296. Synthesis with 1,2-Oxazines. II. Synthesis and Properties of 2,3-Dimethyl-5,6-dihydro-4*H*-1,2-oxaziniumiodide

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Summary. Preparation of 2,3-Dimethyl-5,6-dihydro-4*H*-1,2-oxaziniumiodide was achieved by N-alkylation of 3-methyl-5,6-dihydro-4*H*-1,2-oxazine. Reactions with C-nucleophiles led to the corresponding N-methyl-perhydro-1,2-oxazine derivatives. Reaction with sodium hydride in triglyme led to 3-methyl-4-aza-1,3-pentadiene.

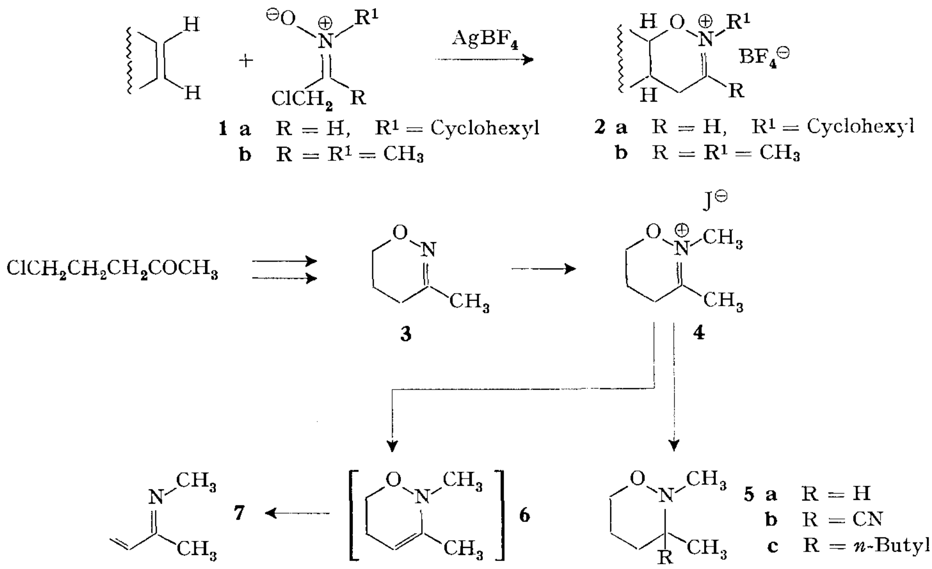
The $AgBF_4$ induced 1,4 dipolar cycloaddition of α-chloronitrones to olefinic [1] and acetylenic [2] systems awoke our interest in the 1,2-oxazine system as a tool in organic synthesis. The intermediate products of the 'carboxolytic' cleavage of C,C-double bonds [3] as well as in the γ-lactone synthesis [4] are N-alkyl-5,6-dihydro-4*H*-1,2-oxazinium salts of type **2a** (see *Scheme*). Since these salts result form cycloaddition with α-chloroaldonitrones **1a**, they carry an H-atom on C(3) of the corresponding oxazine moiety. The object of this work was the preparation of an analogous salt having a methyl group on C(3) (such as **2b**) and the examination of its behaviour in addition and deprotonation reactions.

Previous work on the preparation of α-chloroacetone-N-methylnitrone (**1b**) and $AgBF_4$ induced cycloaddition of this substance to olefinic double bonds unfortunately showed some difficulties of this method in obtaining our desired system [5]. Chloroketonitrones were found to be extremely unstable intermediates and gave rise to systems such as **2b** in low yields (*ca.* 20%). Because of the above reasons we used an alternative method namely N-alkylation of the corresponding six membered cyclic oxime ethers.

N-Alkylation of the known [6] oxime ether **3** with CH_3J in dry acetonitrile gave the desired 2,3-dimethyl-5,6-dihydro-4*H*-1,2-oxaziniumiodide **4** as yellow needles (93% yield). It was possible to keep the salt for a period of a few months at −20°. At room temperature, however, decomposition was observed after a few hours.

Reaction of **4** with $NaBH_4$ in methanol at −70° gave **5a** in 76% yield. Shaking **4** with 25% KCN in water yielded **5b** in 72%. Reaction of **4** with *n*-BuLi in hexane at 0° afforded **5c** in 45% yield. These findings led to the synthesis of 3,3-disubstituted-perhydro-1,2-oxazine derivatives.

Deprotonation of immonium salts of type **2a** could only result in endocyclic enamoid derivatives. It was not clear *a priori* whether an endocyclic enamoid structure **6** would result from the deprotonation of **4**. From data of the enamine synthesis it was doubtful whether an exocyclic enamoid structure would occur as an alternative deprotonation product [7]. Treatment of **4** with NaH in triglyme at room temperature followed by many attempts to isolate the resulting enamoid structures were abortive. On trapping the volatile material resulting from the reaction in vacuum, 3-methyl-4-aza-1,3-pentadiene (**7**) was isolated as a very unstable liquid (*ca.* 60% yield). This liquid polymerizes by itself in a few minutes. In solution, *Scheme*



measurements of its NMR. and IR. spectra were possible, indicating its structure. As an analogy to the well established work on deprotonations of salts such as **2a** [3], the presence of enamoid structure **6** as the deprotonation product of **4** was thereby assumed.

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Experimental Part

^{1}H-NMR. spectra were determined in $CDCl_3$ with tetramethyl silane as internal standard; chemical shifts are expressed in δ values (ppm). Unless otherwise indicated, IR. spectra were determined in chloroform. Melting points were determined on a *Büchi* SMP-20 apparatus and are uncorrected.

Dry solvents were obtained by filtration over 100-fold amount of basic aluminium oxide (activity 1; *Merck*).

*2,3-Dimethyl-5,6-dihydro-4*H*-1,2-oxazinium iodide* (**4**). 14.1 g (0.142 mol) of freshly distilled 3-methyl-5,6-dihydro-4*H*-1,2-oxazine (**3**) [6] was dissolved in 44 ml acetonitrile (2 × dest. over P_2O_5). 44 ml of methyl iodide were added and the resulting solution allowed to stand at RT. overnight in the dark. The yellow reaction mixture was then evaporated to the point of crystallization and crystallized from ether. 32 g (0.133 mol, 93%) yellow crystals of **4** (m.p. 102°) were obtained (melting point tube was sealed. The crystals are very hygroscopic and the product was stored in a tightly closed vial at –20°.) – IR.: 3610, 3410, 2425, 1667, 1446, 1391, 1235, 1045, 995 and 875 cm^{-1}. – NMR.: 2.27 (*m*, 2H); 2.70 (*s*, 3H); 3.19 (*m*, 2H); 3.91 (*s*, 3H) and 4.71 (*d* × *d*, 2H). – MS. (*m/e*): 256 (47), 242 (17), 241 (6), 236 (12), 228 (14), 213 (22), 199 (17), 185 (32), 169 (55), 157 (16), 154 (80), 149 (30), 137 (23), 129 (38), 112 (35), 111 (35), 99 (100), 93 (12), 81 (54), 69 (100), 57 (44), 55 (56) and 41 (100).

$C_6H_{12}INO$ (241.1) Calc. C 29.89 H 5.02 N 5.81% Found C 30.15 H 5.16 N 5.78%

When this product is recrystallized three times from acetonitrile/ether, the melting point rises to 112°, while the spectroscopical data remain unchanged.

2,3-Dimethyl-tetrahydro-1,2-oxazine (**5a**). To 1.01 g sodium borohydride in 20 ml absolute methanol were added 5.74 g (24 mmol) oxazinium compound **4** at –70° with stirring. A spontaneous evolution of gas occurred together with decolorization of the initial yellow solution. The cooling bath was removed and the solution stirred for another 5 min. It was diluted with dichloromethane, shaken with 2 portions (20 ml) of an ice-cooled aqueous solution of 10% ammonium chloride and extracted 3 times with dichloromethane. The organic layers were combined, dried on magnesium sulfate, filtered through cellite and evaporated carefully at 20° bath-temperature resulting in 2.1 g (18.2 mmol, 76%) of colorless liquid. Distillation at 36°/30 Torr yielded 1.58 g (13.7 mmol, 57%) oxazine compound **5a**, the NMR. of which is identical with that of the raw material. – IR.: 1605, 1452, 1436, 1377, 1362, 1330, 1145, 1122, 1069, 1050, 1017 and 982 cm^{-1}. – NMR.: 1.00 (*d*, 6 Hz, 3H); 1.4–1.9 (*m*, 4H); 2.2–2.5 (*m*, 1H); 2.57 (*s*, 3H) and 3.89 (*m*, 2H). – MS (*m/e*): 115 (18), 100 (100), 72 (31), 56 (31) and 42 (44).

$C_6H_{13}NO$ (115.2) Calc. C 62.57 H 11.38 N 12.16% Found C 62.38 H 11.42 N 12.36%

2,3-Dimethyl-3-cyano-tetrahydro-1,2-oxazine (**5b**). 500 mg (2.08 mmol) of the oxazinium-compound **4** was dissolved in 20 ml dichloromethane and shaken with a solution of 2.5 g sodium cyanide in 10 ml water. The aqueous solution was then extracted twice with dichloromethane, the organic layers were combined, filtered through cotton wool and evaporated. The resulting liquid (300 mg) was distilled at 90°/0.02 Torr in a ball tube to yield 210 mg (1.5 mmol, 72%) of colorless compound **5b**. – IR.: 2235, 1605, 1452, 1440, 1380, 1167, 1121, 1095, 1062 and 1020 cm^{-1}. – NMR.: 1.41 (*s*, 3H); 1.6–2.3 (*m*, 4H); 2.67 (*s*, 3H) and 3.96 (*m*, 2H). – MS. (*m/e*): 140 (31), 126 (10), 125 (100), 114 (17), 97 (21), 82 (12), 81 (14), 67 (25) and 56 (12).

$C_7H_{12}N_2O$ (140.2) Calc. C 59.97 H 8.63 N 19.98% Found C 59.64 H 9.00 N 19.76%

2,3-Dimethyl-3-butyl-tetrahydro-1,2-oxazine (**5c**). To 1.8 g (7.5 mmol) oxazinium compound **4** in 20 ml abs. hexane, 20 ml of a *ca.* 4% solution of *n*-butyl lithium was added dropwise under stirring at 0°. The mixture was stirred for another 3 h at 0°. It was then poured onto 40 ml of an ice-cooled aqueous solution of 10% ammoniumchloride and extracted 3 times with ether. The organic layers were washed with another 40 ml portion of 10% ammoniumchloride. The organic layers were combined, dried over sodium sulfate, filtered through cellite and evaporated. The residue was chromatographed on 30 g neutral aluminium oxide (activity $>$ 1 according to *Brockmann*) on an ice cooled column using dry dichloromethane as the solvent. The fractions which contained the product combined and dried over sodium sulfate. The resulting mixture was filtered through cellite and evaporated resulting in 580 mg (3.4 mmol, 45%) of a yellowish liquid. Distillation at 48°/0.02 Torr yielded 440 mg (2.6 mmol, 35%) oxazine compound **5c**, the NMR. of which is identical with that of the chromatographed material. – IR.: 1604, 1468, 1456, 1439, 1373, 1143, 1067 and 1018 cm^{-1}. – NMR.: 0.6–1.9 (*m*, 16H, *s* at 1.04); 2.45 (*s*, 3H) and 3.87 (*m*, 2H). – MS. (*m/e*): 171 (3), 156 (4), 115 (8), 114 (100), 86 (6), 71 (4), 69 (5), 56 (14) and 41 (5).

$C_{10}H_{21}NO$ (171.3) Calc. C 70.12 H 12.37 N 8.18% Found C 69.85 H 12.42 N 8.32%

Reaction of immonium salt **4** *with sodium hydride.* 1.02 g (4.25 mmol) oxazinium compound **4** was added under stirring to a mixture of 210 mg (8.8 mmol) sodium hydride in 20 ml of triethyleneglycol-dimethylether at 0°. After 40 min of vigorous stirring at 0° the system was connected to a vacuum (0.5 Torr), and the reaction mixture heated up to 50°. A colorless liquid distilled out of the mixture, and it was collected in a small trap cooled by dry ice/acetone. After 10 min the system was filled with nitrogen. The trap which contained *ca.* 200 mg (*ca.* 60%) of a colorless liquid was closed immediately and transferred to an ice bath. To record its NMR. spectrum the necessary amount of dry $CDCl_3$ was precooled to 0° in a NMR. tube. Then 3 drops of the liquid were added and the NMR. recorded immediately. In this solution, the lifetime of this highly reactive compound **7** is less than 1 h at RT. – IR.: 1637, 1606, 1370, 1095, 1011, 996 and 928 cm^{-1}. – NMR.: 1.95 (*s*, 3H); 3.23 (*s*, 3H); 5.3–5.9 (*m*, 2H, part of an *ABC*-system); 6.48 ($d \times d$, 1H, $J_{AB(trans)} = 18$ Hz, $J_{AC(cis)} = 10{,}5$ Hz) and impurities at 2.13, 3.38 and 4.75.

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