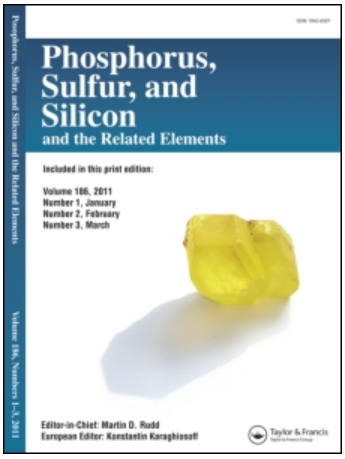

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The synthesis of unsubstituted pyridinium salt containing the 4-oxothiazolidine moiety bonded via *C(5) to the N position of the pyridine nucleus is reported. The nucleophilic displacement of pyridine from pyridinium salt by the selected nucleophiles leads to the formation of new 5-substituted 4-oxothiazolidines in good yields.*

Keywords 4-Oxothiazolidine; methoxy group; neutral nucleophile; nucleophilic substitution; pyridinium salt

INTRODUCTION

Numerous *N*-substituted pyridinium perchlorates **2**, generated from 2,4,6-triphenylpyrilium salt **1** and primary amines, react with various nucleophiles to give substitution products **3** (Scheme 1).[1–3]

Aspects of this two-step sequence, including the preparation of pyrilium salts, the mechanistic study, and synthetic utility of the transfer of *N*-alkyl groups from pyridinium salts to nucleophiles have been extensively reviewed.[4,5] Substitution reactions of 1-(3-cyano-5-nitropyridyl-2)pyridinium salt, in which the unsubstituted pyridine acts as a leaving group,[6] and pyrylium salt-catalyzed substitution reactions

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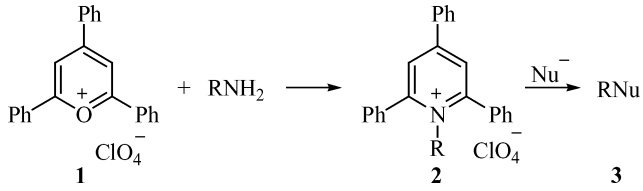


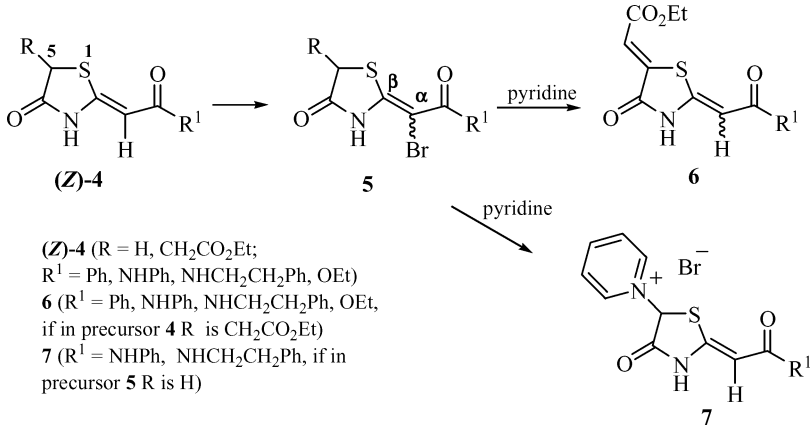
SCHEME 1

of acetals with silylated nuclophiles,[7] represent recent and valuable contributions.

Herein, we report the synthesis of a new piridinium salt of this type, *i.e.* (*Z*)-2-[4-oxo-5-(pyridinium-1-yl)thiazolidin-2-ylidene]-*N*-phenylacetamide bromide (**7**), and preliminary results of the nucleophilic functionalization at the C(5) position.

RESULTS AND DISCUSSION

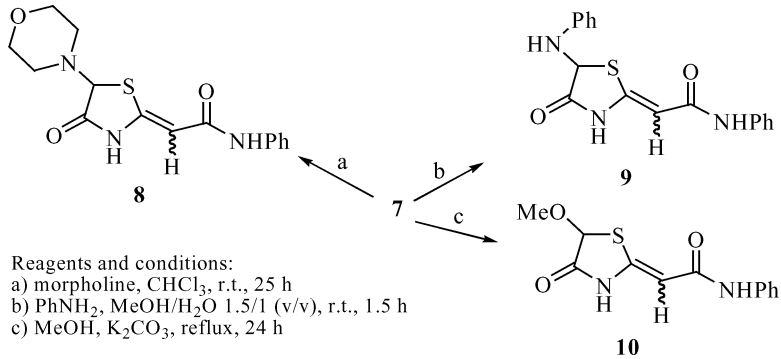
We have recently reported that (Z)-2-alkylidene-4-oxothiazolidines **4**, with an acetate group attached at the C(5) position, undergo the regioselective α-bromination under mild experimental conditions (10–30 min, 0°C to rt), affording α-bromo-α,β-unsaturated compounds **5** (Scheme 2) in good yields (60–66%).[8,9] Isolated, or *in situ*, formed vinyl bromides **5** were subsequently converted, *via* pyridine-induced rearrangement, into the stereodefined push–pull thiazolidines **6** with the two fully delocalized exocyclic C=C bonds at the C(2) and C(5) positions.



SCHEME 2

The overall reactivity of 5-substituted precursors (*Z*)-**4** (R = CH_2CO_2Et) *versus* unsubstituted substrates (*Z*)-**4** (R = H) toward bromine is not varying greatly. By contrast to the facile rearrangement of 5-substituted 4-oxothiazolidines occurring because of an enhanced resonance stabilization of compounds **6**, the reaction of **5a** (R = H, R^1 = NHPh) with a tenfold molar excess of pyrdine in $CHCl_3$ was very slow (97 h, reflux). Based on spectroscopic data (see Experimental), the product, isolated in a clean rearrangement reaction and in good yield, was characterized as the new pyridinium salt **7**. The identical rearrangement of vinyl bromide **5b** (R = H; R^1 = $NHCH_2CH_2Ph$) takes place readily, yielding the corresponding pyridinium salt, while with an enaminone-type thiazolidine precursor **5c** (R = H; R^1 = Ph) stable parent compound **4c** was formed.

Hence, the report by Hutchinson and Tarbell[10] that the unsubstituted pyridine in pyridinium salts can be a potential leaving group, led us to employ the pyridinium salt **7**, which has the 4-oxothiazolidine moiety connected through the C(5) atom to the *N*-position, as the substrate for substitution reactions. Thus, the reactions of pyridinium salt **7** with the selected nucleophiles (Scheme 3) are summarized in Table I. Spectroscopic data and elemental analyses were consistent with the structures of the substitution products **8–10** formed in satisfactory yields.



SCHEME 3

Despite the fact that pyridine is a poor leaving group, and that the pyridinium ring cleavage can occur by nucleophilic attack at the 2, 4, and 6 positions,[11–13] we did not observe a decrease in effectiveness of these substitution reactions, affording the new 5-substituted 4-oxothiazolidines.

TABLE I Selected Analytical and ^{1}H NMR (DMSO-d_6) Data for Products 8–10[a] Obtained by Substitution Reactions of Pyridinium Salt 7

Nucleophile	Product (yield, %)[b]	Mp (°C)	NH_{ring}	C(α)H	C(5)H
Morpholine	**8** (85)	161–3	11.49	5.79	5.44
Aniline	**9** (80)[c]	180–4	11.52	5.41	6.30
Methanol	**10** (70)	155–8	11.42	5.46	5.96

[a]Obtained by column chromatography (silica gel) as Z/E mixtures in various ratios which depend on eluent polarity.[14]

[b]Yields of the isolated products based on vinyl bromide **5a** (Scheme 2, R = H; R^1 = NHPh).

[c]Crude product.

EXPERIMENTAL

Synthesis of (*Z*)-2-[4-Oxo-5-(pyridinium-1-yl)thiazolidin-2-ylidene]-*N*-phenylacetamide Bromide (7)

Pyridine (0.33 mL, 4.2 mmol) was added to a suspension of the 70/30 mixture of (*Z*/*E*)-2-bromo-2-(4-oxothiazolidin-2-ylidene)-*N*-phenylacetamide (**5a**) (0.13 g, 0.42 mmol) in chloroform (8.8 mL). The mixture was brought to reflux and stirred over the period of 97 h, when TLC indicated complete consumption of the starting material. Then, the reaction mixture was evaporated to dryness at 40°C, affording 0.16 g of the crude brownish product **7**, mp 198–200°C, which was not purified because of the decomposition upon column chromatography. Spectral data for the pyridinium salt **7** are as follows: IR (KBr): ν 3250, 3186, 3129, 3024, 1725, 1665, 1599, 1540, 1384, 1309, 1281, 1243, 1150, 830, 758, 694 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 6.13 (s, 1H, =CH), 7.04 (t, 1H, *p*-phenyl, J = 7.4 Hz), 7.06 (s, 1H, CHS), 7.31 (t, 2H, *m*-phenyl, J = 7.4 Hz), 7.62 (d, 2H, *o*-phenyl, J = 7.4 Hz), 8.24 (dd, 2H, *m*-pyridine, $J_{o\text{-H}}$ = 5.8 Hz, $J_{p\text{-H}}$ = 7.8 Hz), 8.75 (t, 1H, *p*-pyridine, J = 7.8 Hz), 9.31 (d, 2H, *o*-pyridine, J = 5.8 Hz), 10.25 (s, 1H, NH_{exo}), 12.50 (broad s, 1H, NH_{ring}); ^{13}C NMR (DMSO-d_6): δ 71.8 (CHS), 96.6 (=CH), 119.1 (*o*-phenyl), 123.4 (*p*-phenyl), 128.7 (*m*-phenyl or *m*-pyridine), 129.1 (*m*-phenyl or *m*-pyridine), 139.4 (C1-phenyl), 144.9 (*o*-pyridine), 148.1 [*p*-pyridine, or C(2)=], 148.8 [*p*-pyridine or C(2)=], 165.2 (CO_{exo}), 168.4 (CO_{ring}); MS (ESI): *m*/*z* (rel. intensity) 312 (M^+, 100), 233 (38).

REFERENCES

[1] A. R. Katritzky, G. Musumarra, and K. Sakizadeh, *J. Org. Chem.*, **46,** 3831 (1981).
[2] E. Anders, J. G. Tropsch, A. R. Katritzky, D. Rasala, and J.-J. V. Eynde, *J. Org. Chem.*, **54,** 4808 (1989).

[3] C. Uncuta, M. T. Căproiu, V. Cămpeanu, A. Petride, M. G. Dňilă, M. Plăveti, and A. T. Balaban, *Tetrahedron*, **54,** 9747 (1998).
[4] A. R. Katritzky and C. M. Marson, *Angew. Chem., Int. Ed. Engl.*, **23,** 420 (1984).
[5] A. T. Balaban, A. Dinculescu, G. N. Dorofeenko, G. W. Fischer, A. V. Koblik, V. V. Mezheritskii, and W. Schroth, "Pyrylium Salts: Syntheses, Reactions and Physical Properties," in *Advances in Heterocyclic Chemistry*, Suppl. Vol. 2, A. R. Katritzky, Ed. (Academic Press: New York, 1982).
[6] M. Yu, Yakovlev, A. V. Kadushkin, N. P. Solov'eva, O. S. Anisimova, and V. G. Granik, *Tetrahedron*, **54,** 5775 (1998).
[7] M. Kamata, S. Nagai, M. Kato, and E. Hasegawa, *Tetrahedron Lett.*, **37,** 7779 (1996).
[8] R. Marković, Z. Džambaski, and M. Baranac, *Tetrahedron*, **57,** 5833 (2001).
[9] R. Marković, M. Baranac, and Z. Džambaski, *Heterocycles*, **63,** 851 (2004).
[10] R. E. J. Hutchinson and D. S. Tarbell, *J. Org. Chem.*, **34,** 66 (1981).
[11] A. R. Katritzky, J. B. Bapat, R. J. Blade, B. P. Leddy, P.-L. Nie, C. A. Ramsden, and S. S. Thind, *J. Chem. Soc., Perkin Trans. 1*, 418 (1979).
[12] S. P. Gromov and N. A. Kurchavov, *Eur. J. Org. Chem.*, 4123 (2002).
[13] H. C. van der Plas, *J. Heterocycl. Chem.,* **37,** 427 (2000).
[14] R. Marković, A. Shirazi, M. Baranac, Z. Džambaski, and D. Minić, *J. Phys. Org. Chem.,* **17,** 118 (2004).