Reaction of 2-Trifluoromethyl-4*H*-3,1-benzoxazin-4-one Derivatives with Carboethoxymethylenetriphenylphosphorane

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Treatment of a series of 2-trifluoromethyl-4*H*-3,1-benzoxazin-4-one derivatives **1** with carboethoxymethylenetriphenylphosphorane **2** yielded the phosphoranes **3** in boiling toluene solution. Thermolysis of these phosphoranes **3** gave esters **6**.

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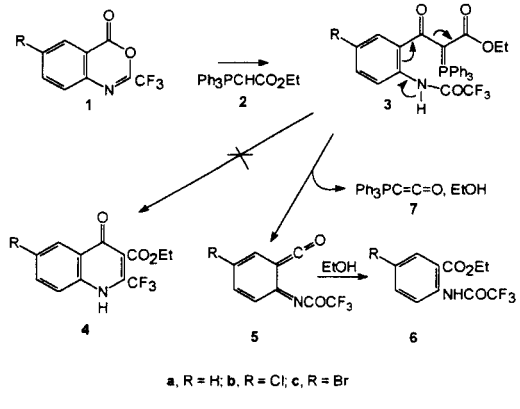
The Wittig reaction of compounds other than aldehydes and ketones, for example anhydrides [1] (including isatoic anhydride [2]) and imides [1,3] is well documented. We were interested in investigating the reaction of 2-trifluoromethyl-4*H*-3,1-benzoxazin-4-one derivatives **1** with carboethoxymethylenetriphenylphosphorane **2** anticipating the formation of the phosphoranes **3** by cleavage of the heterocyclic ring in compounds **1** (Scheme). These new phosphoranes **3** might then be transformed into quinolone derivatives **4** by an intra-molecular Wittig reaction. 4-Quinolone-3-carboxylic acid derivatives form an important class of anti-bacterial agents [4] and a potential synthesis of these compounds from 4*H*-3,1-benzoxazin-4-ones would provide an expedient method for their preparation.

Scheme



a, R = H; b, R = Cl; c, R = Br

When compounds **1a-1c** were treated with phosphorane **2** in boiling toluene solution the corresponding phosphoranes **3a-3c** were formed (70-99% yield) as expected. When phosphorane **3a** was heated (180-200°) in the melt however, quinolone **4a** was not formed and the only product isolated after column chromatography was ethyl *N*-trifluoroacetyl anthranilate **6a** (31% yield). A possible mechanism for this transformation may involve elimination of ketenylidinetriphenylphosphorane **7** [5] and ethanol from compound **3a** giving an intermediate iminoketene **5a** [6] as indicated in the Scheme. Ester **6a** is then formed by addition of ethanol to iminoketene **5a**. Similarly, phosphoranes **3b** and **3c** gave esters **6b** (13%) and **6c** (13%) respectively.

EXPERIMENTAL

Infra-red spectra were recorded as potassium bromide discs. Proton nmr spectra were determined at 90 MHz in deuteriochloroform solution. Compound **1c** was prepared by treating 5-bromoanthranilic acid with trifluoroacetic anhydride and then heating with acetic anhydride [7,8] and was used directly in the reaction with phosphorane **2**. Compounds **1a** [8] and **1b** [9] have been reported previously. Authentic samples of the esters **6a-6c** were prepared by treating the appropriate ethyl anthranilate derivatives with trifluoroacetic anhydride. Ethyl 5-bromoanthranilate and ethyl 5-chloroanthranilate were prepared by Pedersen's method [10].

Phosphoranes **3**. General Method.

A mixture of the 2-trifluoromethyl-4*H*-3,1-benzoxazin-4-one derivative **1** and phosphorane **2** were heated at reflux in toluene. The reaction mixture was allowed to cool to room temperature and the products **3a-3c** were collected by filtration.

Ethyl 2-Triphenylphosphoranylidine-3-(2-trifluoroacetylamino-phenyl)-3-oxopropionate **3a**.

Compound **1a** (0.5 g) and phosphorane **2** (1.6 g) for 6 hours gave phosphorane **3a**, 1.3 g (99%), mp 181-183° (toluene); ir: ν 3240, 1725, 1660, 1500, 1275 and 1150 cm^{-1}; ^1H nmr: δ 10.90 (1H, broad s, >NH), 8.24 (1H, d, J = 8 Hz, ArH), 7.90-7.10 (18H, m, ArH), 3.67 (2H, q, J = 7 Hz, -CH_2-) and 0.63 (3H, t, J = 7 Hz, -Me) ppm.

Anal. Calcd. for $C_{31}H_{25}F_3NO_4P$: C, 66.1; H, 4.5; N, 2.5. Found: C, 66.2; H, 4.3; N, 2.4.

Ethyl 2-Triphenylphosphoranylidine-3-(2-trifluoroacetylamino-5-chlorophenyl)-3-oxopropionate **3b**.

Compound **1b** (0.5 g) and phosphorane **2** (1.25 g) for 6 hours gave phosphorane **3b**, 0.85 g (70%), mp 179-180° (toluene); ir: ν 3450, 1740, 1670, 1505, 1375 and 1275 cm^{-1}; nmr: δ 10.80 (1H, broad s, >NH), 8.20 (1H, d, J = 8 Hz, ArH), 7.80-7.10 (17H, m, ArH), 3.72 (2H, q, J = 7 Hz, -CH_2-) and 0.70 (3H, t, J = 7 Hz, -Me) ppm.

Anal. Calcd. for $C_{31}H_{24}ClF_3NO_4P$: C, 62.3; H, 4.05; N, 2.3. Found: C, 62.5; H, 4.05; N, 2.35.

Ethyl 2-Triphenylphosphoranylidine-3-(2-trifluoroacetylamino-5-bromophenyl)-3-oxopropionate **3c**.

Compound **1c** (0.5 g) and phosphorane **2** (1.18 g) for 4 hours

gave phosphorane **3c**, 0.8 g (73%), mp 116-117.5° (toluene); ir: ν 3450, 1735, 1675, 1500, 1370 and 1270 cm^{-1}; ^1H nmr: δ 10.78 (1H, broad s, >NH), 8.13 (1H, d, J = 8 Hz, ArH), 7.90-7.10 (17H, m, ArH), 3.72 (2H, q, J = 7 Hz, $-CH_2-$) and 0.71 (3H, t, J = 7 Hz, -Me) ppm.

Anal. Calcd. for $C_{31}H_{24}BrF_3NO_4P$: C, 58.0; H, 3.8; N, 2.2. Found: C, 58.5; H, 3.9; N, 2.1.

Formation of Ethyl *N*-Trifluoroacetyl Anthranilates **6a-6c** from Phosphoranes **3a-3c**. General Method.

Phosphorane **3a** (0.5 g) was heated (180-200°, oil-bath temperature) for 0.5 hour under a nitrogen atmosphere. The dark mixture was allowed to cool to room temperature and purified by column chromatography (silica gel, eluent, petroleum ether: ethyl acetate, 8:1) giving ester **6a** 0.09 g (39%), identical with an authentic sample. Similarly, phosphoranes **3b** and **3c** yielded esters **6b** (13%) and **6c** (13%), identical with authentic samples.

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REFERENCES AND NOTES

[1] P. J. Murpy and J. Brennan, *J. Chem. Soc. Rev.*, **17**, 1 (1988).

[2] D. T. Conner and M. von Strandtmann, *J. Org. Chem.*, **38** 1047 (1973).

[3] W. Flitsch and S. R. Schindler, *Synthesis*, 685 (1975).

[4] R. P. Hertzber, Comprehensive Medicinal Chemistry, Vol **2**, C. Hansch, P. G. Sammes and J. B. Taylor, eds, Pergamon, 1990, p 773.

[5] H. J. Bestmann, *Angew. Chem., Int. Edn. Engl.*, **16**, 349 (1977).

[6] T. Kametani, T. Higa, C. V. Loc, M. Ihara, M. Koizumi and K. Fukumoto, *J. Am. Chem. Soc.*, **98**, 6186 (1976).

[7] D. T. Zentmyer and E. C. Wagner, *J. Org. Chem.*, **14**, 967 (1949).

[8] L. A. Errede, H. T. Oien and D. R. Yarian, *J. Org. Chem.*, **42**, 12 (1977).

[9] F. Clémence, O. Le Martret and J. Collard, *J. Heterocyclic Chem.*, **21**, 1345 (1984).

[10] E. B. Pedersen, *Tetrahedron*, **33**, 217 (1977).