HINDERED ORGANOBORON GROUPS IN ORGANIC SYNTHESIS. 13. THE DIRECT PRODUCTION OF KETONES FROM ALIPHATIC ALDEHYDES BY A UNIQUE VARIANT OF THE BORON-WITTIG REACTION

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Summary. In the presence of trifluoroacetic anhydride or *N*-chlorosuccinimide, aliphatic aldehydes react with dimesitylboron stabilised carbanions to give, after work up, the corresponding ketones, a process which is unique among Wittig type reactions. Yields of ketones are satisfactory in all cases except those involving the anion derived from the parent compound dimesitylmethylborane, which gives the corresponding alkenes.
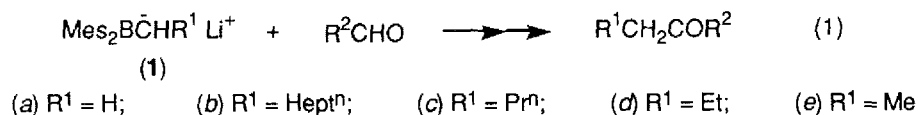
In previous studies[1,2,3] of the boron-Wittig reaction, we showed that condensations of dimesitylboryl stabilised carbanions with aromatic aldehydes may be controlled so as to yield *Z*- or *E*-alkenes[2] or *erythro*-1,2-diols.[3] The reaction thus exhibits a versatility which is unique amongst Wittig type reactions.

In a preliminary investigation we showed that aliphatic aldehydes react with (1a) to give alk-1-enes as expected.[1] We now report the surprising results of a systematic investigation of the reactions of carbanions (1) with aliphatic aldehydes.

We first used (1b), derived from dimesityloctylborane, and found that in the absence of a trapping agent there resulted a plethora of products, no one product being predominant. We had previously[2] used trifluoroacetic anhydride (TFAA) as a convenient trapping agent leading to *Z*-alkenes, and decided to use this reagent standardly in order to try to direct the reaction.

Using TFAA (process A) we found that aldehyde was rapidly consumed (exp. 2, 3) and intermediates were produced that were transformed, not into alkenes *but into ketones*, on passage through a silica column or by exposure to aqueous acid. The ketones were identified by their physical characteristics and by comparison with authentic samples.

We had thus inadvertently accomplished the unique condensation-redox reaction shown in equation (1)

$$\text{Mes}_2\text{B}\bar{\text{C}}\text{HR}^1\ \text{Li}^+\ +\ \text{R}^2\text{CHO}\ \longrightarrow\ \text{R}^1\text{CH}_2\text{COR}^2 \qquad (1)$$

$$(1)$$

(a) $R^1 = H$;   (b) $R^1 = Hept^n$;   (c) $R^1 = Pr^n$;   (d) $R^1 = Et$;   (e) $R^1 = Me$

Experiments 1 - 7 in Table 1 show that the condensation of (**1b**) with aliphatic aldehydes to give ketones is general. We also confirmed our preliminary results that (**1a**) condenses with aliphatic aldehydes to give alk-1-enes (exp. 17, 18, 19). We therefore investigated the reactions of carbanions (**1c**), (**1d**) and (**1e**) to check the effect of the chain length of R^1 upon the reaction.

When R^1 = Pr^n (**1c**) ketones are produced (exp. 8, 9, 10) as with (**1b**) and we assume that ketones are produced with all carbanions (**1**) in which R^1 is an *n*-alkyl group with chain length of C_3 or longer. However, the yields of ketones drop with (**1d**) (R^1 = Et) (exp. 11, 12) and are neglible with R^1 = Me or H (exp. 13, 17, 18, 19).

Of necessity, the process is a redox reaction in which TFAA is a hydride receptor. Hence, a more efficient oxidant than TFAA might encourage ketone formation for compounds (**1,a,d,e**). We chose *N*-chlorosuccinimide (NCS) as an oxidant compatible with the reactants and conditions and were encouraged to find (exp. 11 - 15) that indeed carbanions (**1d**) and (**1e**) do give ketones in acceptable yields by use of this reagent. Even an aromatic aldehyde gives some ketone with the unfavourable anion (**1e**) (exp. 16). With carbanion (**1a**), however, even NCS gives only 20-29% of ketone (exp. 17-19) and we are searching further for a method of converting (**1a**) into methyl ketones.

We are not certain of the reactions involved, but with TFAA, enol trifluoroacetates were produced in some cases (exp. 2,3). We are considering a process such as that shown in the Scheme, in which the enolborinate (**4**) is the primary product with both TFAA and NCS, and this is hydrolysed to ketone. With TFAA, the enoltrifluoroacetates (**5**) are produced in some cases and are also hydrolysed to ketones.
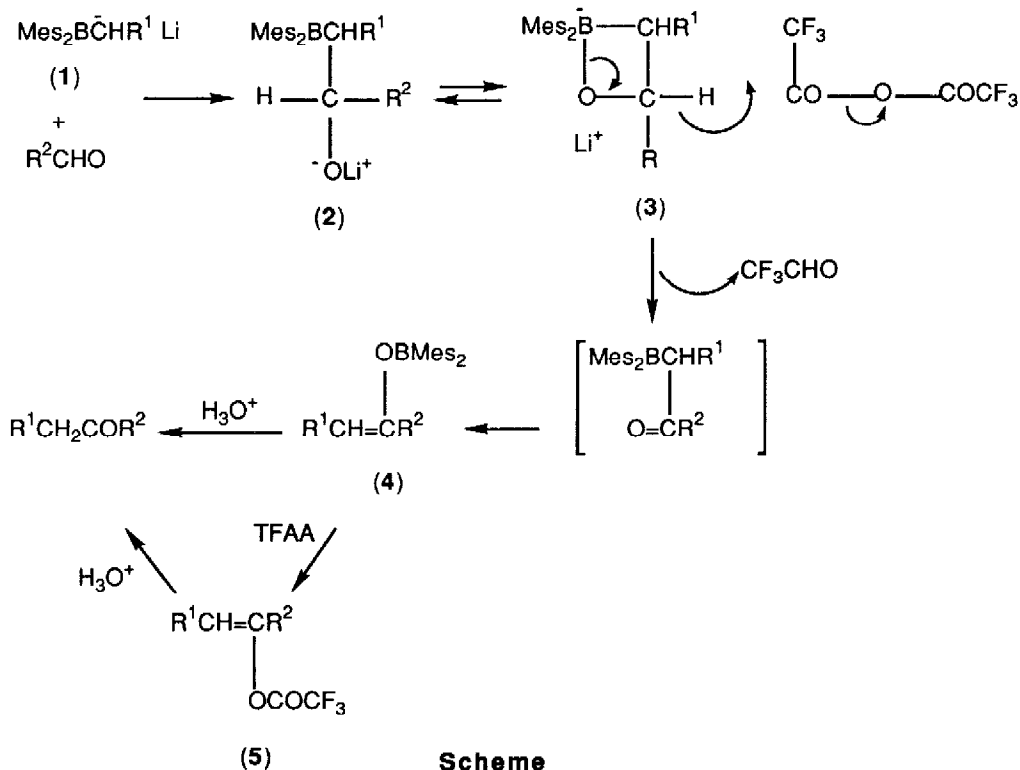
Scheme

TABLE 1
SYNTHESIS OF KETONES BY THE BORON-WITTIG REACTION

$$Mes_2\overset{-}{B}CHR^1 + R^2CHO \longrightarrow R^2COCH_2R^1$$
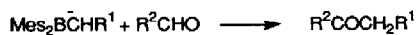
Exp. No.	R^1	R^2	Product	Yield(%)[a]	
				$A^{[b]}$	$B^{[c]}$
1	$Hept^n$	Me	$MeCO.Oct^n$	71	-
2	"	Et	$EtCO.Oct^n$	72	-
3	"	Hept	$Hept^nCO.Oct^n$	76	73
4	"	$Bu^nCH(Et)$	$Bu^nCH(Et)CO.Oct^n$	85	-
5	"	Bu^t	$Bu^tCO.Oct^n$	92	-
6	"	$Cp^{[d]}$	$CpCO.Oct^n$	89	-
7	"	$Chx^{[e]}$	$ChxCO.Oct^n$	78	-
8	Pr^n	$PhCH_2$	$PhCH_2COBu^n$	75	-
9	"	$Bu^nCH(Et)$	$Bu^nCH(Et)COBu^n$	87	-
10	"	Chx	$ChxCOBu^n$	82	-
11	Et	$PhCH_2$	$PhCH_2COPr^n$	41	72
12	"	$Bu^nCH(Et)$	$Bu^nCH(Et)COPr^n$	(41)	79
13	Me	$Hept^n$	$Hept^nCOEt$	0	72
14	"	$PhCH_2$	$PhCH_2COEt$	-	57
15	"	$Bu^nCH(Et)$	$Bu^nCH(Et)COEt$	-	68
16	"	Ph	$PhCOEt$	$0^{[f]}$	16
17	H	Hept	$HeptCOCH_3$	$0^{[f]}$	(28)
18	"	$Bu^nCH(Et)$	$Bu^nCH(Et)COCH_3$	$0^{[f]}$	21
19	"	Chx	$ChxCOCH_3$	$0^{[f]}$	(29)

a)Yields are of isolated, purified, fully characterised ketones except the g.c. yields given in parentheses. b)Aldehyde added and then 1.0-1.2 equiv. of TFAA. c)Aldehyde added and then 4.0 equiv. of NCS. d)Cp=Cyclopentyl. e)Chx=Cyclohexyl. f) Only alkene was isolated.

Discussion of the origin of the unusual effect of the length of the alkyl group on the nature of the process, is deferred. So is any discussion of the stereochemistry of intermediates (2) and (3) until we present the results[4] of our successful attempts to produce alkenes from (2). It suffices to note that the boron-Wittig reaction retains its ability to spring surprises and has yielded a unique and useful method of transforming aldehydes directly into ketones.

General procedure for the preparation of ketones by the boron-Wittig reaction

Reactions are carried out under nitrogen in a septum capped flask equipped with a spiral inlet arm, which is wholly immersed in the cooling bath and through which all additions are made by syringe or double-ended needle.[5]   Mesityl bromide (1.99g, 10 mmol) and THF (10 ml) are added to the flask at -78ºC and then Bu^t Li (9.5 ml, 2.1M in hexane, 20 mmol) added dropwise. The mixture is stirred for 15 min. and then allowed to warm to room temperature over 15 min.   A solution of the dimesitylalkylborane (Mes$_2$BR, 10 mmol) in THF (10 ml) at 25ºC is added and the mixture stirred for 1h (R = Me, Et) or 2h (R = Pr, Bu, Oct).   The deep-red solution is cooled to -127ºC and freshly distilled aldehyde (10 mmol) in THF (10 ml) precooled to -78ºC is added. The reaction is stirred at -127ºC for 1h and then a solution of TFAA (2.52g, 10 mmol) in THF (10 ml) at -78º is added and the mixture stirred for 1h at -127º and then allowed to warm to room temperature and stir for 18h.   Solvents are removed under vacuum, ether (30 ml) is added and the solution is washed with water (3 x 20 ml), dried (MgSO$_4$) and filtered.   The crude product is placed on a silica gel (230-400 mesh) column and eluted with light petroleum and dichloromethane.   Ketone is isolated from eluant consisting of 1% CH$_2$Cl$_2$: 99% light petroleum. The procedure for reaction involving NCS is entirely analogous.

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