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STUDIES IN THE FURAN SERIES. XXXIX.* REACTION OF FURAN AND 2-METHYLFURAN WITH ACRYLONITRILE

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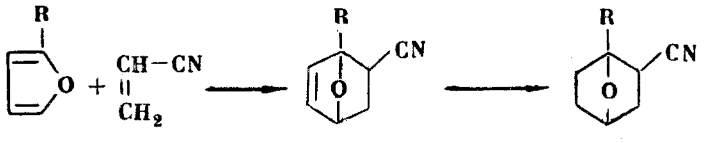
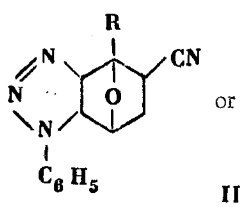
Furan undergoes a diene-synthesis type of reaction with acrylonitrile to give stereoisomeric 3, 6-endoxotetrahydrobenzonitriles whose configurations are established by PMR spectra. 2-Methylfuran undergoes a similar reaction with acrylonitrile. Some aspects of the relationship between the diene substitution reaction and substitutive addition in the furan series are considered.

It was perviously remarked [2, 3] that all the various types of diene synthesis in the furan series can conveniently be classified according to the electronic character of the dienophile. Dienophiles with one electron-accepting group can react mainly in accordance with the diene type of synthesis, though substitutive addition can also take place. It has also been shown that furan, its homologs, and its α, β-unsaturated carbonyl derivatives can undergo the substitutive addition type of reaction, this being a general method of synthesizing furan aldehydes and ketones [3-5]. Even in the cases where the literature states, that the reaction between furan derivatives and α, β-unsaturated carbonyl derivatives is of the diene type, what actually occurs is substitutive addition [4]. Data on the reaction of furan and its derivatives with monofunctional dienophiles having any other electron-accepting group are scarce, and some of them have already been discussed [3]. It was recently shown that 2-alkylfurans react by substitutive addition with nitroethylene [6] and acrylic acid [7], though results show that furan reacts with ethyl acrylate as a diene, giving an adduct [8]. It is also known that 3, 4-dimethoxyfuran reacts with methyl acrylate and acrylonitrile, but the structures of the resultant products are unknown [9]. The reaction of tetrachlorofuran with various dienophiles has been described [10], but the paper lacks kinetic data, so that it is impossible to decide whether in that reaction the donor is the diene or the dienophile [11].

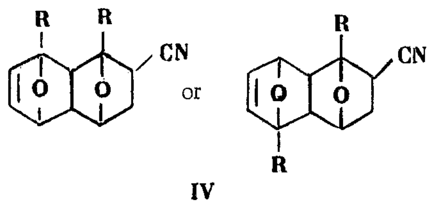
The present paper continues the study of the reaction of furan compounds with monofunctional dienophiles, and establishes that furan and 2-methylfuran react with acrylonitrile, although the literature states [12] that furan does not react. Still it was found that on prolonged boiling of furan with acrylonitrile there is a diene synthesis, giving an approximately 25% yield of 3, 6-endoxo-Δ^4-tetrahydrobenzoic acid (Ia), which with phenyl azide gives a triazoline derivative IIa. Here the diene synthesis does not take place stereospecifically, and thin-layer chromatography demonstrated the formation of a mixture of endo- and exo-isomers Ia, from which the stereoisomeric nitriles were separated by fractional distillation.



I III



II



IV

a $R = H$
b $R = CH_3$

Hydrogenation of the mixed isomeric nitriles Ia afforded a mixture of the corresponding hydro derivatives IIIa, and to separate the endo- and exo- forms of IIIa, fractional distillation was again employed. The PMR spectra given in the figure served as a basis for configuration assignment. The following differences are exhibited in the PMR spectra of each pair of stereoisomeric nitriles Ia and IIIa. In one of the isomers Ia the peak belonging to the bridge proton is split into a triplet (spectrum 1), while in the other there is an unsplit signal (spectrum 2). Further the signal from the proton, adjacent to the nitrile group in spectrum 1, is split into a larger number of peaks, than in spectrum 2. Lastly, in spectrum 1,

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*Communication XXXVIII, see [1].

all the signals are somewhat displaced towards the region of weaker field. According to the literature, in the PMR spectrum of derivatives of 3, 6-endoxocyclohexane, the signal from the protons at the bridgehead and from those at the carbon atoms of the carbon skeleton, which are united in functional groups, move into the region of weaker field [13-15], when, for 3, 6-endoxocyclohexane the peak due to bridgehead protons is unsplit. However, when functional groups are present, this signal is split due to spin-spin interaction of exo-protons with bridgehead protons, while the spin-spin interaction constant of the endo-protons with them is equal to zero. Hence spectrum 1 must belong to the endo form, and spectrum 2 to the exo form of nitrile Ia, since in the first spectrum the signals are shifted into the weaker field region, and there is splitting of the bridgehead protons signal into a triplet due to interaction with two exo-protons. To the right of spectrum 1 are signals due to protons of the grouping NC—CH—CH$_2$, the minimum signal on the right proceeding from an endo-proton of the CH$_2$ group, since this signal is a quartet, but the two other signals proceed from exo-protons, and because of additional interaction with bridgehead protons they are multiplets, and the proton in the weakest field is next to the nitrile group. The endo-proton has two spin-spin interaction constants, 3.5 and 11 cps, which can be ascribed to endo-exo interaction, and to interaction with the CH$_2$ group. It is interesting that in spectrum 1 the signal due to olefin protons is typical of AB systems, while in spectrum 2 the signal of these protons became more complex. This can be ascribed to their interaction with endo-protons, since spatially they are adjacent. The configuration of the IIIa isomers is established by similar PMR spectra considerations, as well as by a correlation arising out of hydrogenation of the endo-isomer Ia to give endo IIIa.

An adduct is also formed when 2-methylfuran is boiled for a long time with acrylonitrile, and from the polarities of the reactants the resultant nitrile is considered to be 6-methyl-3, 6-endoxo-Δ^4-tetrahydrobenzonitrile (Ib). The structure of Ib is also shown by formation of a triazoline derivative. In this latter reaction a second compound, a diadduct, was also isolated along with Ib. It is known that furan and its derivatives can undergo diene type synthesis with strained bicyclic olefins [3], so that the formation of a diadduct is not unexpected. It is most probable that the diadduct is a complex mixture of structural (IVb) and spatial isomers.

Thus the relationship between the diene synthesis reaction and substitutive addition in the furan series is a function of the functional group of the dienophile with only one functional group. From the literature data and the present results it follows that α, β-unsaturated aldehydes, ketones, acids, and nitro-compounds react with compounds of the furan series by substitutive addition, while α, β-unsaturated nitriles and esters undergo the diene type of synthesis.

EXPERIMENTAL

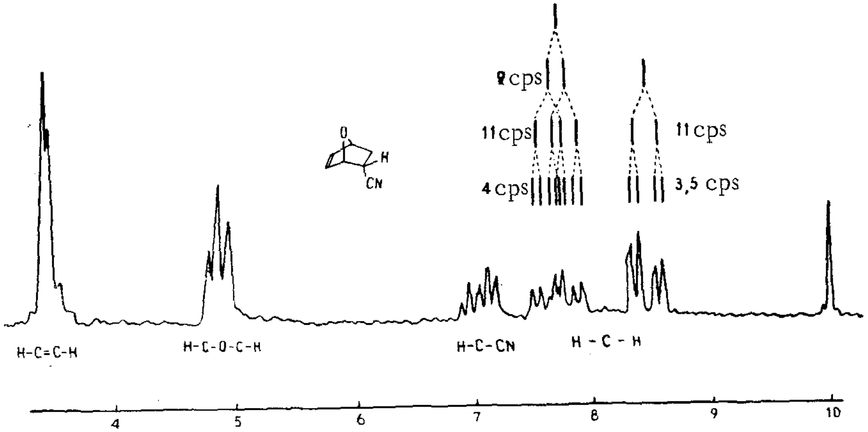
3, 6-Endoxo-Δ^4-tetrahydrobenzonitrile (Ia). 27 g furan, 20 g acrylonitrile, and 0.1 g hydroquinone are boiled together for one month, unchanged furan taken off in a vacuum, and the acrylonitrile and residue fractionated (distillation is accompanied by some retro-diene decomposition). The first distillation gives 12-15 g of a mixture of isomeric nitriles b.p. 70-120° (2 mm), redistillation affording 11-14 g, b.p. 80-100° (2 mm). Found: C 69.62, 69.60; H 6.00, 5.94%. Calculated for C_7H_7NO: C 69.40; H 5.82%. Thin-layer chromatography in benzene on alumina gives two spots, R_f 0.55 and 0.36.

Triazoline derivative IIa. Equivalent amounts of Ia and phenyl azide are mixed, and after standing 24 hr, IIa is obtained in quantitative yield, as white crystals m.p. 213-214° (from methanol). Found: C 64.91, 65.14; H 5.30, 5.46%. Calculated for $C_{13}H_{12}N_4O$: C 64.99; H 5.03%. 12 g mixed isomers Ia are distilled giving two fractions b.p. 81-84° (2 mm) (8 g), and 89-93° (3 mm) (4.5 g). A second distillation gives the endo-nitrile, m.p. 32-33° (from carbon tetrachloride); PMR spectrum no. 1. Further distillation of the second fraction gives the exo-nitrile, b.p. 92° (2 mm), n_D^{20} 1.4875, d_4^{20} 1.1390, MR_D:30.56. Calculated for C_7H_7NO: MR_D:31.12, PMR spectrum no. 2.

3, 6-Endoxohexahydrobenzonitrile (IIIa). 10 g mixed isomeric nitriles Ia in 50 ml acetone are hydrogenated using palladium on barium sulfate catalyst, under the usual conditions, to give 9.9 g IIIa b.p. 70-85° (3 mm), n_D^{20} 1.4751, d_4^{20} 1.1020, MR_D 31.54. Calculated for C_7H_9NO: MR_D 31.58. Found: C 67.83, 67.64; H 7.19, 7.37%. Calculated for C_7H_9NO: C 68.26; H 7.28%. Fractional distillation yields 2.75 g, b.p. 70° (3 mm), 1.8 g b.p. 71-76° (3 mm), and 5.25 g, b.p. 77-85°. Further distillation of the first fraction gives the endo-nitrile IIIa, b.p. 70° (3 mm), n_D^{20} 1.4771, PMR spectrum no. 3. Distillation of the third fraction gives the exo-nitrile IIIa, b.p. 83° (3 mm), n_D^{20} 1.4771, PMR spectrum no. 4. Hydrogenation in the way described above of the endo-nitrile Ia gives the endo-nitrile IIIa.

6, Methyl-3, 6-endoxotetrahydrobenzonitrile. 31.5 g 2-methylfuran and 24 g acrylonitrile with 0.1 g hydroquinone are boiled together for one month, unreacted starting materials vacuum-distilled off, and the residue (10 g) vacuum-fractionated, giving 3.6 g of a fraction, b.p. 72-79° (3 mm), which is the nitrile Ib: n_D^{20} 1.4730, d_4^{20} 1.1057, MR_D 35.85. Calculated for C_6H_9NO: MR_D 35.72. Found: C 71.19, 71.02; H 6.96, 7.07%. Calculated for C_8H_9NO: C 71.08; H 6.71%.

Action of phenylazide on Ib gives the triazoline derivative IIb, m.p. 146-147° (from methanol). Found: C 65.71, 65.61; H 5.75, 5.79; N 22.27, 22.45%. Calculated for $C_{14}H_{14}ON_4$: C 66.12; H 5.55; N 22.03%.



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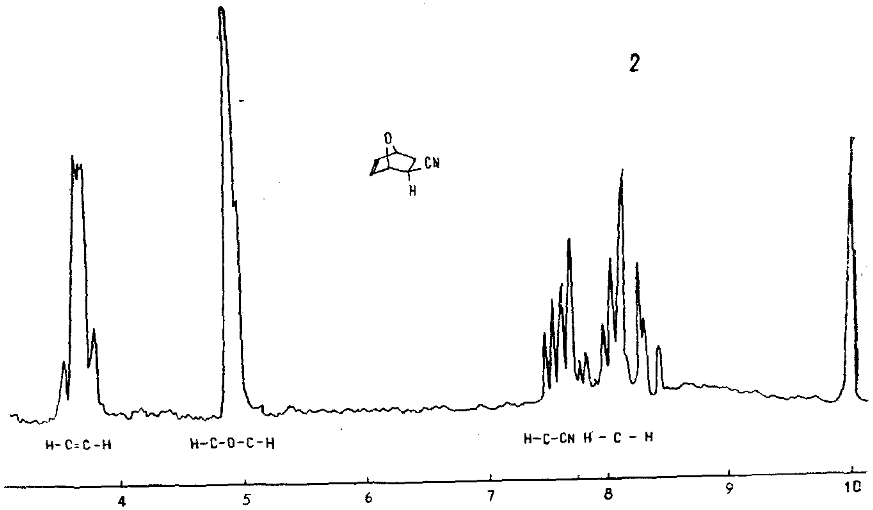
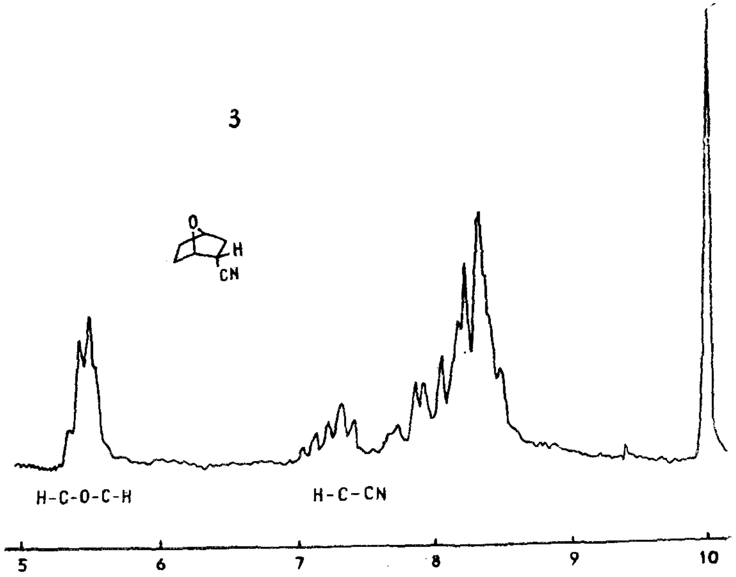


PMR spectra of 3, 6-endoxo-Δ^4-tetrahydrobenzonitrile and -hexahydrobenzonitrile.

3



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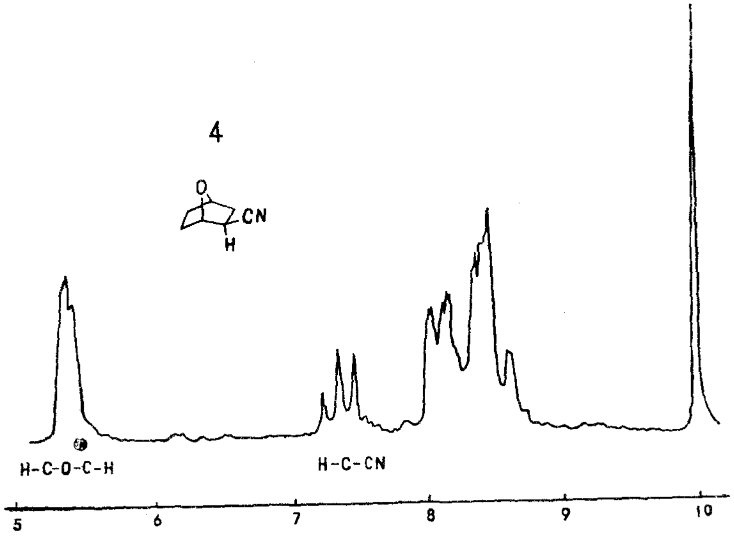

The fraction b.p. 150-155°(3 mm) forming a very viscous oil, is the diadduct IV. Found: C 71.89, 72.10; H 6.89, 6.98%. Calculated for $C_{13}H_{15}NO_2$: C 71.86; H 6.96%.

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