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SAMARIUM DIIODIDE AS COUPLING AGENT BETWEEN ALDEHYDES AND ORGANIC HALIDES FOR THE SYNTHESIS OF HOMOALLYLIC AND HOMOBENZYLIC ALCOHOLS

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Summary
Many aliphatic aldehydes are transformed into secondary alcohols by reaction with allyl halides or benzylic halides in presence of SmI_2.

We have shown that various organic halides react with ketones in presence of SmI_2 to give tertiary alcohols after hydrolysis (1,2). This reaction could not be extended to the synthesis of secondary alcohols by using aldehydes instead of ketones. The reason is that the secondary samarium alkoxide once produced, rapidly gives a Meerwein-Ponndorf reaction with the aldehyde. We have now found that this side reaction can be avoided in the case of organic halides which are reactive enough to suppress further consecutive reactions.

A fast reaction (between a few seconds and five minutes) occurs at room temperature when an aliphatic aldehyde is mixed with allyl iodide or various benzylic bromides in THF solution. This is exemplified by the following experiment :

Cyclohexanecarboxaldehyde (560 mg, 5 mmole) and benzyl bromide (855 mg, 5 mmole) dissolved in 10 ml of THF were added under nitrogen to 100 ml of 0.1 M SmI_2 in THF (10 mmole) at room temperature. After stirring for 2 minutes the typical colour of SmI_2 had disappeared.

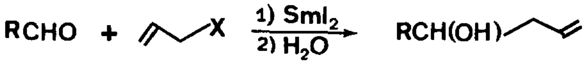
Hydrolysis by 0.1 N HCl, ether extraction and washing with sodium thiosulfate and saturated NaCl solution gave after distillation 800 mg of pure 1-cyclohexyl 2-phenyl-ethanol (78 % yield) identified by nmr, glc, IR and microanalysis.

Representative results are indicated in Tables I and II. Every time the yield of secondary alcohol is low, pinacol formation from the aldehyde is the major competitive process. The main limitation of the method is the lack of regioselectivity with dissymetric allylic halides (3), as found in the condensation on ketones (1). It is also not compatible with the presence of a free carboxyl group and does not work with aromatic aldehydes (which give rise to faster pinacol formation (4)).

Nevertheless, this new method can be favourably compared to some known processes (5-10), because of its smoothness and rapidity in many cases and because it tolerates various functional groups (cyano or ester groups for example). It is also interesting to point out the two following cases : on the one hand, benzyl bromide and acetaldehyde give in 36% yield a carbinol which cannot easily be obtained by the classical Grignard reaction (11) ; on the other hand, propargyl bromide, whose organometallic derivatives are not easily available, can be coupled with octanal (12).

Table I

Reaction of aldehydes and allylic halides in presence of SmI_2 [a]



R	X	Yield[b], (reaction time)[c]	R	X	Yield[b], (reaction time)[c]
n-C_7H_{15}	I	96% (3 min.)	cyclohexyl	Cl	6% (4-5 h)
n-C_7H_{15}	Br	53% (10 min.)	i-Pr	I	71% (1 min.)
n-C_7H_{15}	OTs[e]	17% (25 min.)	i-Pr	Br	28% (1 h)
n-C_7H_{15}	Cl	10% (6 h)	i-Pr	OTs[e]	10% (1·5 h)
cyclohexyl	I	85% (2 min.)	i-Pr	Cl	4% (2 days)
cyclohexyl	Br	54% (6 min.)	t-Bu	I	78%[d,f] (5 min.)
cyclohexyl	OTs[e]	11% (50 min.)			

[a] 1 mmole of each reactant, 2 mmole of SmI_2 in 25 ml THF under nitrogen, at room temperature For other details see the text.

[b] Yields measured on the crude product by glc using a suitable internal standard.

[c] Measured by the change of colour from deep blue-green (Sm^{2+}) to yellow (Sm^{3+}).

[d] Isolated yield on a 5 mmole scale.

[e] For preparation of allylic and benzylic tosylates, see (13).

[f] Purified by distillation of the liquid carbinol.

Table II

Reaction of aldehydes and benzylic halides in presence of SmI_2 [a]

$$RCHO + ArCH_2X \xrightarrow[2)\,H_2O]{1)\,SmI_2} RCH(OH)CH_2Ar$$

R	X	Ar	Reaction time [c]	Yield [b]
n- C_7H_{15}	Br	C_6H_5	2.5 min.	86 %
n-C_7H_{15}	Cl	C_6H_5	1.1 h	23 %
i-Pr	Br	C_6H_5	3 min.	87 %
i-Pr	Cl	C_6H_5	1.7 h	25 %
cyclohexyl	Br	C_6H_5	3 min.	78 % [d,f]
cyclohexyl	Cl	C_6H_5	2.1 h	21 %
n-C_7H_{15}	Br	p-NCC_6H_4	1 min.	41 % [d,g]
n-C_7H_{15}	Br	p-$(CO_2Ph)C_6H_4$	20 min.	75 %
n-C_7H_{15}	Br	p-$(CO_2H)C_6H_4$	3 days	0 % [h]
n-C_7H_{15}	OTs [e]	C_6H_5	-	0 % [i]
CH_3	Br	C_6H_5	1.5 min.	36 % [d,j]

[a,b,c,d,e] See corresponding notes in Table I.

[f] Recrystallisation in ether ; mp = 39°C.

[g] Purification of the product by recrystallisation in cyclohexane/ethyl acetate (80/20) ; mp = 78°C.

[h] In this case, pinacol formation occurs for the aldehyde and reduction to 4-methyl benzoic acid for the bromide.

[i] The blue colour of SmI_2 does not completely disappear. 1-octanol, resulting from reduction of octanal, was identified by glc.

[j] Purification of the product by preparative tlc with acetone/$CHCl_3$ (4/96) as eluent.

Acknowledgements

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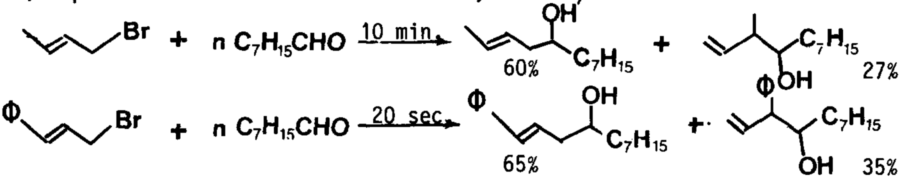
(3) Concerning crotyl and cinnamyl bromides, we obtained the following results (room temperature, experimental conditions as in note a, Table I) :



(4) The behaviour of aldehydes alone in SmI_2 solution has been studied. Pinacol formation from aliphatic aldehydes is a slow process but aromatic aldehydes are very rapidly transformed into corresponding pinacols (paper in preparation).

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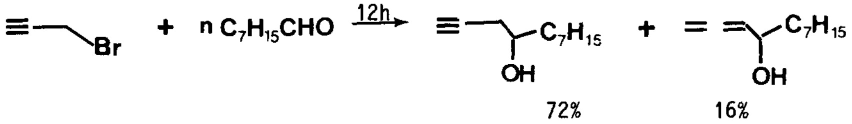
(12) At room temperature (according to conditions of note a, Table I) the results were :



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