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SYNTHESIS AND REACTION OF 6,7-DIHYDROAZIRINO[1,2-a]THIENO[2,3-d]-PYRIDIN-8-ONE

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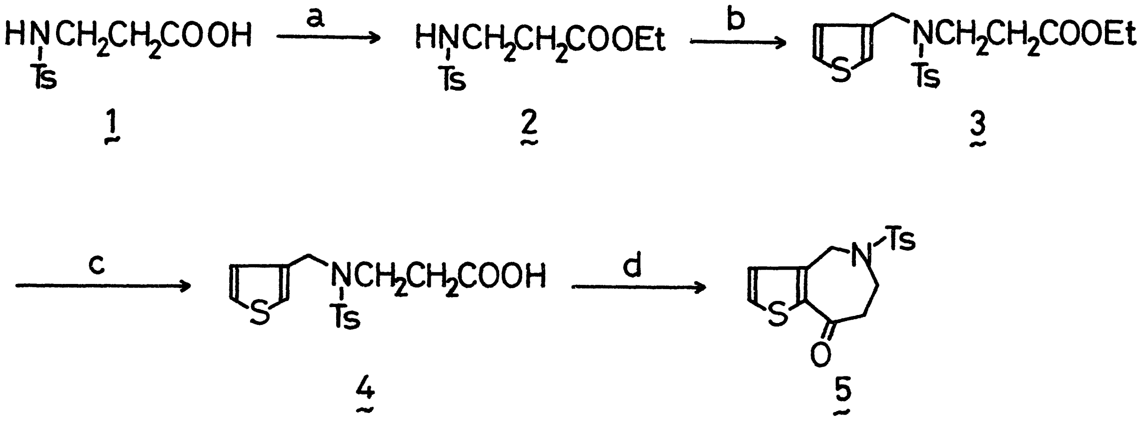
6,7-Dihydroazirino[1,2-a]thieno[2,3-d]pyridin-8-one 7 was synthesized and its base-catalyzed ring-opening leading to 4,5-dihydro-8H-thieno[3,2-c]azepin-8-one 8 was studied.

As a part of the azepine chemistry in our laboratory, the synthesis of 8H-thieno[3,2-c]azepin-8-one 9 was planned. We now report the synthesis and reactions of a tricyclic aziridino compound 7 (precursor to 4,5-dihydro-8H-thieno[3,2-c]azepin-8-one 8) formed on treating 4,5,6,7-tetrahydro-7-bromo-5-tosyl-8H-thieno[3,2-c]azepin-8-one 6 with polyphosphoric acid.

The starting ketone 5 was prepared from 3-(tosylamino)propionic acid 1 $^{1)}$ as shown in Scheme 1. The ketone (^{1}H-NMR ($CDCl_3$) δ=3.10 (t, J=7.0 Hz, 2H), 3.60 (t, J=7.0 Hz, 2H), 2.30 (s, 3H), 4.71 (s, 2H), 6.9-7.8 (aromatic 4H) ; IR (nujol) 1620 cm^{-1}; UVλmax(EtOH) 203 (logε=4.08), 232 (3.96) 271 nm(4.04)) was easily brominated by equimolar pyridinium tribromide in HOAc to give 7-bromo-

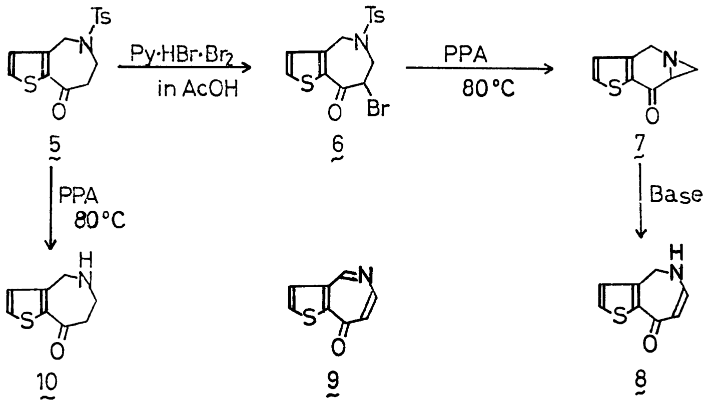


Scheme 1. Synthetic route of 5 from 1 .

a) i) Equimolar PCl_5 in C_6H_6 at r.t. ii) Abs. EtOH
b) 1.3 molar equiv. of 3-thenyl bromide$^{3)}$and excess K_2CO_3 in dry acetone.
c) 0.1N-KOH/t-BuOH at r.t.
d) i) Equimolar PCl_5 at r.t. ii) $SnCl_4$ in C_6H_6 at 5°C, stirring overnight at r.t.

ketone 6 [2](mp 150-151°C(EtOH), 78%), whict resisted to the direct dehydrobromination.

An attempted detosylation [4]of the bromoketone 6 with polyphosphoric acid at 80°C for 30 h under nitrogen resulted in the formation of a tricyclic aziridino compound 7 [5](mp 64-65°C(MeOH), 63%), instead of the corresponding free amine expected, through a 1,3-transannular dehydrobromination after detosylation. The formation of the aziridino compound by 1,3-transannular dehydrohalogenation leading to a bicyclic system may be the first example, though many monocyclic aziridino compounds are reported to form by 1,3-dehydrohalogenation.[6]



No reaction occurred by refluxing 7 in benzene for 48 h under nitrogen without basic catalyst, while, with 1.3 molar amount of Et_3N or DBU, an olefinic ketone 8 (mp 175.5-176°C(H_2O) ; ^{1}H-NMR δ=4.33 (d, J=3.8 Hz, 2H), 4.98 (d, J=8.3 Hz, 1H), 7.02 (d, J=5.3 Hz, 1H), 7.04 (d, J=8.3 Hz, 1H), 7.70 (br s, 1H, D_2O exchangeable) ; IR (nujol) 3210, 1590 cm^{-1}; UVλmax(EtOH) 242 (logε=4.03), 277 (3.84), 343 nm(3.96)) was obtained in 12 and 89% yield, respectively.

Dehydrogenation of 8 to 9 is now under investigation.

References and Notes

1) R.W.Holley and A.D.Holley, J.Am.Chem.Soc.,71,2129(1949).

2) Spectral data of 6 : ^{1}H-NMR ($CDCl_3$) δ=4.22 and 4.79 (AB q, J=16.9 Hz, 2H), 3.34, 4.02 and 4.47 (AMX pattern, J=14.9, 10.8 and 5.1 Hz, 3H), a pair of long-range coupling (J=1.3 Hz) was observed between protons of 4 and 6 positions [7]; IR (nujol) 1640 cm^{-1}; UVλmax(EtOH) 204 (logε=4.19), 229 (4.14), 283 nm(3.95).

3) E.Campaigne and B.F.Tullar, Organic Syntheses, coll.vol.4, Wiley, New York, N.Y.,1963, p.921.

4) N-Detosylation method under this condition is unknown to our knowledge. The starting ketone 5 gives the corresponding free amine 10 (^{1}H-NMR ($CDCl_3$) δ=2.32 (br s, 1H, D_2O exchangeable), 2.90 (m, 2H), 3.20 (m, 2H), 4.26 (s, 2H), 6.93 (d, J=5.3 Hz, 1H), 7.56 (d, J=5.3 Hz, 1H) ; IR (nujol) 3350, 1630 cm^{-1}; UVλmax(EtOH) 277 (logε=4.01), 330 nm(2.72)) in 56% yield by this method.

5) Spectral data of 7 : ^{1}H-NMR ($CDCl_3$) =1.83 (d, J=3.0 Hz, 1H), 2.42 (d, J=6.2 Hz, 1H), 2.85 (dd, J=6.2 and 3.0 Hz, 1H), 4.42 (s, 2H), 6.85 (d, J=5.0 Hz, 1H), 7.68 (d, J=5.0 Hz, 1H) ; IR (nujol) 1630 cm^{-1}; UV max(EtOH) 203 (log =3.78), 281 nm(3.99).

6) K.D.Gundermann, G.Holtmann, H.J.Rose, and H.Schulze, Chem.Ber.,93,1632(1960) ; G.L.Closs and S.J.Brois, J.Am.Chem.Soc.,82,6068(1960).

7) R.M.Acheson, M.W.Foxton, and G.R.Miller, J.Chem.Soc.,1965,3200.

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