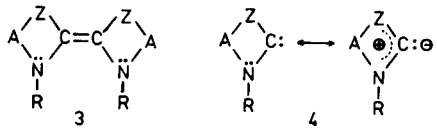
It is well known that the benzoin condensation, which is limited to aromatic aldehydes when cyanide is the catalyst, can be extended to aliphatic aldehydes if a thiazolium salt **1** plus a base is used instead [1]. The formal electronic analogy between H-C≡N and S-CH=N⁺< and some germane experimental evidence on the relatively facile hydrogen isotope exchange at C_2-H of the thiazolium ring [2] has led to the general acceptance that, when a thiazolium salt plus base is used, the actual catalytic species is the conjugate base or thiazolin-2-ylidene **2** (Figure 1). The acidity of "olium" ions and the ylide-carbene nature of the deprotonated species have been the subject of several experimental and theoretical studies [3,4,5].



1 2

Figure 1

Bis(azolin-2-ylidene)s and bis(azolidin-2-ylidene)s **3** (Figure 2) are compounds so closely related to the corresponding azolin-2-ylidenes (of which thiazolin-2-ylidenes



3 4

Figure 2. A: Saturated or unsaturated two carbon chain connection. Z: Frequently, NR or S. Undefined sterochemistry.

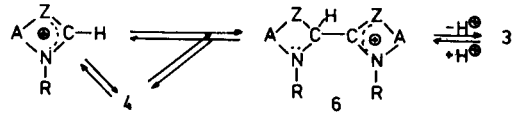
are the most typical representatives) and azolidin-2-ylidenes **4**, respectively, that they are frequently referred to as their "dimers". These "dimers" have been studied intensively within the context of nucleophilic carbene chemistry [6,7,8], but references to their employ as benzoin condensation catalyst are scarce [9,10].

As explained elsewhere [11], during work on the special type of benzoin condensation that uses formaldehyde as substrate and which we have called *formoin reaction*, it was thought desirable to avoid the presence of a base in the reaction medium and, to this end, the use of "dimers" as catalysts was studied.

Preparation and Study of Several "Dimers".

Bis(azolin-2-ylidene)s and bis(azolidin-2-ylidene)s are rather unstable substances which can be prepared by several procedures among which deprotonation of azolium ions **5** [12,13,14,15] is particularly relevant to the present discussion. The accepted mechanism for the formation of these "dimers" is the one shown in Scheme 1: the azolin-2-ylidene species formed by deprotonation of the azolium ion attacks the surrounding azolium ions giving rise to the intermediate dimeric species **6** which is subsequently deprotonated to the bis(azolin-2-ylidenes) **3**, that is to say, to the "dimer". Use of base drives the equilibrium reaction "to the right" and, up to now, isolation of the "dimers" has taken advantage of their insolubility on the reaction medium. This is an important limitation of the procedure.

Scheme 1



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We have developed an alternative general method for the preparation of bis(thiazolin-2-ylidene)s which consist in passing a methanolic solution of the thiazolium salt through a strongly basic ion exchange column, thermostated at 0°, in an inert atmosphere, and collecting the

eluted solution over 3A molecular sieves to avoid the problems due to the high reactivity of these substances. An anhydrous methanolic solution of the "dimer" of the starting salt is obtained; these solutions are relatively stable for variable periods of time, depending on the case, but long enough to permit their manipulation. When necessary, solvent can be removed in high vacuum, low temperature and under an inert atmosphere. We have prepared the "dimers" from the salts shown in Table 1. All of them, except **7** and **8**, are described here for the first time by us, and all except **7** are chiral. Apparently, the bulkier the R_1 group, the more stable the dimer. The mass spectra of some of the dimers have been registered.

The mass spectrum (Figure 3) of the dimer prepared from 3-benzyl-5-(2-hydroxymethyl)-4-methylthiazolium chloride shows a peak at m/e 375 which corresponds to $M_{dimer} - 91$ and that cannot be due to the starting salt. At m/e 233 ($M_{dimer}/2$ or $M_{thiazolium} - 1$) a peak of relative intensity 12.9% is observed while no peak appears at m/e 234 ($M_{thiazolium}$). The significance of these data comes from the fact that in the ms of the thiazolium salt the relative intensity of the peak at m/e 234 is 5.3% while that the one at 233 is only 2.6%.

The ms (Figure 3) of the dimer prepared form 3-[(1*S*,2*S*)-1-hydroxymethyl-2-hydroxy-2-phenylethyl]-4,5-dimethylthiazolium iodide **15** affords similar information. Peaks at m/e 526 (M_{dimer}), 419 (M_{dimer} - PhCHOH) and 263 ($M_{dimer}/2$) are of significant relative intensity.

Use of "Dimers" as Catalysts.

"Dimers" are good benzoin condensation catalysts and, as Table 2 shows, yields of benzoin are in most cases clearly higher than using the corresponding thiazolium salt (plus base). This result is in agreement with that reported by Wanzlick [9].

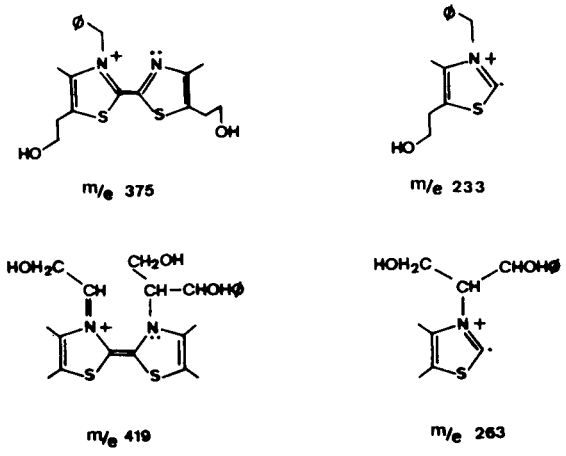
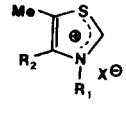


Figure 3

Table 1

2-Unsubstituted Thiazolium Salts



Salt	R_1	R_2	X^-	Mp (°C)	$[\alpha]_D^{20}$	Microanalysis [d] C	H	N	S	X
7	Benzyl	2-Hydroxyethyl	Cl	[a]						
8	(*S*)-1-Phenylethyl	Methyl	I	[b]						
9	Tetra-*O*-acetyl-β-D-glucopyranosyl	Methyl	Br	207-209	−0.60	43.4 (43.5)	5.0 (5.0)	2.5 (2.7)	6.4 (6.1)	15.5 (15.2)
10	β-D-Glucopyranosyl	Methyl	Br	145-147	+18.3	37.1 (37.1)	5.1 (5.1)	3.9 (3.9)	9.2 (9.0)	22.2 (22.4)
11	Tri-*O*-acetyl-β-D-xylopyranosyl	Methyl	Br	157-158	−17.4	42.5 (42.5)	5.0 (4.9)	3.5 (3.1)	7.0 (7.1)	17.6 (17.7)
12	β-D-Xylopyranosyl	Methyl	Br	[c]						
13	Tri-*O*-acetyl-α-D-xylopiranosyl	Methyl	Br	133-135	−37.8	42.4 (42.5)	4.9 (4.9)	3.3 (3.1)	7.0 (7.1)	17.7 (17.7)
14	(2*S*)-1-Hydroxy-3-phenyl-2-propyl	Methyl	I	143-144	−81.2	44.6 (44.8)	4.8 (4.8)	3.6 (3.7)	8.7 (8.5)	33.7 (33.8)
15	(2*S*,3*S*)-1,3-Dihydroxy-3-phenyl-2-propyl	Methyl	I	170-171	+60.0	43.3 (43.0)	4.6 (4.6)	3.6 (3.6)	8.1 (8.2)	32.5 (32.4)

[a] Described in ref [31]. [b] Described in ref [32]. [c] Very hygroscopic product. [d] The values in brackets are the calculated values.

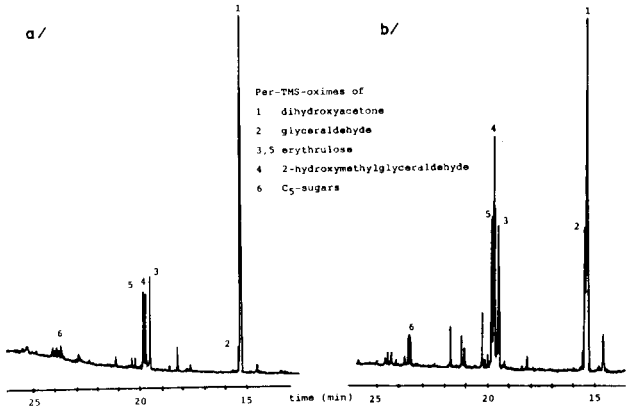


Figure 4. Representative glc chromatograms of TMS-oxime derivatives of formoine mixtures, performed at 60°, with a molar relation formaldehyde:catalyst = 150:1. a/ Conventional procedure, thiazolium salt plus ethyldiisopropyl amine; b/ salt previously converted into its dimer. Observe the different quantitative composition at C_4 area.

Higher yields are obtained also in the formoin reaction. For instance, using salt **7** (plus diisopropylethylamine) the best yield obtained was 35% while using the corresponding "dimer" the yield reached 87% in purified product. However, using a "dimer" as the catalyst, increases the amount of 2-hydroxymethylglyceraldehyde - a branched carbohydrate the presence of which had already been established in the conventional formoin mixtures [16] (Figure 4).

Table 2

Yields in the Catalysed Benzoin Condensation

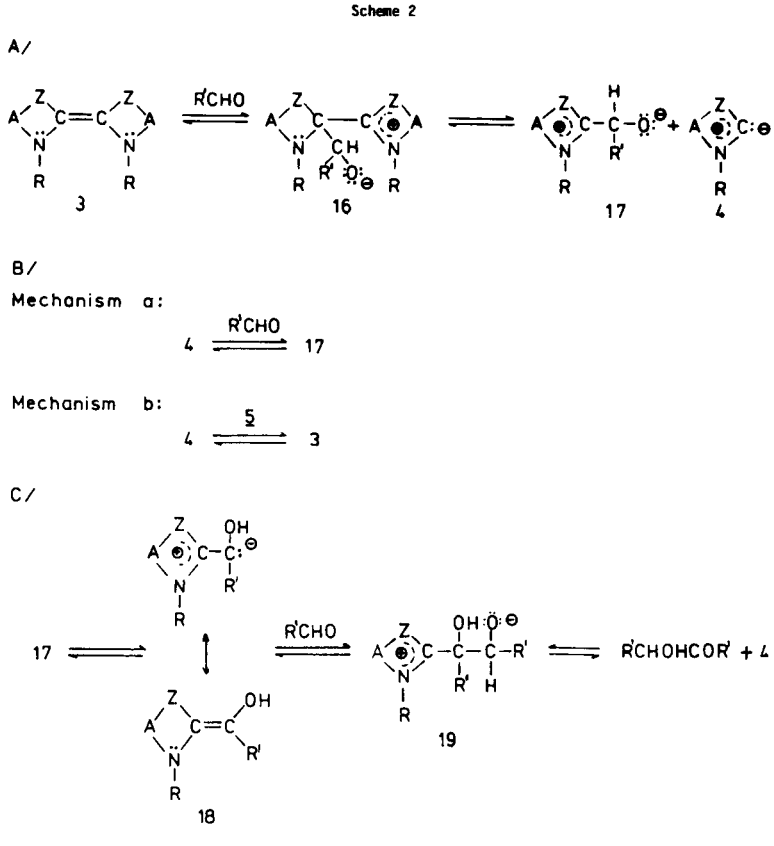
Salt	Basic medium	Dimers
7	94 [a]	93 [a]
9	2 [b,c]	31 [b,c]
10	17 [b,c]	21 [b,c]
11	5 [b,c]	42 [b,c]
12	7 [b,c]	30 [b,c]
14	6 [b,d]	21 [b,d]

[a] Yield in purified benzoin. [b] Yield calculated by quantitative glc. using trimethylsilylated decanol as the internal standard. [c] Reaction conducted in refluxing methanol. [d] Reaction conducted in refluxing ethanol.

Interpretative Discussion.

The excellent benzoin condensation catalytic activity of the "dimers" brings together two closely related fields which, surprisingly enough, seem to have developed ignoring each other. In fact, within the field of catalysis by thiazolium salt plus base [1,17,18,19,20] the unquestioned usage is strict adherence to the more than twenty-five

Scheme 2



years old Breslow's proposals [2], with hardly any reference to knowledge from the nucleophilic carbene field. An extreme example of the prevailing dichotomy can be found in a very recent publication [21] where the isolation of the free conjugate base of thiamine is claimed, apparently ignoring that about twenty years ago a similar claim was made within the field of nucleophilic carbenes [12] and it was shown almost immediately [14] to be wrong. Furthermore, Hunig [22] and Balli [23,24] have established in the case of 3-alkylbenzothiazolin-2-ylidene (which is the only mechanistically studied case) that free species **2** are extremely short-lived and not isolable reactive intermediates.

Without questioning the intermediacy of Breslow species in the benzoin condensation sequence, the catalytic activity of a "dimer" can be explained by two slightly, but significantly, different mechanisms (Scheme 2, part B; part A is common to both mechanisms). Mechanism **a** is a pure extension of Lemal's proposal [25] to the case in which the electrophile is an aldehyde; **b** represents a modified Lemal mechanism in which the free species **4** reacts with the surrounding azolium ions **5** to afford more dimer, which enters in the catalytic cycle.

Part **C** of Scheme 2 shows the classical sequence which leads to benzoins through the participation of Breslow intermediates. The free species **4** which is liberated in the catalytic sequence will react with more aldehyde (mechanism **a**) or with azolium ions (mechanism **b**).

In simplifying terms it can be said that in mechanism **a**, the "dimer" acts as a source of free thiazolin-2-ylidene, which can be considered as the significant catalytic species, while in mechanism **b** free thiazolin-2-ylidene is used up in the formation of "dimer", which is now the exclusive catalytic species.

We think that present evidence favours mechanism **b** more than **a**. To begin with, the omnipresence of "dimers" should be emphasized. In fact, when the catalytic system used is a thiazolium salt plus base, the "dimer" must also be present in the reaction medium; as explained (see above and Scheme 1), deprotonation of thiazolium ions with concomitant nucleophilic attack of the resulting carbene to the surrounding thiazolium ions is the key stage of a standard procedure for the preparation of the "dimers". Furthermore, when a thiazolium salt is treated with a base such as triethylamine the amount of conjugate base which is formed is extremely small and, consequently, the possibility of reaction with the surrounding thiazolium ions is very high.

On the other hand, there have been always some "dark points" on the acceptance of free thiazolin-2-ylidenes **2** as the actual catalytic species. The conjugate bases of thiazolium ions must be stronger bases than cyanide ions because thiazolium ions (pK_a18) [26] are weaker acids than HCN; then, why do they not induce aldol reactions? Furthermore, in a protic medium such as ethanol - frequently used to perform benzoin condensations - it is hardly imaginable that any species **2** could survive long enough to be available for catalytic purposes [27].

It should also be kept in mind that "dimers" *are more* effective benzoin catalysts (see above) and better nucleophilic carbene sources than their related azolium salts plus base [7]. Finally, if mechanism **a** were right, use of a pre-catalyst that could generate thermally a thiazolin-2-ylidene should be the ideal procedure to perform benzoin condensations. However, preliminary results [28] using betaine **19** as pre-catalyst (Figure 5) show that is not the case.

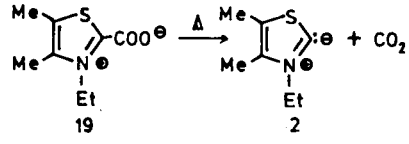
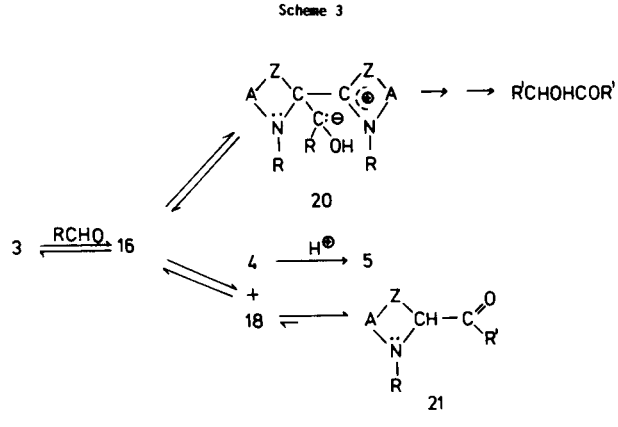


Figure 5

Regarding the much more specific question of the presence of branched sugars in the formoin mixtures it is worth mentioning that Wanzlick [29,30] has shown that ketones are not inert substances in front of "dimers" and it is reasonable to accept that easily enolizable and strongly electrophilic ketones such as dihydroxyacetone, or ketoses in general, should be specially active towards them.

Scheme 3



Once the catalytic activity of the "dimers" (be it through mechanism **a** or **b**) has been established, an important question arises: could not the actual catalytic species preserve the "dimer" skeleton? We believe that all the known facts could be better rationalized by accepting that the actual catalytic species is *always* species **20** (Scheme 3), that derives directly from **16** by tautomerization; species **18** which, after all, is nothing else than an enol, would tautomerize to the acyl derivative **21**. It should be recalled that the poorer the catalytic activity of a "dimer" the higher the yield in which the acyl derivatives **21** are formed [9]. Acyl derivatives from other olium rings

are also known [13,31].

In conclusion, we think that the field of catalysis by thiazolium salt plus base and by related "dimers" should be considered within the broader field of nucleophilic carbene chemistry and that there is no reason to treat aldehydes out of context of the rest of the electrophilic reagents. The mechanistic proposals put forward here are in agreement with this new approach.

EXPERIMENTAL

General Reagents and Methods.

N,N-Dimethylformamide was obtained dry and amine-free by refluxing over phosphorus pentoxide and ninhydrin, vacuum distilled and stored over 4A molecular sieves; the absence of amines was confirmed by the 1-fluoro-2,4-dinitrobenzene test. Analytical-quality pyridine, stored over 4A molecular sieves, was used. Decanol used as internal standard for gl chromatographic quantification was controlled by the same technique. 5-(2-Hydroxyetyl)-4-methylthiazole was supplied by Merck A.G.; 4,5-dimethylthiazole was prepared by the Hantzsch's method [32], acetobromoglucose by the Barczai-Martos and Korosy procedure [33], acetobromoxylose by the method described by Dale [34] and dithioformic acid as described by Engler [35].

The salts 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (**7**) were prepared according to the procedure described by Stetter *et al.* [36] and 3-[(*S*)-1-phenylethyl]-4,5-dimethylthiazolium iodide (**8**) as described by Sheehan *et al.* [37].

The reported temperatures always refer to external heating baths.

A Hewlett-Packard 5790A chromatograph connected to a Hewlett-Packard 3390A integrator was used for glc. A column (2m x 0.125 in) packed with 3% of SE 52 on Chromosorb W 60-80 mesh with a temperature program of 90° for 2 minutes and then 16°/minute was used in the benzoin quantification and a Hewlett-Packard 19091/102 high performance capillary crosslinked column, 5% phenylmethyl silicone, 25 m, in the study of the formoin mixtures. The chromatographic derivatives were TMS-derivatives [38] for the quantification experiments and TMS-oximes [39] for the qualitative study of the composition of formoin mixtures. The ms were recorded on a Hewlett-Packard 5930A mass spectrometer.

Preparation of the Undescribed Salts.

3-(2,3,4-6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4,5-dimethylthiazolium Bromide (**9**).

Acetobromoglucose (16 g, 39 mmoles) was dissolved in anhydrous acetonitrile (40 ml) and added dropwise to 4,5-dimethylthiazole (4.4 g, 39 mmoles) dissolved in boiling anhydrous acetonitrile (30 ml); after refluxing for 18 hours the solvent was removed, the residue washed with anhydrous ethyl ether and recrystallized first from methylene chloride-ethyl ether and afterwards from anhydrous methanol-ethyl ether, yield, 6.1 g, 31%; ^{1}H nmr: δ (H_1) 6.37 ppm ($J_{1,2}$ = 8.6 Hz, *trans*-diaxial).

3-(2,3,4-Tri-*O*-acetyl-β-D-Xylopyranosyl)-4,5-dimethylthiazolium Bromide (**11**).

Acetobromoxylose (3.5 g, 10.3 mmoles) was dissolved in anhydrous acetonitrile (30 ml) and 4,5-dimethylthiazole (1.3 g, 10.3 mmoles) was added; after heating at 40° with stirring for 5 hours the solvent was removed, the residue washed with anhydrous ethyl ether and recrystallized from anhydrous methanol-ethyl ether, yield, 1.2 g, 26%; ^{1}H nmr: δ (H_1) 6.23 ppm $J_{1,2}$ = 8.7 Hz, *trans*-diaxial).

3-(β-D-Glucopyranosyl)-4,5-dimethylthiazolium Bromide (**10**) and 3-(β-D-Xylopyranosyl)-4,5-dimethylthiazolium Bromide (**12**).

The corresponding acetylated salt (9.5 mmoles) was boiled with diluted hydrobromic acid (50 ml, 5%) for 1 hour; the water was removed, the residue washed with anhydrous acetone and crystallized from boiling methanol, yields, 95% of **10** and 90% of **12**. In both cases, the $J_{1,2}$ of the anomeric proton shows no epimerization of the salt.

3-(2,3,4-Tri-*O*-acetyl-α-D-xylopyranosyl)-4,5-dimethylthiazolium Bromide (**13**).

Acetobromoxylose (21.7 g, 64 mmoles) was dissolved in 4,5-dimethylthiazole (14.6 g, 130 mmoles) and left at 5° for 24 hours; the solid that crystallized was filtered out, washed with anhydrous ethyl ether and recrystallized from anhydrous acetone, yield, 13 g, 45%; ^{1}H nmr: δ (H_1) 6.49 ppm ($J_{1,2}$ = 1.7 Hz, *gauche*-H-H).

3-[(2*S*)-1-Hydroxy-3-phenyl-2-propyl]-4,5-dimethylthiazolium Iodide (**14**).

(*S*)-Fenilalaninol (2 g, 13.2 mmoles) was dissolved in ethanol (12 ml) and dithioformic acid (1.03 g, 13.2 mmoles) was suspended in the solution and left under magnetic stirring at room temperature for 20 hours; the solvent was removed, the residue suspended into water (20 ml) and the aqueous suspension extracted with chloroform (5 x 20 ml); the organic layer was dried over anhydrous sodium sulfate and the solvent removed at vacuum. The reddish oily residue (2.1 g, 80% yield), spectrally identified as 2-(*S*)-benzyl-*N*-thioformyl-2-aminoethanol, was mixed with 3-chlorobutan-2-one (2.3 g, 19.7 mmoles) and heated at 75° for 20 hours. After cooling, the mixture was poured into anhydrous ethyl ether (20 ml), and the gelatinous residue was treated with ether three more times with vigorous shaking. The pasty solid obtained was treated with activated charcoal in ethanolic solution, the ethanol evaporated, the product dissolved in water (50 ml) and the aqueous solution saturated with potassium iodide appearing an oil that was extracted with methylene chloride (3 x 40 ml). The organic solution was dried over anhydrous sodium sulfate and the solvent removed. The isolated oil was chromatographied over silica gel; the material eluted with methylene chloride was discarded and the product eluted with methylene chloride-1% methanol was collected. The resulting salt was recrystallized from anhydrous acetone, yield, 1.9 g, 48%; ^{1}H nmr (DMSO-d_6): δ 1.9 (s, 3H, CH_3), 2.1 (s, 3H, CH_3), 3.0 (d, 2H, CH_2Ph), 3.7 (d, 2H, CH_2OH), 4.7 (b. b., 1H, CH-N$^+$), 6.8 (s, 5H, Ph) and 9.8 (s, 1H, C_2-H).

3-[(2*S*,3*S*)-1,3-Dihydroxy-3-phenyl-2-propyl]-4,5-dimethylthiazolium Iodide (**15**).

(1*S*,2*S*)-2-Amino-1-phenyl-1,3-propanodiol (9 g, 54 mmoles) and dithioformic acid (4.2 g, 54 mmoles) were suspended into methanol, methylene chloride (50 ml, 1:1) and left stirring for 2 hours at room temperature. The solvent was removed and the oily residue was dissolved in 3-chlorobutan-2-one (10.1 g, 95 mmoles), heating at 120° for 30 minutes. After cooling, the mixture was poured over anhydrous ethyl ether (50 ml) and the oily residue was vigorously shaken for three more times in the same amount of ether. The residue was dissolved in water (50 ml), extracted with methylene chloride (3 x 10 ml) and the aqueous layer saturated with potassium iodide and extracted with methylene chloride (5 x 20 ml). The organic layer was dried over anhydrous sodium sulfate, the solvent removed and the solid was crystallized from anhydrous acetone/ethyl ether, yield, 1.4 g, 10%; ^{1}H nmr (deuteriochloroform): δ 1.7 (s, 3H, CH_3), 2.1 (s, 3H, CH_3), 3.8 (d, 2H, CH_2OH), 4.6 (d, 1H, PhCHOH), 4.9 (m, 1H, CH-N$^+$), 6.9 (s, 5H, Ph), 9.8 (s, 1H, C_2-H).

Preparation of Bi(thiazolin-2-ylidenes).

A solution of 3.5 mmoles of thiazolium salt in 10 ml of methanol was passed through a 2.7 x 43 cm chromatographic column filled with Kastel A-300 anionic exchange resin (OH^- form) (Amberlite IRA-401 and Ionac A-305 have also been used with the same results) thermostatized at 0° and previously washed with methanol up to neutral *p*H. The eluted was collected at 0° over 3A molecular sieves under an inert atmosphere until the eluate was colorless. The methanolic solution was directly used or evaporated under a nitrogen atmosphere at high vacuum and low temperature.

Measure of Catalytic Activity.

a/ By Isolation of Benzoin.

A solution of 20 mmoles of benzaldehyde, 0.5 mmole of thiazolium salt and 2.0 mmoles of triethylamine (or the same amount of salt previously converted into its bis(thiazolin-2-ylidene)) in 10 ml of alcohol was heated under reflux for 1.5 hours. The reaction mixture was poured into 100 ml of ice-water and filtered. The white solid that appeared was filtered, washed with water, dried at vacuum over phosphorus pentoxide and recognized as benzoin by comparison with an authentical sample. The yields are shown in Table 2.

b/ Benzoin Quantification by GLC.

A mixture of 1.9 mmoles of benzaldehyde, 0.19 mmole of thiazolium salt, 0.20 mmole of triethylamine (or the equivalent amount of salt previously converted into its bis(thiazolin-2-ylidene) derivative) and 50 mg of decanol (as internal standard for glc. quantification) in 1 ml of methanol or ethanol, was heated under reflux for 1.5 hours. After distillation of the solvent, the resulting oil was dissolved in 5 ml of chloroform, washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The resulting material was dissolved in 2 ml of pyridine, silylated by the addition of 0.5 ml of hexamethyldisilazane (HMDSA) and 0.5 ml of trimethylchlorosilane (TMCS) and chromatographied. The yields are shown in Table 2.

Activity in the Formoin Reaction.

A methanolic solution containing the amount of bis(thiazolin-2-ylidene) prepared from 0.9 mmole of the starting thiazolium salt **7** is evaporated to dryness under nitrogen atmosphere, at high vacuum and low temperature. The resulting amorphous material was dissolved in 10 ml of DMF, 1.2 g of paraformaldehyde added and heated with magnetic stirring at 80° for 1.5 hours. After distillation of the solvent at low pressure, the residue was dissolved in 50 ml of water and extracted with chloroform (3 x 25 ml). The aqueous phase, after evaporation and drying at vacuum over phosphorus pentoxide, yielded 1.04 g (87%) of the sugar mixture (the maximum yield obtained in basic medium was 35%, see reference [11].

Acknowledgment.

We acknowledge gratefully the support of the "Comisión Asesora de Investigación Científica y Técnica" (Grant No. 343/81) and a scholarship of the "Ministerio de Educación y Ciencia" to one of us (F. G.).

REFERENCES AND NOTES

[1] H. Stetter, R. Y. Ramsch and H. Kuhlmann, *Synthesis*, 733 (1976).

[2] R. Breslow, *J. Am. Chem. Soc.*, **80**, 3719 (1958).

[3] F. Geijo, F. López-Calahorra and S. Olivella, *J. Heterocyclic Chem.*, **21**, 1781 (1984).

[4] F. Geijo, F. López-Calahorra and S. Olivella, *J. Heterocyclic Chem.*, **21**, 1785 (1984).

[5] A. A. Gallo, J. J. Mieyal and H. Z. Sable, *Bioorg. Chem.*, 147 (1978).

[6] H. W. Wanzlick, F. Esser and H. J. Kleiner, *Chem. Ber.*, **96**, 1208 (1963).

[7] H. W. Wanzlick, H. J. Kleiner, I. Lasch, H. U. Fuldner and H. Steinmaus, *Ann. Chem.*, **708**, 155 (1967).

[8] W. Krasuski and M. Regitz, *Z. Naturforsch.*, **39b**, 1806 (1984).

[9] B. Lachmann, H. Steimans and H. W. Wanzlick, *Tetrahedron*, **27**, 4085 (1971).

[10] M. F. Lappert, R. K. Maskell, *J. Chem. Soc., Chem. Commun.*, 580 (1982).

[11] J. Castells, F. López-Calahorra and F. Geijo, *Carbohydr., Res.*, **116**, 197 (1983).

[12] H. W. Wanzlick and H. J. Kleiner, *Angew. Chem.*, **75**, 1204 (1963).

[13] J. Metzger, H. Larivé, R. Dermilauler, R. Baralle and C. Gaurat, *Bull. Soc. Chim. France*, 2857 (1964).

[14] H. Quast and S. Hünig, *Angew. Chem.*, **76**, 989 (1964).

[15] H. Quast and S. Hünig, *Chem. Ber.*, **99**, 2017 (1966).

[16] We thank Dr. Donald E. Willis, Corporate Research Laboratories, Monsanto Company, for drawing our attention to the presence of this substance.

[17] H. Stetter and G. Lorenz, *Chem. Ber.*, **118**, 1115 (1985).

[18] T. Matsumoto, M. Ohishi and S. Inoue, *J. Org. Chem.*, **50**, 603 (1985).

[19] D. Hilvert and R. Breslow, *Bioorg. Chem.*, **12**, 206 (1984).

[20] M. B. Doughty and D. S. Lawrence, *J. Chem. Soc., Chem. Commun.*, 454 (1985).

[21] H. Sugimoto and K. Hirai, *Tetrahedron Letters*, **26**, 883 (1985).

[22] S. Hünig, *Angew. Chem., Int. Ed. Engl.*, **7**, 335 (1968).

[23] H. Balli, *Chimia*, **22**, 49 (1968).

[24] H. Balli, *Angew. Chem.*, **76**, 995 (1964).

[25] D. M. Lemal, R. A. Lovald and K. I. Kawano, *J. Am. Chem. Soc.*, **86**, 2518 (1964).

[26] D. S. Kemp and J. T. O'Brien, *J. Am. Chem. Soc.*, **92**, 2554 (1970).

[27] R. S. Brown, H. Slebocka-Tilk, J. M. Buschek and J. G. Ulan, *J. Am. Chem. Soc.*, **106**, 5979 (1984).

[28] J. Castells, F. López-Calahorra and L. Domingo, *Tetrahedron Letters*, **26**, 5457 (1985).

[29] H. W. Wanzlick and E. Schikora, *Chem. Ber.*, **94**, 2389 (1961).

[30] H. D. Hartzler, *J. Am. Chem. Soc.*, **91**, 1113 (1969).

[31] H. W. Wanzlick and H. J. Kleiner, *Chem. Ber.*, **96**, 3024 (1963).

[32] J. Metzger and J. Beraud, *Compt. Rend.*, **242**, 2362, (1956).

[33] M. Bárczai-Martos and F. Körösi, *Nature*, **165**, 369 (1950).

[34] J. K. Dale, *J. Am. Chem. Soc.*, **37**, 2745 (1917).

[35] R. Engler and G. Gattow, *Z. Anorg. Allg. Chem.*, **389**, 145 (1972).

[36] H. Stetter and H. Kuhlmann, *Synthesis*, 379 (1975).

[37] J. C. Sheehan and T. Hara, *J. Org. Chem.*, **39**, 1196 (1974).

[38] C. C. Sweeley, R. Bentley, M. Makita and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).

[39] D. E. Willis, *J. Chromatogr. Sci.*, **21**, 132 (1983).