

## 2-ARYL-1,3-THIAZETIDINES FROM ETHYLENE THIOUREA

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**Summary:** Several 2-aryl-1,3-thiazetidine derivatives were prepared by the condensation reaction of ethylene thiourea and aromatic aldehydes using boron trifluoride etherate.

In our investigation directed toward the synthesis of heterocycles from ethylene thiourea (1), it was found that 1 reacted with benzaldehyde in the presence of boron trifluoride etherate to yield 2-phenyl-3,4-dihydroimidazo[2,1-b][1,3]-thiazetidine (3a) in a good yield.

This paper deals with the preparation and the structural assignments of 2-aryl-1,3-thiazetidines (3), a little-known class of compounds<sup>2</sup>.

Compound 3a was prepared by the following procedure:

To a stirred mixture of 1 (1 g, 9.8 mmol), benzaldehyde (2a, 1.04 g, 9.8 mmol), and dry THF (30 ml, distilled over CaH<sub>2</sub>) was gradually added a mixture of boron trifluoride etherate (47 % BF<sub>3</sub>, 3 ml, ca. 16 mmol) and dry THF (5 ml) under cooling in an ice-bath. The resulting solution was stirred for 10 min at this temperature and then for 50 min at room temperature.

The reaction mixture was poured into ca. 100 ml of ice-water, made alkali with an aqueous solution containing 1.6 g of sodium bicarbonate, and kept to stand for 1 hr. A white product was collected and washed with water, ethanol, and then acetone. Drying by Abderhalden apparatus (3 Torr., 180°C, 5 hr) gave white small plates of mp 291-2°C<sup>3,4</sup> (3a, 17 g, yield 95 %).

The structure of 3a was determined on the basis of spectroscopic evidence together with elemental analyses and degradation with hydrogen iodide.

The nmr spectrum (pyridine-D<sub>5</sub>) of 3a showed a singlet methine signal at  $\delta$  8.35, a singlet phenyl signal at  $\delta$  7.35, and a multiplet methylene signal at  $\delta$  ca. 3.7. In ir spectrum an aromatic CH stretching band and an aliphatic CH stretching band appeared at 3040 and 2900 cm<sup>-1</sup>, respectively.

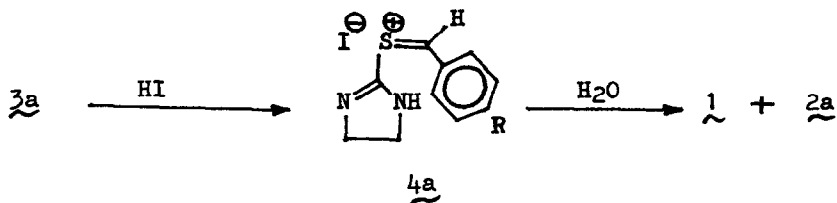
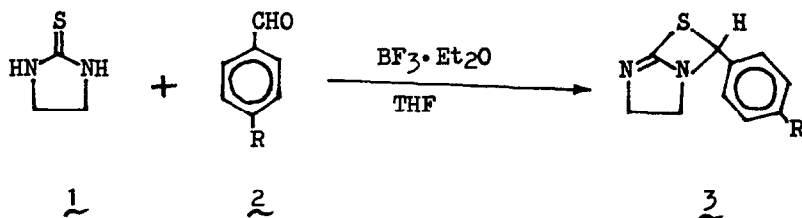
The mass spectrum showed fragmentation to the ions (M-CH<sub>2</sub>NCS)<sup>+</sup>(base peak) and ArCH<sub>2</sub><sup>+</sup>(rel. int. 86 %) together with a parent ion (m/e 190, 6 %).

The treatment of 3a with 57 % hydrogen iodide gave 1 and 2a (detected as benzaldehyde 2,4-dinitrophenylhydrazone) in nearly quantitative yields.

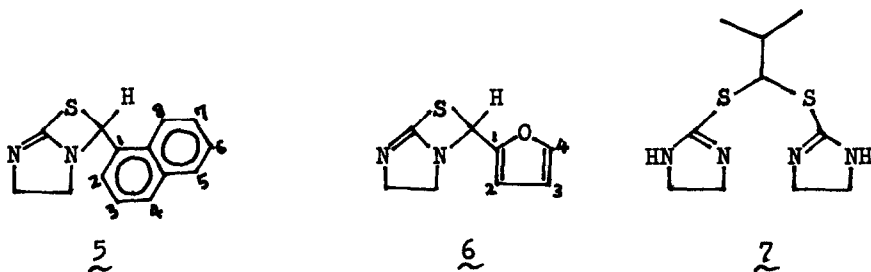
Under mild conditions an intermediacy 4a could be isolated as light yellow prisms of mp 160-1°C<sup>3,5</sup> and easily converted into 1 and 2a by treatment with hot ethanol-water (v/v 10 : 1).

The above results can support the structure of 3a.

The use of p-nitrobenzaldehyde (2b) and p-methylbenzaldehyde (2c) in place of 2a afforded 2-p-nitrophenyl-3,4-dihydroimidazo[2,1-b][1,3]-thiazetidine (3b, light yellow powders of mp 264-5°C, yield 98 %)<sup>3,6</sup> and 2-p-methylphenyl-3,4-dihydroimidazo[2,1-b][1,3]-thiazetidine (3c, white small prisms of mp 273-4°C, yield 88 %)<sup>3,7</sup>, respectively.



2a, 3a, 4a: R = H; 2b, 3b: R = NO<sub>2</sub>; 2c, 3c: R = CH<sub>3</sub>



From  $\alpha$ -naphthaldehyde as an aromatic aldehyde, 2- $\alpha$ -naphthyl-3,4-dihydroimidazo[2,1-b][1,3]-thiazetidine (**5**) also was obtained as light yellow powders of mp 270-1°C<sup>3,8</sup>(recry. from DMSO-ethanol, yield 94 %). And from furfural which could display considerable aromatic character, 2-furfuryl-3,4-dihydroimidazo[2,1-b][1,3]-thiazetidine (**6**) was produced as yellow powders of mp 182-3°Cdec<sup>3,9</sup>(recry. from pyridine-ethanol, yield 68 %).

Compounds **3**, **5**, and **6** should be as dry as possible for satisfactory elemental analyses because they tended to get water of crystallization.

When **1** reacted with isobutyraldehyde as an aliphatic aldehyde under the above conditions, isobutyraldehyde diimidazolinyldithioacetal (**7**) was obtained as white prisms of mp 222-3°C<sup>3,10</sup>(recry. from ethanol, yield 21 %) instead of the corresponding 1,3-thiazetidine derivative.

The present reaction did not occur in the case of ketones. Further, thiourea reacted with benzaldehyde by this method to give intractable tarry materials.

Several preparative methods for 1,3-thiazetidines have been reported: (1) from the reaction of amines, formaldehyde, and hydrogen sulfide<sup>11</sup>; (2) from the reaction of carbodiimide with isothiocyanate or thioketene<sup>12</sup>.

The condensation reaction of **1** and aromatic aldehydes gives us a new and simple preparative method for 2-aryl-1,3-thiazetidines.

Acknowledgment. We thank Prof. T. Takeshima for discussions.

#### References and Notes

- (1) M.Yokoyama, S.Ohtuki, M.Muraoka, and T.Takeshima, *Tetrahedron Lett.*, 3823 (1978).
- (2) consult ref. 12a.
- (3) Elemental analysis gave a satisfactory result.
- (4) uv  $\lambda_{\max}^{99\% \text{ EtOH}}$  245 nm (log  $\epsilon = 4.16$ ), 290 (3.48).
- (5) ir (KBr) 3150 cm<sup>-1</sup>(NH), 3050 (arom. CH), 2850 (aliph. CH); mass m/e 318 (M<sup>+</sup>); uv  $\lambda_{\max}^{99\% \text{ EtOH}}$  241 nm, 292. The yellow aqueous solution of **4a** was treated with silver nitrate to give a white precipitate of silver iodide.
- (6) ir (KBr) 3060 cm<sup>-1</sup>(arom. CH), 2860 (aliph. CH); mass m/e 235 (M<sup>+</sup>, rel. int. 9 %), 163 (M-CH<sub>2</sub>NCS, 100); uv  $\lambda_{\max}^{99\% \text{ EtOH}}$  255 nm, ca. 310.
- (7) ir (KBr) 3010 cm<sup>-1</sup>(arom. CH), 2880 (aliph. CH); mass m/e 204 (M<sup>+</sup>, rel. int. 6 %), 132 (M-CH<sub>2</sub>NCS, 100); uv  $\lambda_{\max}^{99\% \text{ EtOH}}$  244 nm, 288.

- (8) ir (KBr) 3020  $\text{cm}^{-1}$  (arom. CH), 2850 (CH); mass m/e 240 ( $\text{M}^+$ , rel. int. 1%), 156 (100); uv  $\lambda_{\text{max}}^{99\% \text{ EtOH}}$  220 nm, 242, ca. 310; nmr (pyridine- $\text{D}_5$ )  $\delta$  9.00 (br, 1H, C(8)H of naphthalene), 8.40 (br, 1H, CH), 7.95 (br, 2H, C(2,4)H of naphthalene), 7.55 (br, 4H, C(3,5,6,7)H of naphthalene), 3.60 (br, 4H, CH<sub>2</sub>).
- (9) ir (KBr) 3080  $\text{cm}^{-1}$  (furan), 2860 (CH), 880 (furan); mass m/e 180 ( $\text{M}^+$ ); uv  $\lambda_{\text{max}}^{99\% \text{ EtOH}}$  253 nm, 265; nmr (pyridine- $\text{D}_5$ )  $\delta$  8.40 (br, 1H, CH), 7.60 (m, 1H, C(3)H of furan), 6.50 (m, 2H, C(1,2)H of furan), 3.80 (m, 4H, CH<sub>2</sub>).
- (10) ir (KBr) 3220  $\text{cm}^{-1}$  (NH), 2960, 2920, 2880 (CH); mass m/e 258 ( $\text{M}^+$ ); uv  $\lambda_{\text{max}}^{99\% \text{ EtOH}}$  245.5 nm (log  $\epsilon = 4.69$ ); nmr (pyridine- $\text{D}_5$ )  $\delta$  9.30 (s, 2H, NH), 6.50 (d, 1H, CH,  $J = 10\text{Hz}$ ), 4.00 (t, 4H, CH<sub>2</sub>,  $J = 8\text{Hz}$ ), 3.50 (t, 4H, CH<sub>2</sub>,  $J = 8\text{Hz}$ ), 1.50 (m, 1H,  $\text{Me}_2$ CH), 1.10 (d, 6H, CH<sub>3</sub>,  $J = 8\text{Hz}$ ).
- (11) (a) C.G.LeFèvre and R.J.W.LeFèvre, J. Chem. Soc., 1932, 1142.  
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