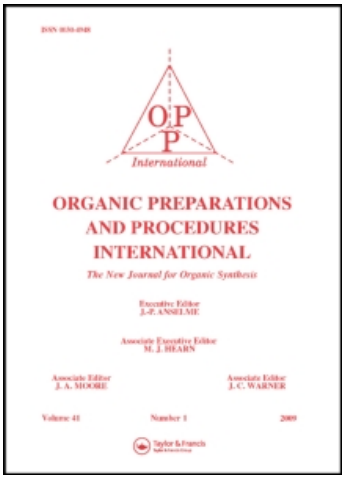

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2,3,4,5,6,7-HEXAHYDROCYCLOPENTA-1,4-THIAZINE AND THE 8,9-DIHYDRO-, 4-ACETYL AND l-OXO - 4-ACETYL DERIVATIVES

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2,3,4,5,6,7-HEXAHYDROCYCLOPENTA-1,4-THIAZINE AND THE 8,9-DIHYDRO-, 4-ACETYL- AND 1-OXO-4-ACETYL DERIVATIVES

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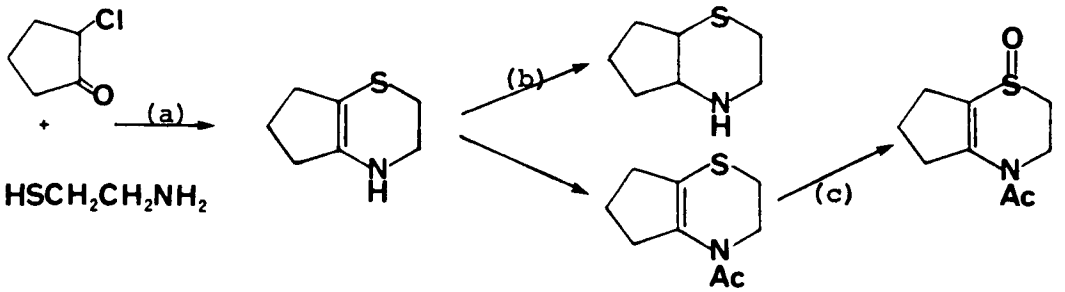
The title compounds are new derivatives of thiazine. The method of Asinger et al.[1] for the formation of a 2,3-dialkyl-5,6-dihydro-1,4-thiazine from an α-haloketone and the anion of β-mercaptoethylamine was used for the preparation of 1. Hydroboration of 1 followed by basic hydrolysis gave 2. Acetylation of 1 gave 3 which was oxidized with periodate to produce 4. Attempts to convert 1 and 2 to the parent cyclopenta-1,4-thiazine by vapor phase (Pd/C) or liquid phase (2,3-dichloro-4,5-dicyanobenzoquinone, sulfur or manganese dioxide) dehydrogenation were unsuccessful.



a) EtO^-, Δ b) B_2H_6; OH^-, H_2O c) $NaIO_4$

EXPERIMENTAL SECTION

2,3,4,5,6,7-Hexahydrocyclopenta-1,4-thiazine (1).- To a solution of 56.8 g (0.5 mol) of 2-mercaptoethylamine hydrochloride in 250 mL of CH_3OH in a 1 L flask equipped with a condenser and pressure-equalizing dropping funnel was added slowly with stirring by N_2 a solution formed from 23 g (1 g-at) of sodium and 200 mL of CH_3OH. To this mixture at 0° (ice bath), was added dropwise (30 min) 59 g (0.5 mol) of 2-chlorocyclopentanone.[2] The bath was removed and the gas stirring was continued for 45 min. after the mixture reached room temperature. After separation of the precipitated sodium chloride, the filtrate was flooded with 300mL of H_2O and then extracted (liquid-liquid extractor) with ether for 36 hrs. Distillation of the dark red oil obtained by removal of the solvent from the dried (Na_2SO_4) extract gave 38 g (54%) of 1 as an unstable, colorless, viscous oil, bp. 76-78°/0.1 mm, n_D^{20} 1.5711; UV (EtOH) (log ε): 268 nm (2.98): IR (neat): 3300 (NH), 1650 cm^{-1} (C=C); ^1H NMR (500 MHz) ($CDCl_3$): δ 1.84 (m, 1, 6βH, $J_{6\beta,6\alpha}$ = 17.7, $J_{6\beta,7\alpha}$ = 9.5, $J_{6\beta,5\alpha}$ = 6.5), 2.06 (m, 1, 6αH, $J_{6\alpha,6\beta}$ = 17.7,

$J_{6\alpha,7\alpha}$ = 2.0, $J_{6\alpha,5\alpha}$ = 1.0), 2.18 (m, 2, 5βH, 7βH, $J_{5\beta,5\alpha}$ = 12.9, $J_{6\beta,7\alpha}$ = 19.8), 2.34 (dd, 1, 5αH, $J_{5\alpha,5\beta}$ = 12.9, $J_{5\alpha,6\beta}$ = 6.5, $J_{5\alpha,6\alpha}$ = 1.0), 2.55 (dd, 1, 7αH, $J_{7\alpha,7\beta}$ = 19.8, $J_{7\alpha,6\beta}$ = 9.5, $J_{7\alpha,6\alpha}$ = 2.0), 2.90 (m, 1, 3βH, $J_{3\beta,3\alpha}$ = 9.65, $J_{3\beta,2\alpha}$ = 6.1, $J_{3\beta,2\beta}$ = 9.65), 3.13 (m, 1, 3αH, $J_{3\alpha,3\beta}$ = 9.65, $J_{3\alpha,2\alpha}$ = 2.1, $J_{3\alpha,2\beta}$ = 1.2), 3.17 (m, 1, 2βH, $J_{2\beta,2\alpha}$ = 11.63, $J_{2\beta,3\alpha}$ = 1.2, $J_{2\beta,3\beta}$ = 9.65), 3.72 (m, 1, 2αH, $J_{2\alpha,2\beta}$ = 11.63, $J_{2\alpha,3\alpha}$ = 2.1, $J_{2\alpha,3\beta}$ = 6.1);[3] MS. (exact mass) 141.0608; $C_7H_{11}NS$ requires 141.0635. The compound was stored at -50°.

The phenylurethane derivative [from 1.19 g (0.01 mol) of phenylisocyanate and 0.7 g (0.005 mol) of 1 heated in 5 mL of dry benzene at 60°] crystallized from 95% ethanol as a colorless solid, mp. 160-162° (dec.).

Anal. Calcd. for $C_{14}H_{16}N_2SO$: C, 64.61; H, 6.16; N, 10.74
Found : C, 64.47; H, 6.11; N, 10.72

2,3,4,5,6,7,8,9-Octahydrocyclopenta-1,4-thiazine (2).- To a solution of 0.85 g (6 mmol) of 1 and 0.426 g of $NaBH_4$ in 10 mL of dry tetrahydrofuran at 0° was added 0.64 g freshly distilled boron trifluoride etherate. The mixture was stirred at room temperature under N_2 for 18 hrs and a colorless solid formed. The addition of 10 mL of 3N NaOH solution caused a vigorous reaction and dissolution of the solid. The basic solution was stirred for 12 hrs., and then was flooded with 150 mL of H_2O. The mixture was extracted with ether (liquid-liquid extractor). Distillation of the oil obtained by removal of the solvent from the ethereal extract gave 0.6 g (70%) of 2 as a colorless oil, bp. 67-68°/0.3 mm. The picrate was crystallized from 95% ethanol, mp. 145-146° (dec.).

Anal. Calcd. for $C_{13}H_{16}N_4SO_7$: C, 41.95; H, 4.36; N, 15.04
Found: C, 42.14; H, 4.58; N, 15.25

4-Acetyl-2,3,4,5,6,7-hexahydrocyclopenta-1,4-thiazine (3).- A mixture of 2.6 g (0.02 mol) of 1 and 40 mL of acetic anhydride was heated 4 hrs. at 70°, the cooled and neutralized with 200 mL of a saturated Na_2CO_3 solution. The whole was extracted with 3 x 50 mL portions of ether and the combined extracts were washed with 25 mL of saturated NaCl solution. Removal of the ether from the dried (Na_2SO_4) solution gave 2.5 g (78%) of 3 as a colorless oil, bp. 130°/0.2 mm.

Anal. Calcd. for $C_9H_{13}NSO$: C, 58.84; H, 7.04; S, 17.45. Found: C, 59.00; H, 7.10; S, 17.50

1-Oxo-4-acetyl-2,3,4,5,6,7-hexahydrocyclopenta-1,4-thiazine (4).- To a solution of 1.1 g (5 mmol) of $NaIO_4$ in 50 mL of CH_3OH and 40 mL of H_2O at 0° was added 0.92 g (5 mmol) of 3 in 5 mL of CH_3OH. The mixture was stirred at 0° for 3 hrs. The precipitated $NaIO_3$ was separated and the filtrate was extracted with 5 x 10 mL of CH_2Cl_2. Removal of the solvent from the combined, dried ($MgSO_4$) organic extracts gave 4 as an unstable oil. IR (neat): 814 and 1048 cm^{-1} (S=O); MS (exact mass): 183.1749; $C_9H_{13}NSO_2$ requires 183.1762. A quantitative yield (0.99 g) of $NaIO_3$ was obtained.

Anal. Calcd. for $NaIO_3$: Na, 11.61; I, 64.40. Found: Na, 11.40; I, 64.41

REFERENCES

1. F. Asinger, F. J. Schmitz and R. Reichel, Ann., 652, 50 (1962).

2. C. H. DePuy, B. W. Ponder and J. D. Fitzpatrick, J. Org. Chem., 29, 3508 (1964).

3. T. Kumeda, T. Nagamatsu, T. Higuchi and M. Hirobe, Tetrahedron Lett, 29, 2203 (1988).

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A FACILE REDUCTION OF 1,8-NAPHTHALIMIDE TO 1,2,3,4-TETRAHYDRO-1,8-NAPHTHALIMIDE

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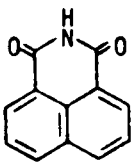
In connection with the synthesis of several targeted heterocyclic compounds for biological evaluation, a large quantity of 1,2,3,4-tetrahydro-1,8-naphthalimide (3a,4,5,6-Tetrahydro-1H-benz[d,e]isoquinoline-1,3[2H]-dione, 2) was needed as an intermediate. A search of the literature revealed only one preparative method of 2 by reduction of 1,8-naphthalimide (1) at high pressure (50 kg/cm^2 or 711 psi) and elevated temperature (80°) over palladium-on-carbon.[1] Although this method of preparation gave a good yield (77%) of 2, it required equipment capable of withstanding rather high pressure and relatively high temperature. These investigators also studied the hydrogenation process with other catalysts, including the use of platinum-on-carbon and rhodium-on-carbon, but again found that only at higher temperature (100°) and high pressure could the compound be reduced, and when rubidium-on-carbon was used, no reduction took place even at elevated temperature and pressure.[1]



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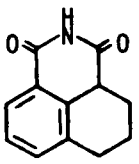

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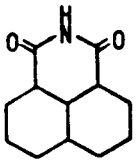

3

The catalytic reduction conditions were reinvestigated in our laboratory in order to uncover