Organic Chemistry

Some features of an SmI_2 -(Me₂N)₃P-THF system. Transformation of esters into dimethylamides

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 Sm^{i1} -intermediates generated upon addition of $(Me_2N)_3P$ to a solution of SmI_2 in THF exhibit the properties of a single-electron reducing agent and an N-nucleophile. In particular, N, N-dimethylamides are formed from esters.

Key words: esters, samarium diiodide, tris(dimethylamino)phosphine, nucleophilic addition, N, N-dimethylamides.

An ether-soluble single-electron reducing agent Sml₂¹ is widely used for synthetic purposes.^{2,3} In THF, Sml₂ readily generates radicals from halogen derivatives, aldehydes, and ketones, which can be captured by olefinic or other appropriate groups. Organosamarium intermediates formed from Sml₂ can be involved in the Barbier, Reformatskii, and similar reactions. Sml2 is an attractive reagent because, first of all, its reactions can be carried out under mild conditions and are highly chemo- and stereoselective. In some cases, multi-step "one-pot" transformations of substrates can be performed, which is extremely important in design of effective strategies for the synthesis of complex natural compounds. The instability (>-50 °C) of organosamarium intermediates derived from Sml₂ and organic iodides and bromides limits the use of the reagent. This drawback is eliminated if SmCp₂ (Ref. 4) and Sm(OTf)₂/LiOTf (Ref. 5) in THF are employed or if THF is replaced by tetrahydropyran (THP). In particular, allyl and benzyl organosamarium derivatives of SmI_2 are stable in THF at 0 to -15 °C.⁶ lt should also be noted that the reducing ability of $\mbox{Sm}\mbox{I}_2$ in THF is not always sufficient for efficient generation of carbon-centered radicals.^{2,3} The reducing ability of SmI_2 -THF is enhanced in the presence of (Me₂N)₃PO⁶ and other strong electron-donating N-ligands (DBU, TMG, or NEt₃).7

While studying reactions of allenvlcyclopentenones (1) and (2) with SmI_2 in THF in the presence of (Me₂N)₃PO, we faced the problem of the reactivity of SmI₂. Mollander et al. widely used this system for intramolecular cyclizations of various functionalized ω -enones.^{8,9} In our case, however, cyclopentenones 1 and 2 were recovered unchanged when treated with an Sm1,-(Me₂N)₃PO-THF system. The situation changes radically when the amide component $((Me_2N)_3PO)$ of the above system is replaced by (Me₂N)₃P. The starting compound 1 is rapidly consumed to produce the expected cyclization product, viz., functionalized derivatives of cycloocta-2,6-dienone.¹⁰ These results provide unambiguous evidence for the formation of a stronger reducing system than the known ones. Taking into account a probable exchange reaction between Sml2 and $(Me_2N)_3P$, its active intermediates are organosamarium(II) compounds of type 3.



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The latter, unlike SmI, and the aforesaid biscyclopentadienyl, triflate, and ligand-type donor-acceptor complexes of SmI₂ with (Me₂N)₃PO and amines (for the structure of a complex of SmI₂ with (Me₂N)₃PO see Ref. 11), contain a Sm-bonded Me₂N substituent. For this reason, a certain dualism can be expected as regards the chemical behavior of 3, i.e., these species can react with carbonyl compounds not only as singleelectron reducing agents but also as rather strong nucleophiles according to a 1.2-addition scheme. To prove this assumption, we studied reactions of 3 with esters. Esters are known to be stable in an Sml_2 -(Me₂N)₃PO-THF system.^{2,3} Our experiments showed that in an SmI₂-(Me₂N)₃P-THF system esters (4) are smoothly transformed into the corresponding N, Ndimethylamides (5). Under similar conditions, dimethyl adipate (6) also gives bisdimethylamide (7). Note that in the absence of SmI₂ esters do not react with (Me₂N)₃P under the experimental conditions (THF, 20-50 °C) (for reactions of (Me₃N)₃P with acids, activated esters, and acid anhydrides, see Refs. 12 and 13).

Scheme 1



A plausible pathway of the formation of amides includes 1,2-addition of an "Me₂N-Sm" reagent to the carbonyl group of the ester and subsequent fragmentation of a tetrahedral intermediate (8), as shown in Scheme 2.

Scheme 2



Hence, one can assume that the amidation of esters in an $\text{Sml}_2-(\text{Me}_2\text{N})_3\text{P}-\text{THF}$ system involves intermediates with an $\text{Me}_2\text{N}-\text{Sm}$ bond whose nucleophilicities are sufficient for 1,2-addition to the ester group. At the same time, it is also obvious that the aforementioned intramolecular cyclization of 1 under the action of $\text{Sml}_2-(\text{Me}_2\text{N})_3\text{P}$ can occur only through the formation of the corresponding ketyl radicals. Apparently, in this case, steric factors are of primary importance: the formation of intermediate tetrahedral complexes of 1.2addition is hindered, and Sm intermediates 3 function as stronger single-electron reducing agents than Sml₃.

Experimental

IR spectra were recorded on UR-20 and Specord-80 spectrometers (thin film). ¹H and ¹³C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75 MHz, respectively) in CDCl₃ with Me₄Si as the internal standard.

Transformations of esters in an SmI₂--(Me₂N)₃P--THF system (general procedure). (Me₂N)₃P (1.63 g, 10 mmol) was added to a solution of SmI₂ (prepared from powdered Sm (0.46 g, 3.04 mg-at.) and CH₃I₂ (0.74 g, 2.76 mmol)) in 25 mL of anhydrous THF (20 °C, 2 h) in an atmosphere of argon. The reaction mixture was stirred for 0.5 h and cooled to 0 °C. A solution of ester 4 (1.25 mmol) in 25 mL of THF was added with stirring over 1.5 h, and stirring was continued at 20 °C for 0.5 h. The reaction mixture was quenched with 5 mL of a saturated solution of NaHCO₃ and the reaction products were extracted with EtOAc (3×15 mL). The combined organic extracts were washed with water and brine, dried with MgSO₄, and concentrated. The residue was chromatographed on SiO₂ (benzene--ethyl acetate, 7 : 3).

N,N-Dimethylarachidonamide (5a). Yield 72%, oil. Found (%): C, 79.53; H, 10.98; N, 3.96. $C_{22}H_{37}$ NO. Calculated (%): C, 79.70; H, 11.25; N, 4.23. IR, v/cm⁻¹: 1648 (C=O). ¹H NMR, δ : 0.84 (t, 3 H, Me, J = 6.2 Hz); 1.20–1.50 (m, 6 H, 3 CH₂); 1.67 (m, 2 H, CH₂); 2.0–2.18 (m, 4 H, 2 CH₂); 2.28 (t, 2 H, CH₂, J = 7.24 Hz); 2.70–2.80 (br.s, 6 H, 3 CH₂); 2.90 and 2.95 (both s, 6 H, NMe₂); 5.33 (br.s, 8 H, 4 CH=CH). ¹³C NMR, δ : 13.92 (CH₃); 22.39 (C(19)); 24.73 (C(3)); 25.45 (C(7), C(10), C(13)); 26.60 (C(4)); 27.02 (C(16)); 29.14 (C(17)); 31.32 (C(18)); 32.44 (C(2)): 117.33, 127.67, 127.91, 128.05, 128.34, 128.39, 129.23, 130.26 (4 CH=CH); 172.74 (C(1)).

N,*N*-Dimethylundec-10-enamide (5b). Yield 66%, oil. Found (%): C, 74.01; H, 12.08; N, 6.49. $C_{13}H_{25}NO$. Calculated (%): C, 73.88; H, 11.92; N, 6.63. 1R, v/cm⁻¹: 1675. ¹H NMR, δ : 1.18 (s. 10 H, 5 CH₂); 1.5 (t, 2 H, CH₂, J = 5.1 Hz); 1.91 (m, 2 H, CH₃); 2.25 (t, 2 H, CH₂-<u>CH</u>, J = 7.4 Hz); 2.81 and 2.88 (both s, 6 H, N(Me)₂); 4.78-4.89 (m, 2 H, <u>CH₂=CH</u>); 5.60-5.74 (1 H, CH=CH₂). ¹³C NMR, δ : 24.88, 28.63, 28.80, 29.06, 29.16, 33.07, 35.51 (8 CH₂); 34.98 and 36.97 (NMe₃); 113.84 and 138.79 (CH=CH₂); 172.87 (CO).

N,N-Dimethylhexanamide (5c) (yield 72%, oil) was identified with an authentic sample by GLC and TLC.

Bis(*N*,*N*-dimethyl)adipamide (7). Yield 60%, oil. Found (%): C, 60.15; H, 9.95; N, 14.29. $C_{10}H_{20}N_2O_2$. Calculated (%): C, 59.97; H, 10.07; N, 13.97. IR, v/cm⁻¹: 1675. ¹H NMR, δ : 1.58 (m, 4 H, 2 CH₂); 2.30 (m, 4 H, 2 CH₂); 2.85 (s, 6 H, 2 CH₃); 3.0 (s, 6 H, 2 CH₃). ¹³C NMR, δ : 24.52 (2 C): 32.35 (2 C); 34.08 (N-Me); 36.12 (N-Me); 172.77 (C=O).

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