

REACTIONS OF ACYL ANIONS GENERATED FROM ACID CHLORIDES AND DIIODOSAMARIUM

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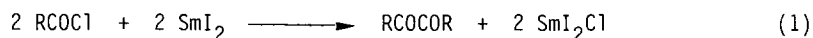
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Abstract

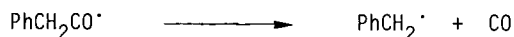
Acid chlorides react with SmI_2 to give α -diketones. Various experiments show that the initially formed acyl radical is rapidly transformed into an acyl anion which is thus generated by quite an unusual route.

This species acylates acid chlorides, aldehydes and ketones in situ to give α -diketones and α -ketols. There are some limitations to this acyl anion chemistry but the reactions are realized with a good efficiency at room temperature in THF solution.

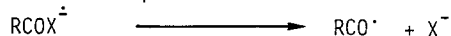
We recently described¹ a new method for the formation of symmetrical α -diketones, using SmI_2 ² as the coupling agent :



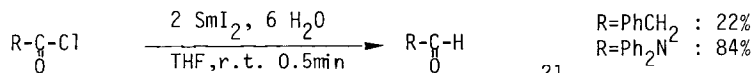
We wish to report results of a mechanistic investigation of this reaction giving support to an acyl anion precursor, and new synthetic developments. Several pathways (a-d, Scheme 1)⁴ can be proposed for reaction (1). In order to gain insight into the mechanism, the reaction between phenylacetyl chloride and SmI_2 was studied. The corresponding acyl radical is known for its rapid decarbonylation^{6a,b} so that this substrate is often used to test for the intermediacy of acyl radical⁷⁻¹⁰:



In a first experiment, a THF solution of PhCH_2COCl was poured into a THF solution of SmI_2 , and the α -diketone $\text{PhCH}_2\text{COCOCH}_2\text{Ph}$ was isolated in 46% yield¹¹. No trace of $\text{PhCH}_2\text{CH}_2\text{Ph}$ could be detected. In a second experiment, a THF solution of SmI_2 was poured into a THF solution of PhCH_2COCl , slowly enough to avoid the persistence of the blue color of SmI_2 . $\text{PhCH}_2\text{CH}_2\text{Ph}$ could then be identified by comparison with authentic samples (19% yield)¹⁴. The latter experiment allows us to exclude pathways where the radical anion $\text{PhCH}_2\text{COX}^{\cdot-}$ would react with PhCH_2COX . Moreover, electrochemical results¹⁵ and ESR studies of the γ -radiolysis of acid halides¹⁶ lead most authors to suggest that the process :



is very rapid. Consequently, pathways (a) and (d) (Scheme 1) can also be excluded. Thus the radical $\text{PhCH}_2\text{CO}\cdot$ is an intermediate in the reaction. The first experiment shows that, in a reductive medium, this radical does not decarbonylate. Considering that coupling of acyl radicals (pathway (b), Scheme 1) is not a very common process¹⁷, it is tempting to speculate that a fast reduction of $\text{PhCH}_2\text{CO}\cdot$ to give the corresponding acyl anion, bound to SmI_2^+ (pathway (c), Scheme 1) takes place. Good support for this hypothesis is the trapping of the RCO^- species by H_2O , giving RCHO :



R=PhCH₂ : 22%
R=Ph₂N⁺ : 84%

Because of the potential of nucleophilic acylation in organic synthesis²¹, we performed various experiments involving the reaction of SmI₂ with a 1:1 mixture of an acid chloride and a second electrophile. We found that in the case of aldehydes or ketones, α-hydroxy ketones are obtained after hydrolysis; the formation of these can be interpreted as involving a nucleophilic acylation. A typical procedure is as follows: 90.3 mg of pivaloyl chloride (0.75 mmol) and 44 mg of propionaldehyde (0.75 mmol) are dissolved under nitrogen in 5 ml of dry THF. The mixture is then added, at room temperature, to 15 ml of a 0.1 M SmI₂ solution in THF (1.5 mmol). Decoloration occurs within 4 min. The usual work up³ gives 69 mg of 2,2-dimethyl 4-hydroxy 3-hexanone (64% yield). The results are collected in Table. We stress that our method requires in situ trapping. In the absence of the second electrophile, the precursor acid chloride is itself acylated²². Up to now, acyl anion chemistry involved either deprotonation by strong bases²³ or organolithium carbonylation²⁴ at low temperatures. Our approach is quite different since the acyl anion is the result of a reductive process. Due to the strong reducing power of SmI₂, we succeeded in our attempt to realize a direct carbonyl "Umpolung"^{25,26} by way of electron transfer. We are currently looking at other electrophiles able to trap the acyl anions generated from acid chlorides and SmI₂.

Scheme 1

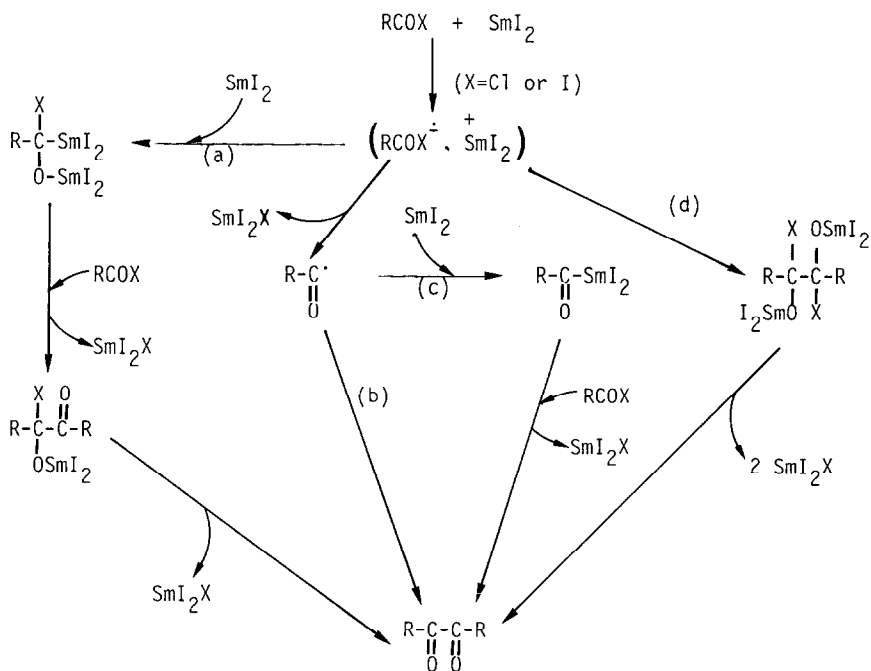


Table : Reduction of Acid Chlorides by SmI_2 in the presence of Aldehydes or Ketones^a

$$\text{RCOCl} + \begin{array}{c} \text{R}_1 \backslash \\ \text{C}=\text{O} \\ / \text{R}_2 \end{array} \xrightarrow[2) \text{H}_3\text{O}^+]{1) 2 \text{SmI}_2} \begin{array}{c} \text{R}_2 \\ | \\ \text{R}-\text{C}-\text{C}-\text{R}_1 \\ || \quad | \\ \text{O} \quad \text{OH} \end{array}$$

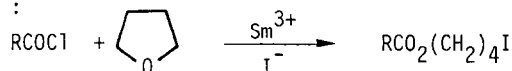
R	R ₁	R ₂	Reaction time ^b	Yield (%)
Ph	<i>n</i> -C ₇ H ₁₅	H	0.5 min	46 ^c
Ph	Ph	H	0.5 min	86 ^d
Ph	Ph	CH ₃	0.5 min	34 ^c
Ph	C ₂ H ₅	C ₂ H ₅	0.5 min	64 ^c
Ph	CH=C(CH ₃) ₂	CH ₃	0.5 min	66 ^{c,e}
<i>n</i> -C ₈ H ₁₇	Ph	H	3 min	27 ^{c,f}
<i>n</i> -C ₈ H ₁₇	C ₂ H ₅	H	1.5 min	63 ^{c,g}
<i>n</i> -C ₈ H ₁₇	Ph	CH ₃	0.5 min	35 ^d
<i>t</i> -Bu	C ₂ H ₅	H	4 min	64 ^d
<i>t</i> -Bu	C ₂ H ₅	C ₂ H ₅	3 min	83 ^c
<i>t</i> -Bu	Ph	CH ₃	2 min	36 ^c
<i>t</i> -Bu	CH=C(CH ₃) ₂	CH ₃	1 min	47 ^{c,h}
PhCH ₂	Ph	H	5 min	48 ^d
Ph ₂ N	<i>n</i> -C ₇ H ₁₅	H	40 min	67 ^d
Ph ₂ N	C ₂ H ₅	C ₂ H ₅	45 min	21 ^{c,i}

a) 1 mmol of each reactant, 2 mmol of SmI_2 in 25 ml THF under nitrogen, at room temperature. For details, see the text. b) Measured by the change of color from deep blue green (Sm^{2+}) to yellow (Sm^{3+}). c) Yields determined by GLC and ¹H NMR. All products gave mass spectra and ¹H NMR spectra in agreement with the structure. d) Isolated yield. e) Only 4% of 1,4-addition product could be detected. f) The keto isomer *n*-C₈H₁₇CH(OH)COPh was also obtained in 27% yield. g) The keto isomer *n*-C₈H₁₇CH(OH)C₂H₅ was obtained in 17% yield. h) No 1,4-addition could be observed. i) Other products: Ph₂NH (43%); HCONPh₂ (4%).

References and Notes

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- It is known⁵ that acyl iodides can be prepared from acyl chlorides. Because of the presence of a stoichiometric amount of SmI_2 , acyl iodides may be formed. We have not investigated whether such exchange occurs and whether the initial electron transfer of Scheme 1 occurs towards RCOCl or RCOI.
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- PhCH₂CO₂(CH₂)₄I was also isolated in 50% yield¹².
- A competitive process of ester formation from THF attack on the acid chloride (similar

reactions are known¹³) may happen :



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Experiments are difficult to reproduce (according to ref.25, footnote p.641).

Acknowledgments

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