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The Wittig Reaction of some Fluorinated Amide Derivatives

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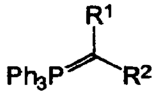
Abstract: Carboethoxymethylenetriphenylphosphorane **1** reacted with fluorinated amides **4**, **6**, **8** and **15** yielding products **12**, **13**, **14** and **3** respectively.

The Wittig reaction[1] of compounds other than aldehydes or ketones[2], for example imides and anhydrides[3] has proved a useful method for the synthesis of heterocycles. We now report the results of our investigations into the Wittig reaction of the amide derivatives **4**, **6**, **8** and **15** with phosphorane **1**.

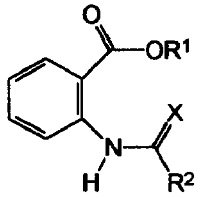
When amide **4**[4] was treated with phosphorane **1** in the melt (180-200°C), the substituted alkene **5** was not isolated but the quinoline derivative **12** was produced together with some product of trans-esterification, quinoline **13**. Amide **6**[5] was therefore reacted with phosphorane **1** under similar conditions yielding quinoline derivative **13** (30% yield) which was fully characterised. In these two transformations **4** to **12**/**13** and **6** to **13** the substituted alkene derivatives **5** and **7** respectively are evidently formed but cyclised under the reaction conditions giving the corresponding intermediates **10** and **11** from which products **12** and **13** are formed by loss of water. In these intermediates **10** and **11**, the most bulky C3 and C4 substituents *ie* the carboethoxy and alkoxy groups adopt an anti-relationship and elimination of water is therefore observed giving quinolines **12** and **13** respectively.

The reaction of amide **8** with phosphorane **1** in the melt (180°C) was next investigated. This reaction did not yield a quinoline derivative but instead gave derivative **14** (32% yield) after column chromatography. The ^{1}H NMR, ^{19}F NMR and mass spectra were in accord with the proposed structure **14** as was microanalytical data. A reasonable explanation which accounts for the formation of compound **14** from the initial product of the Wittig reaction, compound **9** is shown in the Equation. The hydrolytic step presumably occurs during chromatography and an enamine-imine tautomerism must also occur at some stage. Examples of triphenylphosphine oxide behaving as a nucleophile have recently been reported.[6,7]

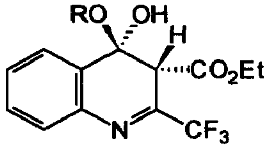
When amide **15**[8] was treated with phosphorane **1** in boiling toluene the only characterisable product was phosphorane **3** (21% yield) whose m.p. and ^{1}H NMR spectrum agreed with those reported[9]. This reaction involves trifluoroacetylation of phosphorane **1** by amide **15** giving phosphorane **2** and pentafluoroaniline. Nucleophilic attack at the ethoxycarbonyl group of phosphorane **2** presumably by pentafluoroaniline then occurs giving phosphorane **3** and urethane **16**, although we have not been able to isolate compound **16**.



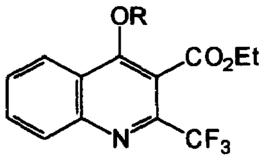
1; $R^1 = CO_2Et$, $R^2 = H$
2; $R^1 = CO_2Et$, $R^2 = COCF_3$
3; $R^1 = H$, $R^2 = COCF_3$



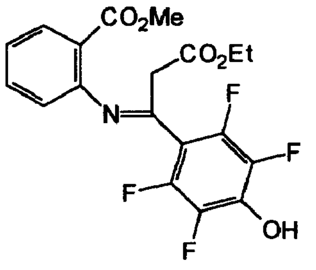
4; $R^1 = Me$, $R^2 = CF_3$, $X = O$
5; $R^1 = Me$, $R^2 = CF_3$, $X = CHCO_2Et$
6; $R^1 = Et$, $R^2 = CF_3$, $X = O$
7; $R^1 = Et$, $R^2 = CF_3$, $X = CHCO_2Et$
8; $R^1 = Me$, $R^2 = C_6F_5$, $X = O$
9; $R^1 = Me$, $R^2 = C_6F_5$, $X = CHCO_2Et$



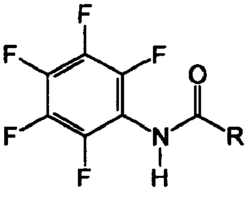
10; R = Me
11; R = Et



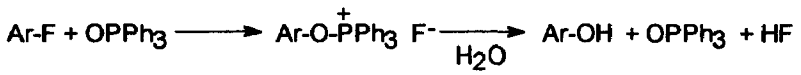
12; R = Me
13; R = Et



14



15; $R = CF_3$
16; R = OEt



$$\text{Ar-F} + \text{OPPh}_3 \longrightarrow \text{Ar-O-}\overset{+}{\text{P}}\text{Ph}_3\ \text{F}^- \xrightarrow[\text{H}_2\text{O}]{} \text{Ar-OH} + \text{OPPh}_3 + \text{HF}$$ Equation

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