

## ELECTROPHILIC ADDITION OF SCHIFF BASES TO ALLENIC ESTERS

Latchezar S. Trifonov and Alexander S. Orahovats\*

Institute of Organic Chemistry with Center of Phytochemistry,  
Bulgarian Academy of Sciences, Sofia 1113, Bulgaria

Abstract — The reaction between the Schiff base 1 and allenic esters 2a and 2b leads to the formation of the butenolide 3a and 1,2-oxaphosphole 3b instead of the Diels-Alder adducts 3a' and 3b' under catalysis with boron trifluoride.

Several examples are known of Schiff bases taking part as an azadiene in a hetero-Diels-Alder reaction<sup>1</sup>.

In a previous paper we described the participation of 1,2-bis(trimethylsilyloxy)cyclobutene in this reaction leading in two steps to benzazocines<sup>2</sup>.

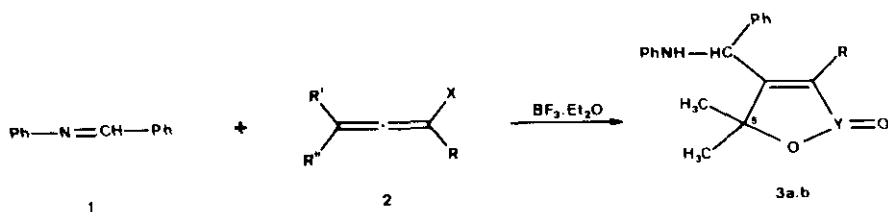
Quite recently Kametani et al. demonstrated that even simple olefins can take part in this cyclisation under rather forcing conditions to give tetrahydroquinolines<sup>3</sup>.

The latter prompted us to investigate the capability of some allenes to act as azadienophiles with the hope to synthesise 3-alkylidene-1,2,3,4-tetrahydroquinolines (see path a, Scheme 2).

Unexpectedly, when the Schiff base 1 was refluxed in toluene with the allenic esters 2a<sup>4</sup> or 2b<sup>5</sup> in the presence of 1 mol-equivalent of BF<sub>3</sub>·Et<sub>2</sub>O the products isolated were shown to have structures 3a or 3b (see Scheme 1), rather than the Diels-Alder adducts 3a' or 3b'. This was evidenced on the one hand by the lack of an ethyl group in the first case and the presence of only one isopropyl group in the latter. On the other hand instead of four one-proton signals in the <sup>1</sup>H NMR spectra characteristic of the aromatic protons of a 1,2,3,4-tetrahydroquinoline<sup>2</sup>, only three signals corresponding to 2, 2 and 1 protons were observed, corresponding to the protons of the phenyl ring bonded to the nitrogen atom.

The 2,5-dihydro-1,2-oxaphosphole 3b was obtained as a diastereomeric mixture of two isomers in a ratio of 1:1 due to the chirotopicity of the carbon and

phosphorous atoms as seen from the overlap of almost all  $^1\text{H}$  and  $^{13}\text{C}$  NMR signals of 3b (see Experimental).



2a:  $\text{R}=\text{R}'=\text{R}''=\text{CH}_3$ ,  $\text{X}=\text{COOEt}$

3a:  $\text{R}=\text{CH}_3$ ,  $\text{Y}=\text{C}$

2b:  $\text{R}=\text{H}$ ,  $\text{R}'=\text{R}''=\text{CH}_3$ ,  $\text{X}=\text{P}(\text{O})\text{OCH}(\text{CH}_3)_2$

3b:  $\text{R}=\text{H}$ ,

2c:  $\text{R}=\text{R}'=\text{R}''=\text{X}=\text{Ph}$

$\text{Y}=\text{P}-\text{OCH}(\text{CH}_3)_2$

2d:  $\text{R}=\text{CH}_3$ ,  $\text{R}'=\text{R}''=\text{Ph}$ ,  $\text{X}=\text{COOEt}$

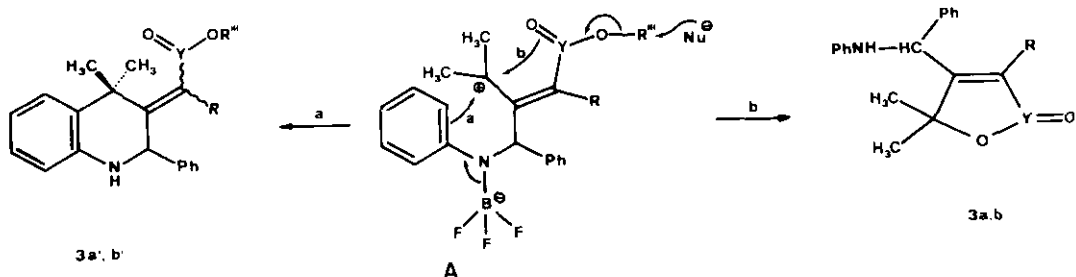
Scheme 1

The Z- and E-stereochemistry of C(5) and CH-N, respectively, with respect to the phosphorous atom is substantiated by the coupling constants  $^3\text{J}_{\text{P}-\text{C}(5)} = 7.9$  Hz and  $^3\text{J}_{\text{P}-\text{CH}-\text{N}} = 20.4$  Hz observed for each of the isomers<sup>6</sup>. The coupling of  $\text{H}-\text{C}(3)$  with the phosphorus ( $^2\text{J}_{\text{P}-\text{H}} = 20.4$  Hz) is also typical of 2,5-dihydro-1,2-oxaphospholes having  $\alpha$ -protons<sup>7</sup>. The large  $^1\text{J}_{\text{P}-\text{C}}$  coupling constant (165.0 Hz) is nearly identical with the known coupling constants of pentacoordinated phosphorus<sup>8</sup>. The presence of two signals at 7.45 and 7.30 ppm in the  $^{31}\text{P}$  NMR spectrum of 3b is also in accordance with the proposed structure.

In the case of tetraphenylallene (2c<sup>9</sup>) as a potential azadienophile the known 1,1,3-triphenylindene was obtained quantitatively as a result of the acid-catalysed autocyclisation<sup>9</sup>. A lactone, analogous to 3a could not be detected in the very complex reaction mixture obtained when using the allene 2d<sup>4</sup>.

The formation of 3a and 3b can be visualized with the participation of an intermediate carbenium ion A as shown in Scheme 2. Path a - electrophilic aromatic substitution does not take place. Instead a five-membered ring cyclisation with the participation of an ester function as nucleophile<sup>10</sup> proceeds (path b). The comparatively low yields of the reaction become clear when one takes into consideration the required proximity of the reactive

centers in A.

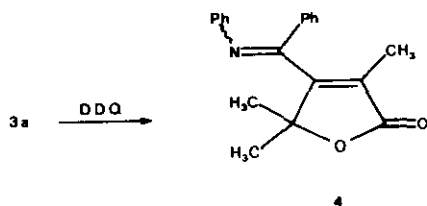


3a and 3a': R=CH<sub>3</sub>, Y=C

3b and 3b': R=H, Y=P-OCH(CH<sub>3</sub>)<sub>2</sub>

Scheme 2

Upon oxidation with DDQ the lactone 3a was converted to 4 with all chromophores conjugated. Consequently the absorption in the UV was shifted from 294 to 345 nm.



The shift of the lactone carbonyl absorption in the IR spectrum from 1735 cm<sup>-1</sup> to 1770 cm<sup>-1</sup> accompanying the conversion of 3a to 4 is noteworthy. This effect is vinylogous to the observed influence of an azomethine group on the absorption of the neighbouring carbonyl group<sup>2</sup>.

#### EXPERIMENTAL

Melting points were determined on a Kofler apparatus and were not corrected. IR spectra were obtained on a UR-10 (Zeiss, Jena) infrared spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a Bruker WM-250 spectrometer at 250 MHz. Chemical shifts (δ) are given in ppm downfield from internal TMS. <sup>13</sup>C NMR spectra were recorded on a Varian XL 100 apparatus at 25.2 MHz. Chemical shifts (δ)

are given in ppm downfield from internal TMS. The  $^{31}\text{P}$  NMR spectrum was taken on a Varian XL 200 apparatus at 80 MHz. Chemical shifts ( $\delta$ ) are expressed in ppm downfield from external 85%  $\text{H}_3\text{PO}_4$ .

Synthesis of 3a. To a stirred solution of 1 (1.81 g, 10 mmol) and 2a (1.54 g, 10 mmol) in dry toluene (10 ml) was added dropwise under argon at room temperature a solution of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.42 g, 10 mmol) in toluene (1 ml). After refluxing for 7 h the solvent was removed under vacuum and the residual oil was subjected to preparative TLC on silica gel using petroleum ether-chloroform-ethanol-acetone (70:25:2.5:2.5) mixture as eluant. The UV (254 nm) active zone ( $R_f = 0.3-0.4$ ) was eluted with chloroform, the eluant was removed under vacuum and the residue recrystallised from ether-hexane to afford 3a (396 mg, 12%) as colourless crystals, mp 149.0-152.0°C; IR( $\text{CHCl}_3$ ): 3500 m sh, 3420 m, 1735 s, 1610 w; UV(EtOH): 244(19500), 294(4400);  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 7.18 (t,  $J=8.0$  Hz, 2H, m-H in  $\text{C}_6\text{H}_5\text{-N}$ ), 6.78 (t,  $J=8.0$  Hz, 1H, p-H in  $\text{C}_6\text{H}_5\text{-N}$ ), 6.57 (dxd,  $J=8.0, 1.0$  Hz, 2H, o-H in  $\text{C}_6\text{H}_5\text{-N}$ ), 7.5-7.3 (m, 5H,  $\text{C}_6\text{H}_5$ ), 5.21 (br.s, 1H, CHN), 3.94 (br.s, 1H,  $\text{D}_2\text{O}$ -exchangeable, NH), 1.80 (d,  $J=0.5$  Hz, 3H,  $\text{CH}_3\text{-C}(3)$ ), 1.56 and 1.31 (each s, 3H,  $2 \times \text{CH}_3\text{-C}(5)$ );  $^{13}\text{C}$  NMR( $\text{CDCl}_3$ ): 172.7 (s, C(2)), 164.7 (s, C(4)), 146.3 (s,  $\text{C}_{\text{arom}}\text{-N}$ ), 138.6 (s,  $\text{C}_{\text{arom}}\text{-CH-N}$ ), 128.9, 128.6 and 126.8 (each d, m-C in  $\text{C}_6\text{H}_5\text{-N}$ , o- and m-C in  $\text{C}_6\text{H}_5$ ), 127.8 (d, p-C in  $\text{C}_6\text{H}_5$ ), 124.5 (s, C(3)), 118.0 (d, p-C in  $\text{C}_6\text{H}_5\text{-N}$ ), 112.7 (d, o-C in  $\text{C}_6\text{H}_5\text{-N}$ ), 85.7 (s, C(5)), 55.8 (d, CH-N), 26.0 and 25.6 (each q,  $2 \times \text{CH}_3\text{-C}(5)$ ), 9.1 (q,  $\text{CH}_3\text{-C}(3)$ ); MS(70 eV): 308(25), 307( $\text{M}^+$ , 100), 292( $\text{M}^+\text{-CH}_3$ , 1), 230( $\text{M}^+\text{-C}_6\text{H}_5$ , 10), 215( $\text{M}^+\text{-C}_6\text{H}_5\text{-CH}_3$ , 50), 182( $\text{C}_6\text{H}_5\text{CHNHC}_6\text{H}_5^+$ , 15), 169(28), 157(60), 129(98), 93(70), 77(35); Anal. Calc. for  $\text{C}_{20}\text{H}_{21}\text{NO}_2$  (307.396): C 78.15, H 6.89, N 4.56. Found: C 78.87, H 7.23, N 4.05.

Synthesis of 3b. To a solution of 1 (1.81 g, 10 mmol) and 2b (2.32 g, 10 mmol) in dry toluene (10 ml) was added dropwise under argon at room temperature  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.42 g, 10 mmol). After refluxing for 2.5 h the solvent was removed under vacuum and the residue chromatographed on silica gel employing the solvent system described above. From the colourless but UV (254 nm) active band ( $R_f = 0.25-0.35$ ) after elution with chloroform, removal of the solvent under reduced pressure and recrystallisation from ether-heptane afforded 3b (605 mg, 15%) as colourless crystals, mp 160-172°C; IR(KBr): 3450 w sh, 3330 m, 1602 s, 1258 s (P=O), 1010 s (P-O); UV(EtOH): 224 sh(8600), 246(14300), 285(sh(3400));  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 7.5-7.3 (m, 5H,  $\text{C}_6\text{H}_5\text{-CH-N}$ ), 7.25-7.10 (m, 2H, m-H in  $\text{C}_6\text{H}_5\text{-N}$ ),

6.85-6.70 (m, 1H, p-H in  $C_6H_5-N$ ), 6.60-6.50 (m, 2H, o-H in  $C_6H_5-N$ ), 6.14 (dxd,  $J=20.4$ , 1.0 Hz, 0.5H, H-C(3)), 6.01 (dxd,  $J=20.4$ , 1.0 Hz, 0.5H, H-C(3)), 5.00 (s, 1H, H-C-N), 4.80-4.55 (m, 1H, OCH), 4.05 (br. m,  $D_2O$ -exchangeable, 1H, NH), 1.73, 1.72, 1.31 and 1.30 (each s, total 6H,  $2 \times CH_3-C(5)$ ), 1.4-1.1 (m, 6H,  $(CH_3)_2CHO$ );  $^{13}C$  NMR( $CDCl_3$ ): 169.8 (d,  $J=18.6$  Hz, C(4)), 169.3 (d,  $J=18.8$  Hz, C(4)), 145.9 (s,  $C_{arom}-N$ ), 139.1 and 138.5 (each s,  $C_{arom}-CH-N$ ), 129.3, 129.2, 128.7, 128.5, 127.6, 118.5, 113.3 and 113.2 (each d, aromatic carbons), 114.0 (dxd, C(3)), 86.2 (d,  $J=7.9$  Hz, C(5)), 86.1 (d,  $J=7.9$  Hz, C(5)), 71.1 (d,  $J=6.5$  Hz, OCH), 58.1 (d,  $J=20.4$  Hz, CH-N), 57.8 (d,  $J=20.4$  Hz, CH-N), 28.6, 28.5, 27.8 and 27.4 (each q,  $2 \times CH_3-C(5)$ ), 24.0, 23.9, 23.8 and 23.7 (each q,  $(CH_3)_2-CH-O$ );  $^{13}C$  NMR ( $CDCl_3$ ) heteronuclear double resonance: irradiation at 6.1 ppm (H-C(3)) gave 114.0 (d,  $J=165.0$  Hz);  $^{31}P$  NMR( $CDCl_3$ ): 7.45 (dxd,  $J=29.6$ , 8.2 Hz), 7.30 (dxd,  $J=30.2$ , 8.8 Hz); MS(70 eV): 371( $M^+$ , 10), 248(13), 237(12), 182( $C_6H_5CHNHC_6H_5^+$ , 95), 155(60), 115(100), 104(30), 77(80); Anal. Calc. for  $C_{21}H_{26}NPO_3$  (371.422) : C 67.91, H 7.06, N 3.77. Found: C 67.75, H 7.61, N 3.20.

Oxidation of 3a to 4. To a stirred solution of 3a (102 mg, 0.33 mmol) in dry benzene (5 ml) was added DDQ (100 mg, 0.44 mmol) and stirring was continued at  $60^\circ C$  for 9 h. The solvent was removed under vacuum and the residue subjected to column chromatography on silica gel with petroleum ether-ether-chloroform-ethanol (70:20:8:2) as eluent. The front part of the yellow zone (TLC-monitored) was collected, the eluant was removed under vacuum and the residue was recrystallised from chloroform-heptane to afford 4 (64 mg, 64%) as lemon yellow prisms, mp  $165.0-167.0^\circ C$ ; IR(KBr): 3080 m, 3005 m, 2950 m, 2880 m, 1770 s, 1625 s, 1600 s; UV(EtOH): 230 sh(32800), 254(38000), 345(4100);  $^1H$  NMR( $CDCl_3$ ): 7.85 (d,  $J=7.1$  Hz, 1H), 7.55-7.45 (m, 2H), 7.35-7.25 (m, 2H), 7.25-7.10 (m, 2H), 7.05-6.95 (m, 1H), 6.83 (d,  $J=7.1$  Hz, 1H), 6.63 (d,  $J=8.3$  Hz, 1H), 2.03 (s, 1H), 1.76 (s, 2H), 1.56 (s, 2H), 1.36 (s, 1H), 1.24 (s, 2H), 0.80 (s, 1H); MS(70 eV): 306(15), 305( $M^+$ , 70), 290( $M^+-CH_3$ , 30), 276(40), 262(45), 234(80), 220(30), 180( $C_6H_5C=NC_6H_5^+$ , 25), 142(30), 77(100), 51(40); Anal. Calc. for  $C_{20}H_{19}NO_2$  (305.380) : C 78.66, H 6.27, N 4.59. Found: C 79.02, H 6.52, N 4.34.

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#### REFERENCES

1. D.L.Boger, Tetrahedron, 1983, 39(18), 2869.
2. L.S.Trifonov and A.S.Orahovats, Heterocycles, 1984, 22(2), 355.
3. T.Kametani, H.Takeda, Y.Suzuki and T.Honda, Heterocycles, 1984, 22(2), 275.
4. H.J.Bestmann and H.Hartung, Ber., 1966, 99, 1198.
5. V.M.Ignat'ev, B.I.Ionin and A.A.Petrov, Zh.Obshch.Khim., 1967, 37(8), 1898.
6. M.Duncan and M.J.Callagher, Org.Magn.Res., 1981, 15(1), 37.
7. C.M.Angelov, K.V.Vachkov, B.I.Ionin and M.Kirilov, Zh.Obshch.Khim., 1979, 49, 2438.
8. G.W.Buchanan and C.Benezra, Can.J.Chem., 1976, 54, 231.
9. D.Vorländer and C.Siebert, Chem.Ber., 1906, 39, 1027.
10. S.Braverman and D.Reisman, Tetrahedron Letters, 1977, 1753.

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