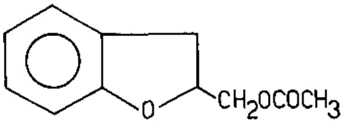
INTRAMOLECULAR CYCLIZATION REACTION OF SOME 2-ALKENYLPHENOLS WITH Tl(III) NITRATE

Maria Luigia Forcellese,* Carlo Alfonsi, Settimia Calvitti, and Enrico Mincione

Centro di Studio per la Chimica delle Sostanze Organiche Naturali del Consiglio Nazionale delle Ricerche and Institute of Organic Chemistry, University of Rome, 00185 Rome, Italy

Abstract - Some 2-allylphenols give an intramolecular cyclization by reaction with Tl(III) nitrate (TTN) leading to 2-substituted 2,3-dihydrobenzofurans; 2-substituted 2,3-dihydrobenzopyran is obtained from 2-(3-butenyl)phenol with the same reagent.

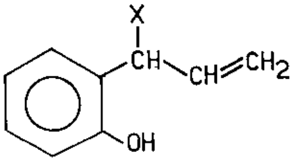
It is known[1] that by treatment of 2-allylphenol with Tl(III)acetate an organothallium derivative is formed, from which 2-acetoxymethyl-2,3-dihydrobenzofuran (1) is obtained.


1

It seemed interesting to investigate this intramolecular cyclization reaction using Tl(III) nitrate in the attempt to obtain 2,3-dihydrobenzofuran derivatives without organothallium intermediates. This reaction could be of some utility in the synthesis of 2,3-dihydrobenzofurans because of their interesting physiological activities.

In this paper we report our results on the action of Tl(III) nitrate[2] on some 2-allylphenols and 2-(3-butenyl)phenol.

2-Allylphenols[3] 2 are transformed into compounds 3 and 4 by Tl(III) nitrate, at room temperature and in a mixture of dry CH_3OH / trimethyl orthoformate (TMOF).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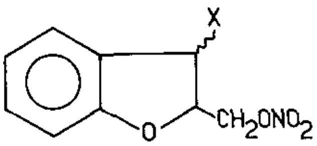
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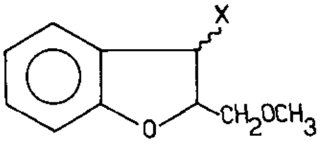
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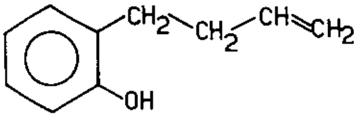
2a,3a,4a X = H
2b,3b,4b = CH_3
2c,3c,4c = C_6H_5

In the same way 2-(3-butenyl)phenol[4] (5) reacts with Tl(III) nitrate giving 5a and 6a.



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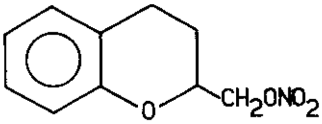
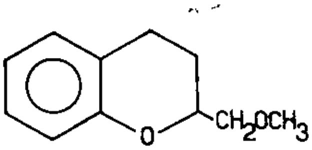


5a



6a

Structures 3a–c, 4a–c and 5a, 6a are supported by their ^{1}H-NMR, infrared, and mass spectra which are summarized in the Experimental.

In the case of X = CH_3, 3b (yield 20%) and 4b (yield 10%) are each a 1:3 mixture of cis- and trans-isomers ($3b_{cis}$ and $3b_{trans}$, $4b_{cis}$ and $4b_{trans}$). The predominant isomers are assigned the trans configuration by assuming that the trans isomer, with less interaction between the two groups at C-2 and C-3, should be the thermodynamically more stable one. The NMR data of the compounds are consistent with the assigned structures; as a matter of fact, the spectra of the cis compounds show the doublet arising from the methyl group at a field higher than those of the trans ones, whereas the H-C-2 and H-C-3 protons are more deshielded in the cis isomers than in the trans ones.

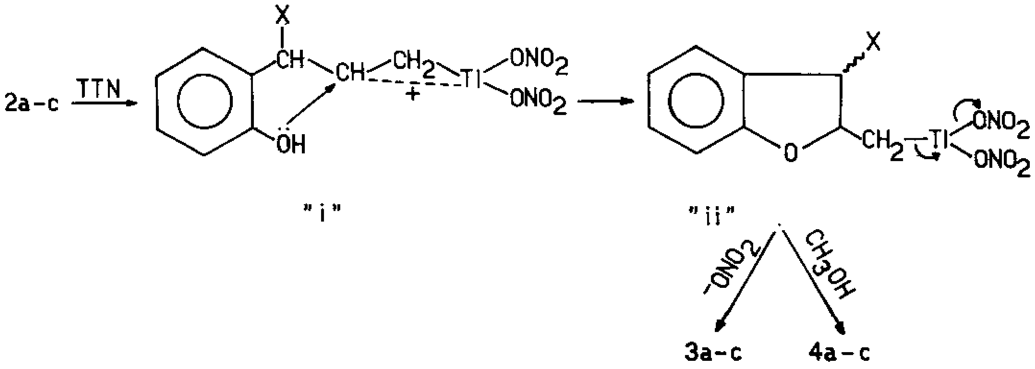
In the case of X = C_6H_5, 3c and 4c are pure compounds to which the trans configuration is assigned on the basis of the higher stability, which reflects the lower steric compression.

No starting material is recovered from the reaction but some polymeric residue is formed. As to the reaction solvent, complex mixtures are obtained by carrying out the reactions in dry CH_3OH, whereas in dioxane compounds 3a–c are formed with yields lower than in CH_3OH/TMOF. Intramolecular cyclization does not occur in hexane; with this solvent the allylic side-chain is unchanged and nitration occurs on the aromatic ring.

As far as the structure of 2-allylphenol is concerned, ring closure does not occur when substituents are present on the aromatic ring.[5]

The formation of 2-substituted 2,3-dihydrobenzofurans can be understood as shown in the Scheme.

Scheme



The reaction of 2-allylphenols with Tl(III) nitrate probably involves the initial electrophilic attack of the thallium salt in the olefinic double bond with formation of the cationic intermediate "i". The nucleophilic attack of the phenolic oxygen occurs at the internal carbon of "i" leading to the organothallium derivative "ii", where the presence of the -ONO_2 group weakens the C-Tl bond. The 2,3-dihydrobenzofuran derivative "ii" undergoes the heterolytic cleavage of the C-Tl bond with the subsequent nucleophilic attack of CH_3OH or $^-ONO_2$ to the carbon atom. The reaction of phenol (5) takes place following the same steps.

EXPERIMENTAL

^{1}H-NMR spectra were recorded in CCl_4; chemical shifts are reported in parts per million (δ) using TMS as an internal standard. Infrared spectra were recorded in CCl_4. Boiling points were determined by microdistillation. Yields, evaluated from the starting material, correspond to the pure isolated products. Satisfactory elemental analyses were obtained for all the described compounds.

General procedure

Phenol (1 mmol) was dissolved in a 1:1 mixture of dry CH_3OH / trimethyl orthoformate (~2 ml), whose solution was stirred at room temperature under a stream of N_2. After the slow addition of 1.5 mmol of Tl(III) nitrate in dry CH_3OH / trimethyl orthoformate (1:1, ~ 2 ml), the reaction mixture was stirred for 3-4 h; during this time a precipitate of Tl(I)nitrate was formed. The solution was diluted with H_2O and extracted several times with ether; the organic layer was washed with H_2O. After drying (Na_2SO_4) and solvent evaporation under reduced pressure, the residue was chromatographed on silica gel to obtain pure samples.

3a (bp 152°C/18 torr, yield 30%): IRν_{max} 1650, 1480, 1280, 1230, 1000 cm^{-1}; ^{1}H-NMR 2.80 - 3.50 (2H, m, H_2-C-3-), 4.45 - 4.60 (2H, m, CH_2-ONO_2), 4.75 - 5.10 (1H, m, H-C-2), 6.65 - 7.20 (4H, m, aromatic protons); mass spectrum, m/e 195 (M^+), 119, 118, 91 (base).

3b cis (bp 148°C/18 torr): IRν_{max} 1640, 1480, 1275, 1225 cm^{-1}; ^{1}H-NMR 1.28 (3H, d, J = 7 cps, CH_3), 3.40 - 3.80 (1H, m, H-C-3), 4.50 - 5.00 (3H, complex pattern, CH_2-ONO_2 and H-C-2), 6.60 - 7.20 (4H, complex pattern, aromatic protons); mass spectrum, m/e 209 (M^+), 162, 163, 164, 133, 132, 131, 118, 105 (base).

3b trans (bp 143°C/18 torr): IRν_{max} 1640, 1480, 1450, 1275, 1050 cm^{-1}; ^{1}H-NMR 1.36 (3H, d, J = 7 cps, CH_3), 3.10 - 3.40 (1H, m, H-C-3), 4.30 - 4.70 (3H, complex pattern, CH_2ONO_2 and H-C-2), 6.60 - 7.20 (4H, complex pattern, aromatic protons); mass spectrum, m/e 209 (M^+), 162, 163, 164, 131, 132, 133, 118, 105 (base).

3c (bp 120°C/1 torr, yield 25%): IRν_{max} 1650, 1480, 1460, 1280, 1260, 1100, 1000 cm^{-1}; ^{1}H-NMR 4.35 (1H, two signals, H-C-3), 4.60 - 4.80 (2H, m, CH_2ONO_2), 4.90 - 5.20 (1H, broad signal, H-C-2), 6.60 - 7.40 (9H, complex pattern, aromatic protons); mass spectrum, m/e 271 (M^+), 226, 195 167 (base),152, 131, 118.

4a (bp 128°C/18 torr, yield 30%): IR ν_{max} 1600, 1470, 1100, 1050 cm^{-1}; ^{1}H-NMR 2.60 - 3.90 (complex patter, H_2-C-3 and CH_2OCH_3), 3.36 (s, OCH_3), 4.60 - 4.90 (1H, broad signal, H-C-2), 6.50 - 7.10 (4H, complex pattern, aromatic protons); mass spectrum, m/e 164 $(M^+$, base), 131, 132, 118.

4b cis (bp 125°C/18 torr): IR ν_{max} 1600, 1480, 1100 cm^{-1}; ^{1}H-NMR 1.20 (3H, d, J = 7 cps, CH_3), 3.10 - 3.80 (complex pattern, H-C-3 and CH_2OCH_3), 3.35 (s, OCH_3), 4.50 - 4.80 (1H, broad signal, H-C-2), 6.50 - 7.10 (4H, complex pattern, aromatic protons); mass spectrum, m/e 178 (M^+), 161, 145, 131, 133, 105 (base).

4b trans (bp 114°C/18 torr): IR ν_{max} 1600, 1480, 1140, 1100 cm^{-1}; ^{1}H-NMR 1.34 (3H, d, J = 7 cps, CH_3), 3.20 - 3.80 (complex pattern, H-C-3 and CH_2OCH_3), 3.35 (s, OCH_3), 4.28 (1H, m, H-C-2), 6.60 - 7.10 (4H, complex pattern, aromatic protons); mass spectrum, m/e 178 (M^+), 145, 131, 133, 105 (base).

4c (bp 115°C/1 torr, yield 25%): IR ν_{max} 1600, 1480, 1460, 1225, 1130 cm^{-1}; ^{1}H-NMR 3.35 (3H, s, OCH_3), 3.50 - 3.70 (2H, broad signal with splitting, CH_2OCH_3), 4.30 - 4.70 (2H, broad signal with splitting, H-C-3 and H-C-2), 6.50 - 7.40 (9H, complex pattern, aromatic protons); mass spectrum, m/e 240 (M^+), 207, 208 (base), 209, 181, 165, 167, 131.

5a (bp 85°C/1 torr, yield 20%): IR ν_{max} 1640, 1480, 1450, 1280, 1225, 1100, 1000 cm^{-1}; ^{1}H-NMR 1.80 - 2.20 (2H, complex pattern, H_2-C-3), 2.60 - 3.00 (2H, complex pattern, H_2-C-4), 4.05 - 4.80 (3H, complex pattern, H-C-2 and CH_2ONO_2), 6.50 - 7.10 (4H, complex pattern, aromatic protons); mass spectrum, m/e 209 (M^+), 164, 131, 132, 133 (base), 134, 105.

6a (bp 130°C/18 torr, yield 20%): IR ν_{max} 1610, 1580, 1480, 1450, 1230, 1110, 1050 cm^{-1}; ^{1}H-NMR 1.70 - 2.10 (2H, complex pattern, H_2-C-3), 2.60 - 2.90 (2H, complex pattern, H_2-C-4), 3.35 (s, 3H, OCH_3), 3.40 - 3.60 (2H, m, CH_2-OCH_3), 3.90 - 4.20 (1H, broad signal, H-C-2), 6.50 - 7.10 (4H, complex pattern, aromatic protons); mass spectrum, m/e 178 (M^+), 133 (base), 105.

REFERENCES AND FOOTNOTES

1. H.J. Kabbe, *Ann. Chem.*, 1962, **656**, 204.
2. Thallium(III) nitrate was prepared according to A. McKillop, J.D. Hunt, F. Kienzle, E. Bigham, and E.C. Taylor (*J. Am. Chem. Soc.*, 1973, **95**, 3635).
3. Phenols 2a-c were prepared by known methods: D.S. Tarbell, "Organic Reactions", Vol. 2, eds; by R. Adams, Wiley, New York; 1944, pp 27-28; L. Claisen and E. Tietze, *Ber.*, 1925, **58**, 275; L. Claisen and E. Tietze, *Ber.*, 1926, **59**, 2344.
4. M. Ōki and H. Iwamura, *Bull. Chem. Soc. Japan*, 1960, **33**, 681.
5. When the aromatic ring is substituted by CH_3 or Cl groups, very complex mixtures are obtained. When NO_2 is the substituent, the only reaction is a nucleophilic attack by $^-ONO_2$ or CH_3OH on the olefinic double bond.

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