1,4-ADDITION REACTIONS TO  $\alpha,\beta$  UNSATURATED TERTIARY AMIDES

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 $\frac{Summary}{1}: Ketones, phenylacetonitrile, ethylmalonate, cyanoethyl acetate, nitromethane$  $and nitroethane were found to add directely to <math>\alpha,\beta$ -unsaturated tertiary amides in the presence of CsF/Si(OMe)<sub>4</sub> to give 1,4-addition products in fair to good yields.

Examples of 1,4-additions of Grignard reagents to  $\alpha,\beta$ -unsaturated tertiary amides have been known for some time (1,2). The 1,4-addition of organolithium reagents has been the subject of more recent studies (2a, 3,4) but includes only one example of 1,4 addition reaction of lithium enolate to  $\alpha,\beta$ -unsaturated tertiary amides (4).

In previous studies (5,6), we have shown the efficiency of  $CsF/Si(OR)_4$  for Michael addition of ketones and phenylacetonitrile to  $\alpha,\beta$ -unsaturated ketones, esters and nitriles. Since Michael addition is recognized to be an useful method for carbon-carbon bond formation, we have extended our studies to the use of  $CsF/Si(OR)_4$  for promotion of 1,4-addition to  $\alpha,\beta$ -unsaturated tertiary amides and report the results of these investigations here in.

As demonstrated in Table I,  $CsF/Si(OR)_4$  allows direct Michael additions of compounds with active methylene group such as  $PhCH_2CN$ ,  $NCCH_2CO_2Et$  and  $CH_2(CO_2Et)_2$  as well as ketones,  $CH_3NO_2$  and  $CH_3CH_2NO_2$  to tertiary cinnamamide and crotonamides in fair to good yields. We observed no reaction when  $\beta,\beta$ -dimethylacrylamide (entries 13 and 14) is taken as the Michael acceptor even with an active methylene compound (entry 14). It is worth to note that the 1,5-difunctional product can be obtained in situ without hydrolysis.

The reaction of ethylcyanoacetate with crotonomorpholide illustrates the standard procedure : 20 mmol of  $CNCH_2CO_2Et$ , 20 mmol of crotonomorpholide and 10 mmol of  $Si(OMe)_4$  were added to 20 mmol of CsF under a nitrogen atmosphere. The well-stirred mixture was heated at 80°C. The course of the reaction was monitored by following the disappearance of the C = C stretch in the IR spectrum. When reaction was complete (1 hour), 50 ml of  $CH_2Cl_2$  were added to the mixture ; filtration on Hyflosupercel and evaporation gave the crude product. Recrystallization from ethanol-pentane gave the expected product (mp : 76-78°C) (7).

Nucleophilic activation of Si(OR)<sub>4</sub> by fluoride ion to give a basic species able to promote enolate formation is proposed to explain the observed results. This enolate would be rapidly silylated to the corresponding silyl enol ether. The salt-activated silyl

|                           | tions reaction product<br>T °C) isolated yield (%) (a) | 80 Dh CON(E1)2 (86)                 | $65 \begin{array}{ c c } Ph & CON(Ef)_2 & (92) \\ Ph & CN \\ Ph & CN \end{array}$ | 65 X CON (E1)2 (79)         | $\begin{array}{c c} & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & &$ | $\begin{array}{c c} & & \\ & &$ | 25 Ph CON 0 (81)                            | 65 2 2 CON 0 (50) |
|---------------------------|--|-------------------------------------|---|-----------------------------|---|---|---|-------------------|
| Cs F/ Si (0R)4            | reaction condi<br>t(h)                                 | ß                                   |   | 0.75                        | ۲   | F   | σ   | m                 |
| ary amides in presence of | Michael donor  | 0<br>  <br>(1eq)                    | Ph CH <sub>2</sub> CN (1eq )  | Ph CH <sub>2</sub> CN (1eq) | $CH_2 \sim \frac{CO_2 E^{\dagger}}{CN}$ (1eq)   | CH <sub>2</sub> (CO <sub>2</sub> Et) <sub>2</sub> (1eq)   | (Ph CH <sub>2</sub> ) <sub>2</sub> CO (1eq) | 0<br>(1 eq)       |
| ichael additions on terti | Michael acceptor                                       | Ph /// CON (E t) <sub>2</sub> (1eq) | (1eq)   | ✓✓>CON(Et) 2 (1eq)          | √CON0 (1eq)   | // (1eq)  | " (2eq)                                     | 1eq)              |
| Σ                         | entry  | -                                   | 2   | m                           | t   | ъ   | Q   | 7                 |

| 1               | (1eq)            | рь со сн <sub>з</sub>  | (1eq)                    | 7 8                      | Ph 2 CON        | 0(76)  |
|-----------------|------------------|--|--------------------------|--------------------------|-----------------|--------|
| 1               | (1eq)            | ∘=∕  | (1 eq)                   | 5 7                      |                 | 0 (75) |
| 1               | (1eq)            | ( CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> | CO (1eq)                 | 4                        |                 | (72)   |
| "               | (1eq)            | N 02 CH3   | (10 eq)                  | 32 8                     | 0 NO2 CON O     | (82)   |
|                 | (1eq)            | N02 CH2 CH3  | (5eq)                    | 74 8                     | 0 X CONC        | ( 14 ) |
| CON             | (1eq)            | Ph CO CH <sub>3</sub>  | (1eq)                    | 24 7                     | 0 no reaction   |        |
| 2               | (1eq)            | <sup>CH2</sup> CO2 Et  | (1eq)                    | 72 7                     | 0 no reaction   |        |
| the pr<br>R and | oducts<br>NMR) C | gave satisfactory<br>onsistent with th                           | elemental<br>neir struct | analysis and spe<br>ures | ectral data are |        |

enolether would promote formation of the 1,4-adduct from the  $\alpha$ , $\beta$ -unsaturated tertiary amide. This adduct would react in situ with the alcohol obtained to give the 1,5-difunctional compound.

The ability of  $\alpha$ , $\beta$ -unsaturated primary and secondary amides to function as Michael acceptors is the subject of further study.

## References and Footnotes

- E.P. Kohler and G. Heritage, J. Am. Chem. Soc., <u>33</u>, 21 (1905); N. Maxim and N. Ioanid, Bull. Soc. Chim. Romania, <u>10</u>, 29 (1928); N. Maxim, Ann. Chiu., <u>9</u>, 55 (1928); Bull. Soc. Chim. Romania, <u>10</u>, 97 (1928), <u>10</u>, 116 (1928); <u>11</u>, 123 (1930); N. Maxim and N. Ioanid, Bull. Soc. Chim. Romania, <u>12</u>, 28 (1930); N. Maxim and I. Zugravescu, Bull. Soc. Chim. Fr., <u>1</u>, 1087 (1934); G. Gilbert, J. Am. Chem. Soc., <u>77</u>, 4413 (1955).
- 2 a) G. Gilbert and F. Aycock, J. Org. Chem., 22, 1013 (1957), b) J. Klein, Tetrahedron, 20, 465 (1964); c) G. Daviaud and P. Miginiac, Tetrahedron Letters, 3251 (1971).

3 - J.E. Baldwin and W.A. Dupont, Tetrahedron Letters, 1881 (1980).

- 4 G.B. Mpango, K.K. Mahalanabis, Z. Mahdavi-Damghani and V. Snieckus, Tetrahedron Letters, 4823 (1980).
- 5 J. Boyer, R.J.P. Corriu, R. Perz and C. Reyé, J. Chem. Soc. Chem. Comm., 122 (1981).
- 6 J. Boyer, R.J.P. Corriu, R. Perz and C. Reyé, Tetrahedron (in press).
- 7 The spectroscopic data are the following : IR (CHCl<sub>3</sub>) cm<sup>-1</sup> 2260, 1745, 1640 ; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ : 1.1 (d, 3H), 1.3 (t, 3H) 2.4 (d, 2H) 2.88 (m, 1H) 3.6 (s, 8H) 4.2 (m, 3H). Analysis (Found C 57.93, H 7.58, N 10.43 ; Calc. for C<sub>13</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub> C 58.20, H 7.46 N 10.44).

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