

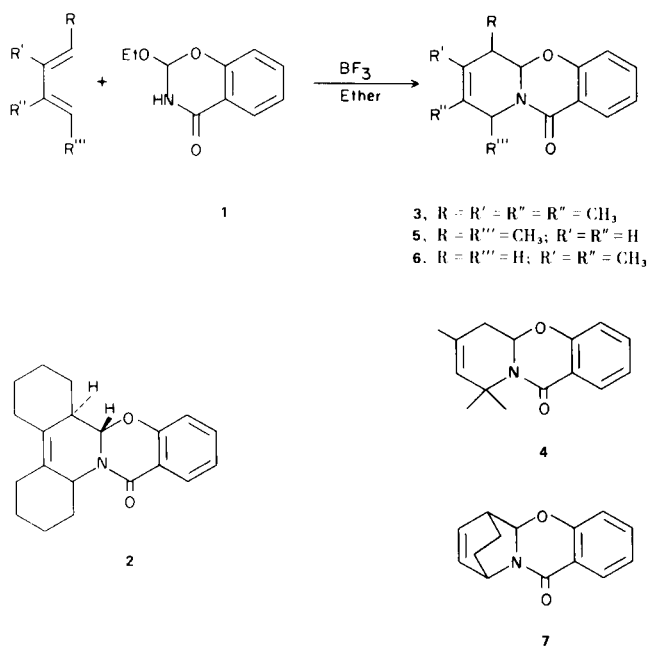
## The Reactions of 2-Ethoxy-2,3-dihydro-4*H*-1,3-benzoxazin-4-one with Conjugated Dienes

D. Ben-Ishai and A. Warshawsky

Department of Chemistry, Israel Institute of Technology, Haifa, Israel

Received March 19, 1971

In recent publications we have described the reactions of *N*- $\alpha$ -methoxylactams (1) and 5-methoxyhydantoin (2) with conjugated dienes to give Diels-Alder type adducts. This reaction has now been extended to 2-ethoxy-2,3-dihydro-1,3-benzoxazin-4-one (3) (1) which also possesses the alkoxy lactam group and which, on the elimination of ethanol, should afford a cyclic acylimine system conjugated with the lone pair of the phenoxy oxygen.



Reacting 1,1-bicyclohexenyl and 1,2,3,4-tetramethylbutadiene with two equivalents of the ethoxybenzoxazine, in ether solution and in the presence of borontrifluoride-ether complex for 16 hours afforded crystalline products in 90 and 86% yield. The products showed CO absorptions at 1670-1660  $\text{cm}^{-1}$  but lacked the NH absorption of the starting material at 3420  $\text{cm}^{-1}$  in the infrared. The nmr spectra showed a characteristic doublet (1H) at 5.0-5.5 ppm of the acetate type methine group (C-2 of the oxazine ring). The coupling constants of these protons suggest that the *trans* isomer was obtained in the first case (2,  $J = 9$  cps) and the *cis* isomer (3,  $J =$

4 cps) was obtained in the case of tetramethylbutadiene. If the reaction with the bicyclohexenyl was quenched after one hour the product which was obtained in 78% overall yield was a mixture of *cis* and *trans* isomers in a ratio of 2:3. The tetramethyl *cis*-isomer was found to isomerize in the presence of borontrifluoride, slowly to the *trans* isomer. After 5 days the product contained about 15% of the *trans* isomer.

2,4-Dimethyl-1,3-pentadiene and 2,3-dimethylbutadiene reacted with the ethoxybenzoxazine, under the same experimental conditions, to give the adduct 4 and 6 in 44 and 42% yield. The proton at C-2 of the oxazine ring in compound 4 appeared as a triplet at  $\delta$  5.40 ppm which supports the assigned structure (4). 2,4-Hexadiene (*t,t*) gave a mixture of *cis-trans* isomers in a 3:1 ratio. The *cis* isomer was found to isomerize, in the presence of borontrifluoride, to the *trans* isomer. 1,3-Cyclohexadiene afforded the adduct 7 on treatment with the ethoxy oxazine in ether solution and in the presence of borontrifluoride etherate. The less substituted dienes, piperylene, isoprene and butadiene reacted sluggishly with the ethoxyoxazine to give complex mixtures of products. An attempt to obtain thermal reactions with the dienes in sealed tubes at elevated temperatures failed to give Diels-Alder adducts.

### EXPERIMENTAL

Melting points are corrected, infrared spectra were measured in chloroform solutions and nmr in deuterio chloroform.

#### 2-Ethoxy-2,3-dihydro-4*H*-1,3-benzoxazin-4-one (3).

A suspension of salicylamide (50.0 g.) in triethylorthoformate (200 ml.) containing  $\beta$ -naphthalenesulfonic acid (2.0 g.) was refluxed for 3 hours. During the reaction the ethanol was distilled off. The solution was kept in the refrigerator overnight, the solid was filtered and crystallized from ethyl acetate-hexane. The yield was 45.2 g. (67%), m.p. 121°; lit. (3) gives m.p. 120-121° and 124°. It showed NH and CO absorptions at 3420 and 1695  $\text{cm}^{-1}$ ; nmr:  $\delta$  8.50 (s, 1H, broad) 8.0 (q, 1H); 7.3-6.9 (m, 3H); 6.10 (s, 1H, broad); 3.75 (q, 2H) and  $\delta$  1.2 (t, 3H) ppm.

The Reaction of 2-Ethoxy-2,3-dihydro-4*H*-1,3-benzoxazin-4-one with Dienes.

#### 1,1'-Bicyclohexenyl affording 2.

A mixture of the ethoxyoxazine (1.93 g., 0.01 mole), diene

(0.82 g., 0.005 mole) and freshly distilled boron trifluoride etherate (1.4 ml., 0.01 mole) in dry ether (50 ml.) was left overnight at room temperature. The mixture was diluted with ether (100 ml.) and aqueous bicarbonate (50 ml., 5%) was added. The ether solution was separated, washed with water, dried and evaporated. The residue (2.0 g.) was chromatographed over neutral alumina (60 g.) and the product eluted with benzene methylene chloride (1:1). It was crystallized from hexane, m.p. 138-139°, yield 1.45 g. (90%); ir: 1665 and 1655  $\text{cm}^{-1}$ ; nmr:  $\delta$  7.94 (q, 1H); 7.6-6.8 (m, 3H), 5.19 (d, 1H,  $J = 8$  cps), 5.0-4.7 (m, 1H), 3.0-1.0 (m, 17H) ppm;  $m/e = 309$ .

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{23}\text{NO}_2$ : C, 77.64; H, 7.49; N, 4.53. Found: C, 77.86; H, 7.48; N, 4.80.

If the reaction is quenched after 1 hour and the solution work out as described above a mixture of two products is obtained (*cis-trans* isomers) in 78% overall yield which showed an additional doublet at  $\delta$  5.42 ( $J = 4$  cps) in the nmr.

#### 1,2,3,4-Tetramethylbutadiene affording 3

1,2,3,4-Tetramethylbutadiene was treated with the ethoxyoxazine as described above. The product obtained after chromatography was crystallized from methanol, m.p. 105-106°, yield 86%; ir: 1670  $\text{cm}^{-1}$ ; nmr:  $\delta$  7.98 (q, 1H), 7.6-6.8 (m, 3H), 5.38 (d, 1H,  $J = 5$  cps), 4.52 (m, 1H), 2.8-2.1 (m, 1H), 1.75 (s, 3H), 1.72 (s, 3H), 1.44 (d, 3H,  $J = 7$  cps), 1.24 (d, 3H,  $J = 7$  cps) ppm;  $m/e = 257$ .

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{19}\text{NO}_2$ : C, 74.68; H, 7.44; N, 5.44. Found: C, 74.60; H, 7.43; N, 5.72.

The *cis* isomer slowly isomerized under the conditions of the reaction to the *trans* isomer. After 5 days at room temperature in ether solution and in the presence of boron trifluoride etherate the mixture showed, according to the nmr spectrum, only 15% of the *trans* isomer,  $\delta$  5.25 ( $J = 8$  cps) ppm.

#### 2,4-Dimethyl-1,3-pentadiene affording 4

The above procedure was used and the product was crystallized from methanol, m.p. 74-75°, yield 44%; ir: 1665  $\text{cm}^{-1}$ ; nmr:  $\delta$  7.95 (q, 1H), 7.6-6.8 (m, 3H), 5.43 (t, 1H,  $J = 7$  cps), 5.25 (s, 1H, broad), 2.59 (d, 2H,  $J = 7$  cps), 1.78 (s, 3H), 1.68 (s, 3H), 1.58 (s, 3H);  $m/e = 243$ .

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{17}\text{NO}_2$ : C, 74.05; H, 7.04; N, 5.76. Found: C, 74.39; H, 6.97; N, 6.00.

#### 2,4-Hexadiene (*t,t*) affording 5

A mixture of the ethoxyoxazine (1.93 g., 0.01 mole), the diene (0.58 ml., 0.005 mole) and borontrifluoride etherate (1.4 ml., 0.01 mole) in dry ether (50 ml.) was left at room temperature for 48 hours. The reaction mixture was diluted with ethyl acetate (100 ml.) and washed with aqueous bicarbonate (5%) and water.

The oily residue obtained after the removal of the solvent (1.6 g.) was chromatographed over neutral alumina (60 g.). The product (*cis*-isomer) which was eluted with benzene-methylenechloride (3:1) was crystallized from hexane; m.p. 102-103°, yield 0.20 g. (18%).

The crude product before crystallization was, according to the nmr spectrum, a mixture of *cis-trans* isomers (3:1). The *cis* isomer isomerized in the presence of borontrifluoride to the *trans* isomers (nmr). The *cis* isomer showed a carbonyl absorption at 1670  $\text{cm}^{-1}$  in the infrared; nmr:  $\delta$  7.97 (q, 1H); 7.6-6.8 (m, 3H), 5.90 (s, 1H), 5.81 (s, 1H), 5.43 (d, 1H,  $J = 5$  cps), 4.64 (q, 1H), 2.9-2.6 (m, 1H), 1.44 (d, 3H,  $J = 7$  cps), 1.26 (d, 3H,  $J = 7$  cps);  $m/e = 229$ .

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{15}\text{NO}_2$ : C, 73.34; H, 6.59; N, 6.11. Found: C, 73.66; H, 6.54; N, 6.31.

#### 2,3-Dimethylbutadiene affording 6

A mixture of the ethoxyoxazine (0.96 g., 0.005 mole), 2,3-dimethylbutadiene (0.3 ml., 0.0025 mole) and borontrifluoride etherate (0.7 ml., 0.005 mole) was left at room temperature for 48 hours. The reaction mixture was worked up as described above to give 0.242 g. (42%) of the Diels-Alder adduct. It melted at 93-94° after crystallization from hexane; ir: 1660  $\text{cm}^{-1}$ ; nmr:  $\delta$  7.95 (q, 1H), 7.6-6.8 (m, 3H), 5.46 (q, 1H), 4.09 (q, 2H), 2.6 (m, 1H) and  $\delta$  1.71 (s, 6H) ppm;  $m/e = 229$ .

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{15}\text{NO}_2$ : C, 73.34; H, 6.59; N, 6.11. Found: C, 71.40; H, 6.49; N, 6.28.

#### 1,3-Cyclohexadiene affording 7

A mixture of the ethoxyoxazine (1.93 g.) the diene (0.475 ml.) and borontrifluoride etherate (1.4 ml.) in dry ether (50 ml.) was treated as described above (48 hours). The product was eluted with benzene:methylene chloride (1:1) and crystallized from hexane; m.p. 105-106°, yield 0.38 g. (34%); ir: 1665  $\text{cm}^{-1}$ ; nmr:  $\delta$  7.92 (q, 1H), 7.6-6.2 (m, 4H), 5.5-4.9 (m, 2H), 3.4-3.1 (m, 1H), 2.3-1.2 (m, 4H);  $m/e = 227$ .

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{13}\text{NO}_2$ : C, 73.99; H, 5.77; N, 6.16. Found: C, 74.20; H, 5.74; N, 6.31.

#### REFERENCES

- (1) D. Ben-Ishai, Z. Inbal and A. Warshawsky, *J. Heterocyclic Chem.*, **7**, 615, 917 (1970).
- (2) D. Ben-Ishai and E. Goldstein, *Tetrahedron* (in press), *Tetrahedron Letters*, 2631 (1969).
- (3) T. Irie, E. Kurosawa and T. Hanada, *Nippon Kagaku Zasshi*, **79**, 1401 (1958); *Chem. Abstr.*, **54**, 5657 (1960); C. Runti, V. D'Osualdo and F. Ulian, *Ann. Chim. (Rome)*, **49**, 1668 (1959); *Chem. Abstr.*, **54**, 22601 (1960).