Quaternization and Catalytic Activity of Poly(vinylthiazoles)

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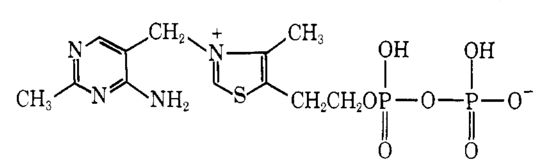
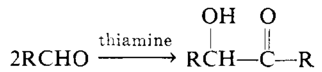
ABSTRACT: Attempts to quaternize 4-vinylthiazole with methyl iodide resulted in the formation of a quaternized polymer. Partially quaternized polymers of 4-vinylthiazole and 5-vinyl-4-methylthiazole were obtained by treating the respective poly(vinylthiazoles) with methyl iodide. The latter polymers serve as catalysts for the conversion of furfural to furoin. A comparison is made of the polymer catalytic activity with that of model compounds.

Thiamine pyrophosphate (I) is a coenzyme for a number of enzymic reactions. For example, I



I

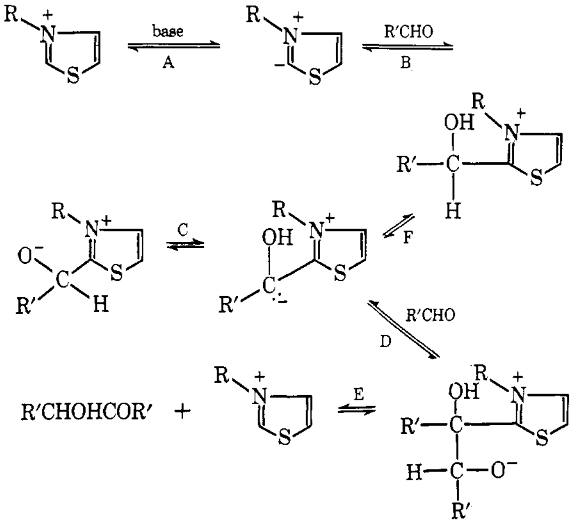
catalyzes the acyloin condensation. A number of



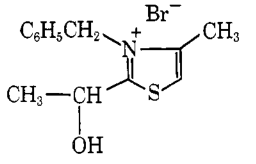
$$2\mathrm{RCHO} \xrightarrow{\text{thiamine}} \mathrm{R}\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{H}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{R}$$

thiamine dependent nonenzymic reactions which are closely similar to the enzymatic process have been discovered, and the mechanism of this process has been elaborated by Breslow[2-4] with the discovery that the hydrogen at the 2 position of the thiazolium ring exchanges with deuterium oxide at neutral pH. The generally accepted sequence of events is shown in Scheme I.

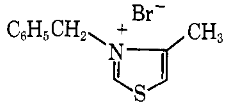
Scheme I



It was of interest to examine the catalytic activity of polymers containing thiazolium units as well as other functional groups which might assist the reaction. In the case of the acetoin condensation, Breslow[4] has shown that 3-benzyl-2-(1-hydroxyethyl)-4-methylthiazolium bromide (II) is more reactive than 3-benzyl-4-methylthiazolium bromide (III). However, II was



II



III

not as effective as thiamine, and, therefore, steps C, D and E (Scheme I) are probably important in determining the rate of reaction.

The simplest polymeric system seemed to be a copolymer containing thiazole and thiazolium units which could be prepared from the previously described vinyl and isopropenylthiazoles.[5] The presence of a high concentration of basic thiazole rings in the vicinity of the polymer coil could facilitate steps A, F, and E by internal proton removal, just as the presence of the amino group on the pyrimidine ring in thiamine may be responsible for the enhanced reactivity of thiamine relative to simple model compounds.[4]

Results and Discussion

Treatment of 4-vinylthiazole with methyl iodide in ethyl ether did not result in the expected product. That a quaternized thiazole was formed was apparent from an immediate positive silver nitrate test and from the fact that the lowest field nmr signal at τ −0.03—which is due to H-2 on the thiazole ring—disappeared because of exchange with deuterium oxide, a characteristic of thiazolium salts.[2] In addition the nmr revealed the absence of olefinic protons and the presence of signals attributable to methylene and methine groups. Inasmuch as 4-vinylthiazole in the absence of methyl iodide does not polymerize under the reaction conditions, it appears that the quaternized monomer is readily polymerizable by the nucleophilic iodide ion just as 4-vinylpyridine is polymerized when quater-

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(1) Continental Oil Co. Fellow, 1966–1967.

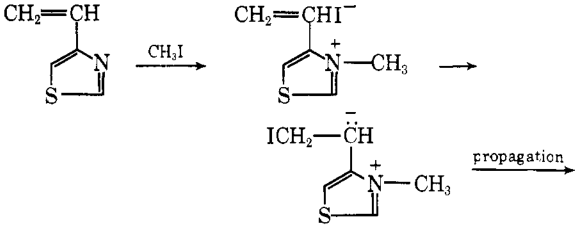
(2) R. Breslow, *J. Amer. Chem. Soc.*, **79**, 1762 (1957).

(3) R. Breslow, *ibid.*, **80**, 3719 (1958).

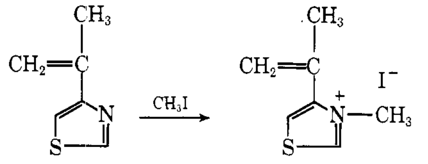
(4) R. Breslow and E. McNelis, *ibid.*, **81**, 3080 (1959).

(5) C. L. Schilling, Jr., and J. E. Mulvaney, *Macromolecules*, **1**, 445 (1968).

nization with alkyl halides is attempted.[6] A similar fully quaternized polymer was obtained from 2-vinylthiazole and methyl iodide.



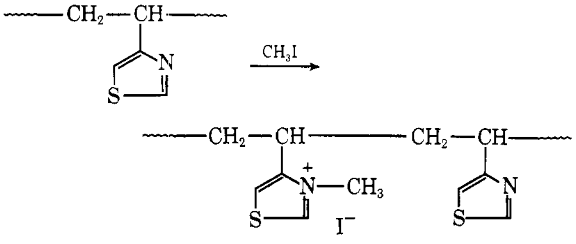
In contrast 4-isopropenylthiazole could be successfully quaternized with no polymerization. It is not



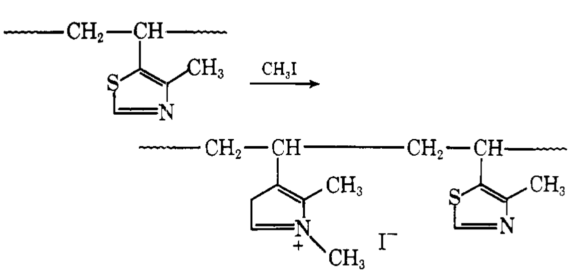
unexpected that the α-methyl group should decrease the polymerizability of the quaternary salt by virtue of its steric and inductive effect. A number of attempted free radical polymerizations of 3-methyl-4-isopropenylthiazolium iodide using radical initiators was unsuccessful.

The simplest method for obtaining copolymers containing thiazole and thiazolium units was by direct quaternization of the previously described[5] poly(vinylthiazoles) as shown in Scheme II. Poly(4-isopropenylthiazole) was quaternized also to the extent of 37.4%.

SCHEME II



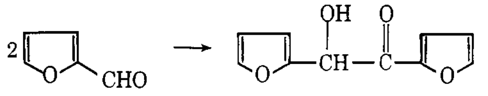
IV, 42% quaternized



V, 78% quaternized

A number of thiazolium salts, some of which are new compounds, were prepared for comparison of catalytic activity. These are listed in Table I.

Because the quaternized polymers were not water soluble, catalytic activities were determined in methanol. The yields of furoin from furfural were used as a criterion for relative reactivity, and results are shown in Table I (average of three determinations). It should be noted that none of the compounds tested produced furoin in the absence of triethanolamine under these conditions. Control experiments established that no furoin was produced in the absence of thiazolium salts and that furoin itself could be recovered at least to the extent of 95% under the reaction conditions. Therefore, the yields presented are a measure of relative rates. The "pH" values have only relative significance because reactions were run in methanol solution. All of the compounds both monomeric and polymeric showed true catalytic activity in the sense of producing considerably more than 1 mol of furoin/mole of thiazolium salt. It is interesting that in this system thiamine chloride hydrochloride (runs 6 and 7) is significantly less reactive than any of the other thiazolium salts which were tested. This is in contrast to results obtained in aqueous systems.[2–4] Run 6 is run under exactly the same conditions as all the others, but thiamine is obtained as the chloride hydrochloride and the pH of the reaction mixture is significantly lower than that of other runs. In run 7 sufficient sodium ethoxide was added to bring this reaction mixture to nearly the same pH as the others. The addition of sodium ethoxide creates sodium chloride and, therefore, in run 9 the reaction was carried out using 3-benzyl-4-methylthiazolium bromide as catalyst in the presence of an equal amount of sodium chloride (~2.0 *M*) as was produced in run 7. The added salt had no measureable effect on the reactivity of this compound (compare runs 3 and 9). It does not seem likely that any salt effects are responsible for the low reactivity of thiamine in run 7.



A comparison of runs 1–5 reveals little difference in activity between the polymer and various monomeric compounds which were chosen for comparison in spite of the fact that unquaternized thiazole units are present in the polymer.

The most efficient catalyst is the partially quaternized poly(4-methyl-5-vinylthiazole) (run 10). Whether or not the presence of unquaternized thiazole accelerates the reaction in this case is not known at this time. Further work will be necessary to clarify this point.

Experimental Section[7]

Furoin Test. All thiazolium salts were recrystallized and vacuum dried just prior to use with the exception of the copolymers which were washed with ether and vacuum dried. Triethanolamine was vacuum distilled at 135° (0.05 mm) and was used as a 0.2 *M* solution in absolute methanol. Furfural was vacuum distilled prior to use at 54° (6.0 mm) and had $n^{23}\text{D}$ 1.5247. Reagent grade absolute methanol was used without further purification.

Test reagents were combined in 15-ml flasks fitted with stopcock adapters, and were degassed twice under vacuum

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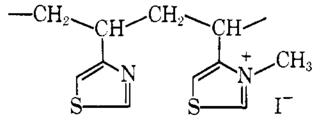
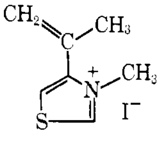
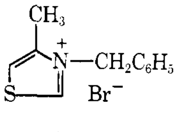
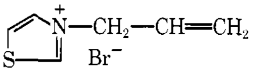
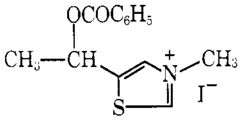
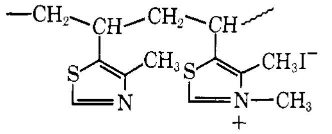
[6] V. A. Kabanov, K. V. Aliev, O. V. Kargina, T. I. Patrikeeva, and V. A. Kargin, *J. Polym. Sci., Part C*, 16, 1079 (1967).

[7] See the first paragraph of the preceding paper[5] for details concerning spectra and analyses.

TABLE I
RESULTS OF FUROIN TEST
(IN METHANOL CONTAINING 2.00 M FURFURAL AND 0.020 M THIAZOLIUM SALT AT 50° FOR 24.0 HR)

Run no.	Catalyst	[TEA],[a] mol/l.	Yield of furoin, %	Mol of furoin/mole of thiazolium units	pH
1[b]		0.050	33 ± 3	17	7.3
2		0.050	26 ± 1	13	7.3
3		0.050	24 ± 2	13	7.3
4		0.050	37 ± 5	19	7.3
5		0.050	42 ± 2	22	7.3
6	Thiamine chloride hydrochloride	0.050	1.5 ± 0.5	0.8	6.7
7[c]	Thiamine chloride hydrochloride	0.050	5.7 ± 0.6	2.9	7.4
8	Same as 3	0.030[f]	5.0 ± 2.0	2.6	6.8
9[d]	Same as 3	0.050	19 ± 3	9.8	
10[e]		0.050	72 ± 1	37	7.3

[a] TEA is triethanolamine. [b] 42 mol % quaternized. [c] Added sufficient sodium ethoxide to give the indicated pH. [d] Solution was made 2.0 M in sodium chloride. [e] 78 mol % quaternized. [f] Also added 0.20 mol/l. of TEA·HCl.

at −78° before being placed in a water bath at 50.0 ± 0.05° for 24 hr. Furoin was isolated by pouring each solution into 30 ml of ice water, collecting the precipitated furoin by filtration, extracting the aqueous solution three times with 125-ml portions of ethyl ether, evaporating the ether and subjecting the total solid product to vacuum sublimation at 95° (0.05 mm) in a sublimation apparatus.

In general, tests were determined in triplicate, each test containing 0.12 mmol of catalyst, 0.30 mmol of triethanolamine, 5.0 ml of methanol, and 1.0 ml (1.2 g, 12 mmol) of furfural. See Table I and discussion for further details.

Copolymer of 4-Vinylthiazole and 3-Methyl-4-vinylthiazolium Iodide. Poly(4-vinylthiazole) (0.62 g) was treated with 9.0 g (0.063 mol) of methyl iodide in 20 ml of chloroform under reflux for 5 hr. The product which precipitated was vacuum dried, ground with mortar and pestle under ethyl ether, and redried prior to submission for iodide analyses. The degree of quaternization was calculated to be 42.5%.

Anal. Found: I, 31.39, 31.67.

Copolymer of 4-Methyl-5-vinylthiazole and 3,4-Dimethyl-5-vinylthiazolium Iodide. Poly(4-methyl-5-vinylthiazole) (0.68 g) was dissolved in 10 ml of chloroform and ethyl iodide (7.0 g, 0.050 mol) was added. The mixture was heated at reflux for 12 hr and the solid product collected, ground, washed with chloroform and ethyl ether, and vacuum dried before submission for iodide analyses. The degree of quaternization was calculated to be 78.0%.

Anal. Found: I, 42.18, 41.94.

3-Methyl-4-(1-benzoxyethyl)thiazolium Iodide. 4-(1-Benzoxyethyl)thiazole[5] (17 g, 0.072 mol) was treated with 18 g (0.13 mol) of methyl iodide at room temperature for 9 days and at 50° for 2 days. The white crystalline product was collected and vacuum dried (12 g, 43%). An analytical sample, recrystallized three times from methanol–ethyl ether, had mp 148–150°. The nmr spectrum (D_2O) showed peaks at τ 8.19 (doublet, 3 H) assigned to the methyl group of the benzoxyethyl side chain, 5.78 (singlet, 3 H) assigned to the 3-methyl group, 3.75 (quartet, 1 H) assigned to the methine proton, 2.46 and 2.01 (two multiplets, 3 H and 2 H, respectively) assigned to the *meta*, *para* protons and the *ortho* protons of the phenyl ring, respectively, and 1.66 (singlet, 1 H) assigned to H_5 on the thiazolium ring. The proton at H_2 on the thiazolium ring was not observed due to exchange with deuterium.

Anal. Calcd for $C_{13}H_{14}INO_2S$: C, 41.60; H, 3.75; S, 8.53; Found: C, 41.98; H, 4.04; S, 8.35.

3-Methyl-4-isopropenylthiazolium Iodide. 4-Isopropenylthiazole (15.6 g, 0.125 mol) and 43.0 g (0.303 mol) of methyl iodide were heated at reflux for 48 hr. The addition of 50 ml of ethyl ether precipitated the crude product (30.0 g, 90.0%, after washing with ethyl ether and vacuum drying). An analytical sample, recrystallized three times from methanol–ethyl ether, had mp 117–118°. The nmr spectrum (D_2O) showed peaks at τ 7.83 (singlet with fine splitting, 3 H) assigned to the isopropenyl methyl group, 5.80 (singlet, 3 H) assigned to the 3-methyl group, 4.47 and 4.18 (two singlets with fine splitting, 1 H each) assigned to the vinylic protons, and 1.93 and 0.05 (two doublets, 1 H each) assigned to H_5 and H_2 on the thiazolium ring, respectively.

Anal. Calcd for $C_7H_{10}INS$: C, 31.46; H, 3.75; S, 11.98; I, 47.57. Found: C, 31.74; H, 3.93; S, 11.97; I, 47.70.

The free radical polymerization of this thiazolium salt was attempted with azobisisobutyronitrile as initiator in aqueous solution at 80°, after degassing through three freeze–thaw cycles, for 21–72 hr according to the method of Price.[8] No polymer was obtained.

3-Methyl-4-(2-benzoxy-2-propyl)thiazolium Iodide. 4-(2-Benzoxy-2-propyl)thiazole[5] (6.0 g, 0.024 mol) was treated with 14.2 g (0.100 mol) of methyl iodide in 3.0 ml of ethyl ether at reflux for 4 hr. The crystalline precipitate, 0.60 g (6.4% after recrystallization from methanol–ethyl ether), had mp 179–181°. The nmr spectrum (D_2O–dimethyl sulfoxide-d_6) showed peaks at τ 7.80 (singlet, 6 H) assigned to the geminal methyl groups; 5.58 (singlet, 3 H) assigned to the 3-methyl group, 2.07 and 1.65 (two multiplets, 3 H and 2 H, respectively) assigned to the *meta*, *para* protons and the *ortho* protons of the phenyl ring, respectively, and 1.37 (singlet, 1 H) assigned to H_5 on the thiazolium ring. The proton at H_2 on the thiazolium ring was not observed due to exchange with deuterium.

Anal. Calcd for $C_{14}H_{16}INO_2S$: C, 43.19; H, 4.11; S, 8.22; I 32.65. Found: C, 43.45; H, 4.23; S, 8.25; I, 32.69.

3-Benzyl-4-methylthiazolium Bromide. 4-Methylthiazole (1.8 g, 0.018 mol) was quaternized with benzyl bromide (4.0 g, 0.023 mol) in 75 ml of ethyl ether heated at reflux for 30 min. The product, after recrystallization from methanol–ethyl ether, had mp 183.5–184.5° (lit.[3] mp 183.5–184°). The nmr spectrum (D_2O) showed peaks at τ 7.45 (singlet with fine splitting, 3 H) assigned to the 4-methyl group, 4.30 (singlet, 2 H) assigned to the methylene group, 2.45 (broad singlet, 5 H) assigned to the phenyl ring, and 2.09 (singlet with fine splitting, 1 H) assigned to H_5 on the thiazolium ring. The proton at H_2 on the thiazolium ring was not observed due to exchange with deuterium.

3-Allylthiazolium Bromide. Thiazole[9] (4.5 g, 0.053 mol) was quaternized with allyl bromide (10 g, 0.083 mol) in 13 ml of ethyl ether heated at reflux for 1 hr. The product, recrystallized from methanol-ethyl ether, had mp 143.5–145°. The nmr spectrum (D_2O) showed peaks at τ 4.89 (two singlets with fine splitting, 1 H each) assigned to the protons on C_3 of the allyl group, 4.62 (two multiplets, 1 H total) assigned to the proton on C_2 of the allyl group, 4.38 (singlet with fine splitting, 2 H) assigned to the methylene group, and 1.46 (AB quartet, 2 H) assigned to H_4 and H_5 on the thiazolium ring. The proton at H_2 on the thiazolium ring was not observed due to exchange with deuterium.

Anal. Calcd for C_6H_8BrNS: C, 34.95; H, 3.88; S, 15.53; Br, 38.83. Found: C, 34.84; H, 4.15; S, 15.51; Br, 38.78.

Copolymer of 4-Isopropenylthiazole and 3-Methyl-4-isopropenylthiazolium Iodide. Poly(4-isopropenylthiazole) (0.65 g) was treated with methyl iodide (4.0 g, 0.028 mol) in 5.0 ml of benzene for 9 days at room temperature. The product which precipitated was ground under ethyl ether, filtered, and vacuum dried before submission for iodide analyses. The degree of quaternization was calculated to be 37.4%.

Anal. Found: I, 26.58, 26.70.

Quaternization of 4-Vinylthiazole. 4-Vinylthiazole (5.7 g) was treated with methyl iodide (20 g, 0.14 mol) at reflux for 24 hr. Ethyl ether (30 ml) was added, precipitating the product, which was filtered, ground under ethyl ether, and vacuum dried. The product softened at 225–228°. The nmr spectrum (D_2O) of the product showed peaks at τ 7.78 (broad band, 2 H) assigned to the methylene groups, 6.95 (broad band, 1 H) assigned to the methine protons, 5.61 and 5.80 (two singlets, 3 H total) assigned to the 3-methyl groups, 2.07 (multiplet, 1 H) assigned to H_5 on the thiazolium rings, and -0.03 (multiplet, 1 H) assigned to H_2 on the thiazolium rings. This spectrum is consistent with the structure of poly(3-methyl-4-vinylthiazolium iodide). The peak at τ -0.03 disappeared on standing overnight, while that at 2.07 became a singlet, indicating exchange with deuterium at H_2 of the thiazolium ring. Treatment of the product with alcoholic silver nitrate produced a copious white precipitate.

Quaternization of 2-Vinylthiazole. A freshly distilled sample of 2-vinylthiazole was treated with excess methyl iodide at room temperature for 12 hr. The nmr spectrum of the product, after washing with ethyl ether and drying, was consistent with the structure of poly(3-methyl-2-vinylthiazolium iodide). The nmr spectrum (D_2O) showed peaks at τ 8.38 (triplet, 2 H) assigned to the methylene groups, 6.78 (quintet, 1 H) assigned to the methine protons, 5.75 (asymmetric doublet, 3 H) assigned to the 3-methyl groups, and 1.80 (AB quartet, 2 H) assigned to H_4 and H_5 on the thiazolium rings. The product, an orange solid, softened at 135–145°. The silver nitrate test was positive.

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(8) C. C. Price and I. Duling, *J. Amer. Chem. Soc.*, **84**, 578 (1962).

(9) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci., Sect. A*, **22**, 362 (1945).