Stereoselective formation of a 3,5-*trans*-disubstituted 1,4-tetramethylene-(tetrahydro-2,2-furylidene)ammonium salt in bromination of 2-phenylthiopent-4-enoic acid dialkylamide

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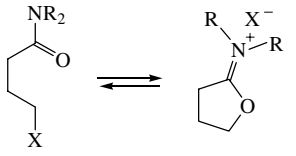
The reaction of *N*-(2-phenylthiopent-4-enoyl)pyrrolidine with bromine results in the stereoselective formation of 1,4-tetramethylene(5*S**-bromomethyl-3*R**-phenylthiotetrahydro-2,2-furylidene)ammonium bromide.

Previously,[1,2] we reported a new type of ring–chain tautomerism that involved a reversible transformation of γ-halobutyric dialkylamides **1** into dialkyl(tetrahydro-2,2-furylidene)ammonium halides **2**. For instance, for X = Br and R = Me, the ratio of tautomers **1** and **2** in a solution in $CDCl_3$ at 30 °C amounts to 58:42; it changes to 80:20 at 45 °C (^{1}H NMR data). The purpose of this study is to determine whether similar immonium salts can result from halogen addition to the dialkylamides of γ-unsaturated carboxylic acids and whether they can undergo ring–chain conversion.

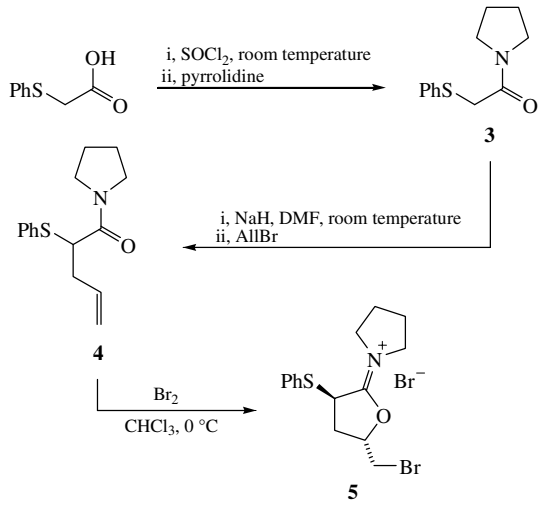


1 **2**

X = Cl, Br, I

Enamide **4**,† which can be easily obtained by the allylation of corresponding acetic acid derivative **3**† (96% yield), was the test compound.

We found that the reaction of dialkylamide **4** with bromine (1.06 equiv.) in $CHCl_3$ at 0 °C smoothly and stereospecifically gives 1,4-tetramethylene(5*S**-bromomethyl-3*S**-phenylthiotetrahydro-2,2-furylidene)ammonium bromide **5**† (94% yield).



3 **4** **5**

The structure of hitherto unknown salt **5** was confirmed by a combination of elemental and spectroscopic analyses. In particular, the relative configuration of substituents in compound **5** was established using ^{1}H NMR spectroscopic data. The B3LYP calculations in the 6-31G basis showed that the preferable conformations of both possible stereoisomers were characterised by a considerable deviation of the C-4 atom from the plane of the tetrahydrofuran ring (Figure 1). The coupling constants calculated from these data using the known procedure[3] for the HC-3, H_2C-4 and HC-5 protons in *trans*-isomer **5** are in good agreement with experimental data (Table 1). For *cis*-**5**, the deviation of the calculated constants from the observed values is more considerable, up to the full discrepancy for $J_{\alpha\text{-HC-4–HC-5}}$ 2.72 Hz (J_{exp} 6.4 Hz). The final conclusion on the relative *trans*-configuration of substituents in salt **5** was made based on measurements of Overhauser's nuclear effects, which showed a spatial proximity of the α-HC-4 and HC-5 protons with the phenyl group's *ortho* protons, as well as an NOE for the HC-3 and β-HC-4 protons with one of the CH_2Br protons.

A thorough NMR study of the solutions of analytically pure salt **5** in $CDCl_3$ did not show any additional signals that could suggest its reversible transformation into the corresponding chain form (*cf.* refs. 1 and 2).

Note that immonium salts like compound **5** are postulated to be likely intermediates in the halolactonisation of γ-unsaturated

Table 1 Calculated coupling constants (J_{calc}) and H–C–C–H torsion angles (φ_{calc}) for proton pairs in stereoisomers **5**.

	trans-**5**		*cis*-**5**		J_{exp}
	φ_{calc}/°	J_{calc}/Hz	φ_{calc}/°	J_{calc}/Hz	
HC-3 – β-HC-4	23.3	7.69	23.5	8.91	8.5
HC-3 – α-HC-4	87.8	0.98	95.9	1.17	1.0
β-HC-4 – HC-5	158.5	9.34	14.4	8.39	9.8
α-HC-4 – HC-5	38.0	5.42	105.2	2.72	6.4

† N-*(Phenylthioacetyl)pyrrolidine* **3**: prepared by routine procedures from known[5] phenylthioacetic acid as colourless crystals, mp 78–79 °C (from a hexane–Bu^{t}OMe mixture). ^{1}H NMR (200.13 MHz, $CDCl_3$) δ: 1.90 (m, 4H, 2CH_2), 3.45 (m, 4H, 2CH_2N), 3.64 (s, 2H, CH_2S), 7.25 and 7.45 (2m, 5H, H-aryl). IR (KBr, ν/cm^{-1}): 684, 728, 812, 912, 1028, 1068, 1164, 1192, 1228, 1252, 1344, 1416, 1436, 1484, 1572, 1588, 1620, 1636, 2872, 2948, 2968, 3060. Found (%): C, 65.31; H, 6.80; N, 6.24; S, 14.22. Calc. for $C_{12}H_{15}NOS$ (%): C, 65.12; H, 6.83; N, 6.33; S, 14.49.

*(±)-*N*-(Phenylthiopent-4-enoyl)pyrrolidine* **4**: colourless crystals, mp 46–47 °C (from a hexane–Bu^{t}OMe mixture). ^{1}H NMR (200.13 MHz, $CDCl_3$) δ: 1.80 (m, 4H, 2CH_2), 2.45 and 2.76 (2m, 2H, HC-3), 3.40 (m, 4H, 2CH_2N), 3.70 (dd, 1H, CHS, *J* 11 and 6 Hz), 5.10 (m, 2H, H_2C=), 5.80 (m, 1H, HC=), 7.30 and 7.50 (2m, 5H, H-aryl). IR (KBr, ν/cm^{-1}): 692, 752, 808, 928, 1012, 1064, 1112, 1192, 1256, 1328, 1440, 1472, 1572, 1628, 1640, 2876, 2908, 2932, 2968, 3064. Found (%): C, 69.07; H, 7.17; N, 5.47; S, 12.01. Calc. for $C_{15}H_{19}NOS$ (%): C, 68.92; H, 7.33; N, 5.36; S, 12.27.

*1,4-Tetramethylene(5*S**-bromomethyl-3*R**-phenylthiotetrahydro-2,2-furyliden)ammonium bromide* **5**: colourless crystals (from MeCN), mp 131–136 °C. ^{1}H NMR (200.13 MHz, $CDCl_3$) δ: 1.90–2.35 (m, 4H, 2CH_2), 2.58 (ddd, 1H, HC-4e, *J* 1.0, 6.4, 13.9 Hz), 3.44 (ddd, 1H, H-4a, *J* 8.5, 9.8, 13.9 Hz), 3.50–3.70 (m, 2H, CH_2N), 3.69 (dd, 1H, CH–Br, *J* 6.3 Hz, *J* 10.8 Hz), 3.86 (dd, 1H, CH–Br, *J* 7.1, 10.8 Hz), 3.90–4.00 (m, 1H, CHN), 4.19–4.32 (m, 1H, CHN), 4.68 (dddd, 1H, HC-5, *J* 6.3, 6.4, 7.1, 9.8 Hz), 5.11 (dd, 1H, HC-3, *J* 8.5, 1.0 Hz), 7.37–7.54 (m, 5H, H-aryl). IR (KBr, ν/cm^{-1}): 508, 656, 708, 780, 800, 852, 976, 1060, 1128, 1152, 1208, 1248, 1300, 1344, 1404, 1420, 1452, 1692, 2840, 2876, 2948, 3012. Found (%): C, 43.16; H, 4.60; Br, 37.48; N, 3.40; S, 7.48. Calc. for $C_{15}H_{19}Br_2NOS$ (%): C, 42.77; H, 4.55; Br, 37.94; N, 3.33; S, 7.61.

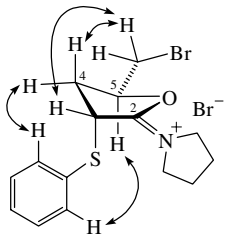


Figure 1 Overhauser effects observed in salt **5**.

carboxamides.[4] We believe that the obvious possibility of hydrolysis of bromide **5** (and similar compounds obtained using other electrophilic reagents for cyclisation of 4-type substrates) to give the corresponding disubstituted butyrolactone, as well as the character of functionalisation of the latter offer a considerable synthetic potential.

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