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The Synthesis of 2-Amino-3-cyano Derivatives of 4,5-Dihydrofuran and 5,6-Dihydro-4H-pyran, and their Transformation to Lactones

SVEIN MORGENLIE*

Department of Chemistry, University of Oslo, Blindern, Oslo 3, Norway

Recently, the synthesis of some substituted 2-amino-3-cyano-4,5-dihydrofurans from the sodium derivative of malononitrile and substituted ethylene oxides was reported. This prompts the following report of a convenient preparation of 2-amino-3-cyano-4,5-dihydrofuran (I) and 2-amino-3-cyano-5,6-dihydro-4H-pyran (II) from the sodium salt of malononitrile with H2O/H+. The low infrared stretching frequency of the cyano group at 2175 cm⁻¹, and the presence of three and four NMR absorptions of equal intensities for the compounds (I) and (II), respectively, can only be explained by the enamine structure.

Acid hydrolysis rapidly transformed the dihydrofuran (I) and the dihydropyran (II) derivatives to the α-cyano-γ- (III) and δ- (IV) lactones, respectively.

Experimental. 2-Amino-3-cyano-4,5-dihydrofuran (I). To finely divided sodium (7.8 g) in toluene (200 ml) and diethyl ether (200 ml) was added malononitrile (22 g) in ether (200 ml). The reaction mixture was heated to 50°, and dry ethanol (25 ml) added in small portions under stirring. When all the sodium was dissolved, 2-bromoethanol (42 g) was added dropwise, and the stirring continued for 12 h at 50°. After cooling, the reaction mixture was filtered, the solid matter washed with ether, and the solutions combined. The solvents were evaporated under reduced pressure, giving a yellowish, crystalline residue, which on recrystallisation from benzene gave almost colourless crystals (3.6 g, 10 %), m.p. 113 – 114°. (Found: C 54.76; H 5.52; N 25.20. Calc. for C₉H₈N₃O: C 54.54; H 5.49; N 25.49.) IR absorption bands (CHCl₃) were found at 3450, 3350, 2175, 1640, and 1550 cm⁻¹. NMR (DMSO-d₆) shifts were observed at

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* Present address: Department of Chemistry, Agricultural College, Vollebekk, Norway.

δ 6.8 (broad), 4.33 (triplet), and 2.72 (triplet); the relative intensities were 1:1:1. UV absorption (MeOH) was found at 256 μm (log ε 4.00).

2-Amino-3-cyano-5,6-dihydro-4H-pyran (II). Sodium (7.8 g) and malononitrile (22 g) gave with 3-bromopropanol (47 g) under the same conditions colourless crystals (21 g, 51 %), m.p. 107—108°. (Found: C 58.31; H 6.47; N 22.38. Calc. for C₆H₆N₃O: C 58.05; H 6.50; N 22.57.) IR absorptions were located at 3460, 3350, 2175, 1630, and 1580 cm⁻¹. NMR (DMSO-d₆) signals at δ 6.0 (broad), 4.08 (triplet), 2.12 (triplet), and 1.8 (quintet) with relative intensities 1:1:1, and UV absorption at 254 μm (log ε 3.83).

α-Cyano-γ-butyrolactone (III). A solution of 2-amino-3-cyano-4,5-dihydrofuran (I) (3.5 g) in 1 N sulphuric acid (60 ml) was kept at room temperature for 30 min. During this period it was extracted with ether at short intervals. The combined ether extracts were dried with sodium sulphate, and the solvent evaporated under reduced pressure. Distillation of the residue gave the lactone (1.4 g, 40 %), b.p. 169—172°. The NMR and IR spectra were identical with those of an authentic sample, prepared by a different method.⁴

α-Cyano-δ-valerolactone (IV). Hydrolysis of 2-amino-3-cyano-5,6-dihydro-4H-pyran (II) (6 g) in 1 N sulphuric acid (100 ml) under the same conditions, afforded a colourless liquid (3.5 g, 55 %), b.p. 128—130°, which crystallized within a few minutes, m.p. 61—52°. (Found: C 57.44; H 5.72; N 10.58. Calc. for C₆H₆NO₂: C 57.59; H 5.64; N 11.20.) IR absorptions (KBr) were found at 2250 and 1730 cm⁻¹. NMR signals (CDCl₃) were located at δ 4.45 (triplet), 3.79 (four lines), and about 2.2 (multiplet); the relative intensities were 2:1:1. These data are consistent with the structure (IV).

BOND-BOND INTERACTIONS IN ORGANIC OXYGEN COMPOUNDS

PART III. ENTHALPY OF FORMATION OF 2-(METHOXYETHOXY)TETRAHYDROPYRAN AND THE CONTRIBUTORY GROUP INCREMENTS

KALEVI PIHLAJA and MARJA-LEENA TUOMI

Department of Chemistry, University of Turku, Turku 2, Finland

2-(Methoxyethoxy)tetrahydrofuran (I) is a very suitable compound for study of bond-bond interactions since several increments including those due to oxygen atoms are involved.

One rabbit-ear effect and one methyl-oxygen gauche interaction exist in the most stable rotamer of the equatorial conformer of 2-alkoxytetrahydrofurans (eqn. 1; E). Similarly, the most stable rotamer of the axial conformer (eqn. 1; A) is that in which two 1,3-diaxial hydrogen-oxygen interactions and one methyl-oxygen gauche interaction contribute.⁵ The enthalpy difference between IA and IE (eqn. 1) is hence nearly equal to the difference between the enthalpy of interaction due to one rabbit-ear effect and that due to one axial alkoxy group. The latter interaction is obviously slightly greater than in methoxy-cyclohexane where ΔG° is 0.4 kcal/mole in favor of the equatorial conformation.⁷ de Hoog and coworkers⁶ have reported that the enthalpy difference between axial and equatorial conformers of 2-alkoxytetrahydrofurans is about 1.05 kcal/mole. If it is assumed that ΔH° for an axial alkoxy group in position 2 of tetrahydrofuran is about 0.7 kcal/mole,


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