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# Catalytic Barbier-type reactions of lactones and esters mediated by the Mischmetall/$SmI_{2(cat.)}$ system or the Mischmetall/$[SmI_2/NiI_{2(cat'.)}]_{(cat.)}$ system

Marie-Isabelle Lannou, Florence Hélion and Jean-Louis Namy*

*Laboratoire de Catalyse Moléculaire, associé au CNRS, ICMO, Bat 420, Université Paris-Sud, 91405, Orsay, France*

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**Abstract**—Barbier-type reactions using $SmI_2$ in catalytic amounts together with Mischmetall as a coreductant, involving lactones or esters and a variety of organic halides (allylic, benzylic and alkyl), have been performed. With alkyl halides and five- or six-membered ring lactones, catalytic quantities of nickel diiodide (with respect to $SmI_2$) must be added to achieve reactions. Thus, a 'two-stage catalysis' is carried out. Unexpectedly, it was found that with esters or an unstrained lactone the Mischmetall/$SmI_2$ (catalytic) system is more reactive than samarium diiodide in stoichiometric amounts. Tentative interpretations of the catalytic role of $NiI_2$ are proposed. © 2002 Elsevier Science Ltd. All rights reserved.

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## 1. Introduction

We have recently reported that Mischmetall is an efficient coreductant in samarium diiodide-catalysed reactions. With the Mischmetall/$SmI_2$ (catalytic) system, Barbier-type reactions have been achieved according to a catalytic Barbier procedure (**Catalytic-BP**).[1] Sequential reactions could also be achieved in the presence of this system and allylic or benzylic halides with ketones aldehydes or esters. In that case the procedure can be termed a catalytic Grignard procedure (**Catalytic-GP**).[2] Besides, it has been shown that lactones and esters are poor electrophiles in stoichiometric samarium diiodide-mediated reactions.[3] However, Barbier-type reactions involving lactones or esters and alkyl halides yield the expected products in the presence of small amounts of nickel diiodide (1 mol% with respect to $SmI_2$) (Scheme 1).[4]

This experimental process can be termed a $NiI_2$-catalysed Barbier procedure (**BP/$NiI_{2(cat.)}$**).

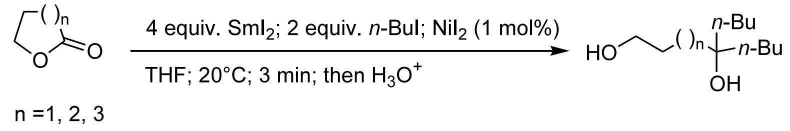
Recently, $SmI_2$ in the presence of catalytic amounts of $NiI_2$ has also been used to promote intramolecular conjugate additions of alkyl halides onto α,β-unsaturated lactones.[5]

Here we report some Barbier-type reactions of lactones or esters performed with samarium diiodide in catalytic amounts together with Mischmetall as the coreductant.

## 2. Results and discussion

We first studied reactions of lactones with activated halides (allyl bromide and benzyl bromide) mediated by the Mischmetall/$SmI_2$ (catalytic) system using a **Catalytic-BP** and readily observed the formation of diols. The results are collected in Table 1.

Yields of diols[7] were good or excellent, except with coumarin (entries 7 and 8) and 5*H*-furan-2-one (entry 11), which gave a mixture of unidentified by-products



**Scheme 1.**

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*Keywords*: Barbier reactions; catalysis; lactones; nickel diiodide; mischmetall; samarium diiodide.

* Corresponding author. Fax: +33-1-69-15-4680; e-mail: jelonamy@icmo.u-psud.fr

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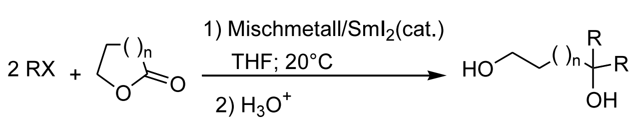
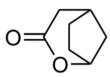
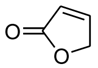
**Table 1.** Catalytic Barbier-type reactions of lactones with activated halides[6]



| Entry | RX | Electrophile | Product: yield (%)[a] |
|---|---|---|---|
| 1 | AllylBr | γ-Butyrolactone | 72 |
| 2 | BenzylBr | γ-Butyrolactone | 78 |
| 3 | AllylBr | ε-Caprolactone | 78 |
| 4 | BenzylBr | ε-Caprolactone | 72 |
| 5 | AllylBr | Dihydrocoumarin | **1**: 88 |
| 6 | BenzylBr | Dihydrocoumarin | 95 |
| 7 | AllylBr | Coumarin | **2**: 20 |
| 8 | BenzylBr | Coumarin | 0 |
| 9 | AllylBr |  | **3**: 42 |
| 10 | BenzylBr | ″ | 90 |
| 11 | AllylBr |  | **4**: 13 |

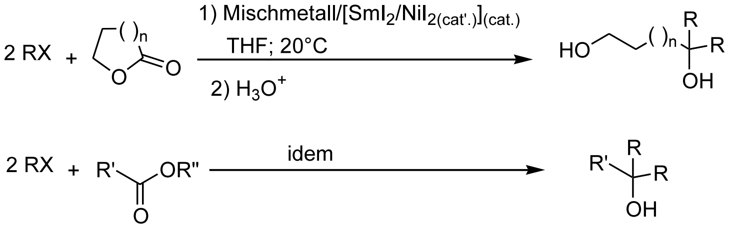
[a] Isolated yields.

(in reaction between coumarin and benzyl bromide, the main product was dibenzyle obtained in 15% yield). In the absence of samarium diiodide, the starting materials were recovered unchanged, indicating that reactions are not mediated by lanthanide metals. Nickel diiodide was not required for these reactions. This feature is not really surprising, since it is well known that allylic and benzylic halides are very reactive in samarium diiodide-mediated Barbier-type reactions. Next, we examined the reactions of the less active alkyl halides. We anticipated a catalytic amount of $NiI_2$ (with respect to $SmI_2$) would be necessary. Therefore, the Mischmetall/[$SmI_2$/$NiI_{2(cat'.)}$]$_{(cat.)}$ system was used in a catalytic Barbier procedure catalysed with $NiI_2$ (**Catalytic-BP/NiI$_{2(cat.)}$**) and compared to the Mischmetall/$SmI_{2(cat.)}$ system in a catalytic Barbier procedure (**Catalytic-BP**).

The results are collected in Table 2.

We checked that both Mischmetall alone and Mischmetall in the presence of nickel diiodide (without $SmI_2$) were unreactive in the reactions indicated above. In several cases (entries 1, 3, 8 and 10) minor amounts of diols[7] (6–30%) resulting from the addition of a THF moiety onto lactones were detected (Scheme 2).

**Table 2.** Catalytic Barbier-type reactions of lactones or esters with alkyl halides



| Entry | Electrophile | RX | Product: yield (%)[a] | |
|---|---|---|---|---|
| | | | Catalytic-BP[b] | Catalytic-BP/NiI$_{2(cat.)}$[c] |
| 1 | β-Propiolactone | 1-Iodoheptane | 37[d] | 47[d] |
| 2 | δ-Butyrolactone | 1-Iodoheptane | 0 | 83 |
| 3 | δ-Butyrolactone | 1-Iodododecane | 0[e] | 71[f] |
| 4 | δ-Valerolactone | 1-Iodoheptane | 0 | 66 |
| 5 | Coumarin | 1-Iodoheptane | 0 | 0 |
| 6 | Dihydrocoumarin | 1-Iodoheptane | 0 | **5**: 80 |
| 7 | Dihydrocoumarin | Iodoethane | 0 | 60 |
| 8 | Dihydrocoumarin | 1-Iodododecane | 0[e] | 78[g] |
| 9 | ε-Caprolactone | 1-Iodoheptane | 91 | 68 |
| 10 | ε-Caprolactone | 1-Iodododecane | 80[h] | 48[i] |
| 11 | Ethyl benzoate | 1-Iodoheptane | 74 | 78 |
| 12 | *tert*-Butyl acetate | 1-Iodoheptane | 70 | 72 |
| 13 | Ethyl *iso*-butyrate | 1-Iodoheptane | 76 | 81 |

[a] Isolated yields.

[b] For the experimental procedure, see Ref. 6.

[c] For the experimental procedure see Ref. 6, except that before addition of an alkyl halide, $NiI_2$ (0.035 mmol) in THF (3.5 mL) was added and the mixture was then stirred for 10 min.

[d] 3-(Tetrahydrofuran-2-yl)-decane-1,3-diol: (**6**) was also obtained in 30% yield.

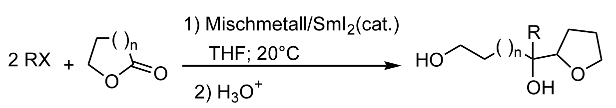
[e] Wurtz coupling of iodododecane occurred.

[f] 4-(Tetrahydrofuran-2-yl)-hexadecane-1,4-diol: was also obtained in 14% yield.

[g] 2-[3-Hydroxy-3-(tetrahydrofuran-2-yl)-pentadecyl]-phenol was also obtained in 15% yield.

[h] 6-(Tetrahydrofuran-2-yl)-octadecane-1,6-diol was also obtained in 6% yield.

[i] 6-(Tetrahydrofuran-2-yl)-octadecane-1,6-diol was also obtained in 12% yield.



**Scheme 2.**

The results (entries 2–8) obtained with the five- or six-membered ring lactones were in good agreement with the expectations since good yields in diols[7] were obtained with nickel diiodide, whereas in the absence of this catalyst, starting materials were recovered unchanged. Thus, this 'double-stage catalysis' is efficient in those cases. In contrast, with β-propiolactone, the diol was obtained as well in **Catalytic-BP** and **Catalytic-BP/NiI$_{2(cat.)}$**. However, due to the strain on the cycle, it is known that this lactone reacts in a peculiar way in the presence of lanthanide salts.[8] More unexpectedly, the diols were obtained with ε-caprolactone in excellent yield in the absence of nickel diiodide. It was thus anticipated that esters should behave as this unstrained lactone. This was confirmed by the results reported in entries 11, 12 and 13: good yields in tertiary alcohols were obtained in both procedures. Thus, with ε-caprolactone and esters the catalytic Barbier procedure does not require the presence of nickel diiodide, while the stoichiometric Barbier procedure demands it. These results are difficult to explain, since the precise part of NiI$_2$ in samarium diiodide-mediated reactions has not been cleared up. However, the following hypotheses can be proposed.

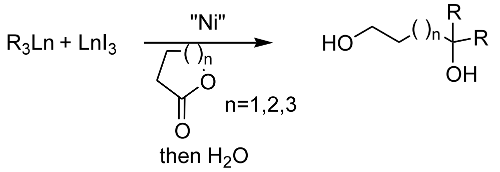
In **BP** (SmI$_2$ in stoichiometric amounts, without NiI$_2$), an organosamarium reagent is slowly produced. Due to its low reactivity towards esters and lactones, it reacts preferentially with the solvent (THF) giving a hydrocarbon and the expected alcohol does not form.

In **BP/NiI$_{2(cat.)}$** (SmI$_2$ in stoichiometric amounts, in the presence of NiI$_2$ in catalytic amounts), NiI$_2$ (or another nickel derivative which could result from a reaction with SmI$_2$) accelerates the formation of an organosamarium reagent as well as facilitating its addition onto esters or lactones (Scheme 3).

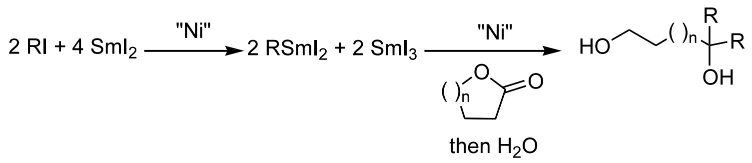
In **Catalytic-BP** (Mischmetall with SmI$_2$ in catalytic amounts), an organosamarium reagent is initially produced (along with SmI$_3$). Its reaction with a lanthanide metal (Ln = Ce, La, Nd, Pr) regenerates SmI$_2$ and furnishes another organolanthanide species, which is able to react with esters and ε-caprolactone but not with five or six-membered-ring lactones (Scheme 4).

In **Catalytic-BP/NiI$_{2(cat.)}$**, NiI$_2$ catalyses both processes: formation of an organosamarium compound and subsequent addition of organolanthanide to electrophiles including five- or six-membered ring lactones (Scheme 5).

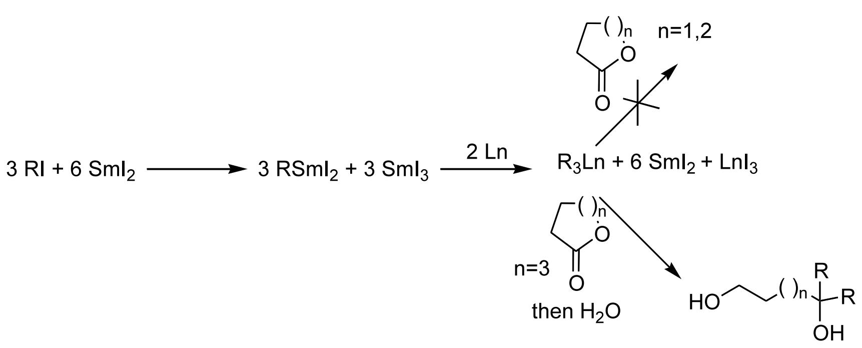
In conclusion, catalytic Barbier-type reactions with SmI$_2$ in catalytic amounts and Mischmetall as a coreductant have been performed between lactones (and esters) and a variety of organic halides (allylic, benzylic and alkyl halides). With an alkyl halide, a catalytic quantity of nickel diiodide (with respect to SmI$_2$) must be added in some cases to achieve reactions. Then a 'two-stage catalysis' is carried out. However, it was found that nickel diiodide is not always necessary, showing that the Mischmetall/SmI$_2$ (catalytic) system can be more reactive than samarium diiodide in stoichiometric amounts. We are currently studying the mechanisms involved in those catalytic reactions.



**Scheme 5.**



**Scheme 3.**



**Scheme 4.**

## Acknowledgements

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6. Mischmetall powder (0.7 g, 5 mmol) was suspended in THF (7 mL), with 0.7 mmol of $SmI_2$ in a Schlenk tube under argon at room temperature. A solution of an electrophile (lactone, 2 mmol) and an organic halide (4 mmol) in THF (7 mL) was slowly added over 2.5 h to the THF/$SmI_2$/Mischmetall suspension. The mixture was then stirred for an additional period of 0.5 h, then diluted with ether, quenched with HCl (1 M) and stirred for 15 min to obtain a clear solution, which was extracted with ether. The combined extracts were washed with brine, aqueous sodium thiosulfate and brine again. The organic layer was dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude material was purified by flash chromatography on silica gel.
7. Selected spectral data. **2-(3-Allyl-3-hydroxy-hex-5-enyl)-phenol (1)**: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ (ppm): 1.76 (2H, m, C(2′)$H_2$); 2.30 (4H, m, C(4′), $C\underline{H}_2$-CH=$CH_2$); 2.65 (1H, s, C(3′)OH); 2.71 (2H, m, C(1′)$H_2$); 5.13 (4H, m, C(6′)$H_2$, $CH_2$-CH=$CH_2$); 5.88 (2H, m, C(5′)H, $CH_2$-C$\underline{H}$=$CH_2$); 6.85 (2H, m, Har); 7.10 (2H, m, Har); 7.19 (1H, s, C(1)OH). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 24.2; 38.9; 43.4; 74.4; 116.0; 119.1; 120.4; 127.4; 128.5; 130.1; 133.2; 153.9. FTIR ($CaF_2$) $\nu_{max}$: 3528, 3338, 3075, 3006, 2977, 2930, 2863, 1839, 1640, 1609, 1593, 1504, 1490, 1457, 1413, 1376, 1242, 1186. GC–MS (IE) *m*/*z* (% base peak): 41 (18), 77 (18), 107 (100), 121 (16), 149 (12), 173 (13), 191 (3), 232 (2). HRMS (IE) calcd for $C_{15}H_{20}O_2$: 232.1463, found: 232.1254. ***Z*-2-(3-Allyl-3-hydroxy-hexa-1,5-dienyl)-phenol (2)**: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ (ppm): 2.34 (1H, s, C(3′)OH); 2.34 (4H, d, C(4′)$H_2$, $C\underline{H}_2$-CH=$CH_2$, $J=7.3$ Hz); 5.13 (5H, m, C(1)OH, C(6′)$H_2$, $CH_2$-CH=$C\underline{H}_2$, $J_{trans}=17.6$ Hz, $J_{cis}=10.3$ Hz); 5.79 (1H, d, C(2′)H, $J_{2'-1'}=$ 12.7 Hz); 5.85 (2H, ddt, C(5′)H, $CH_2$-C$\underline{H}$=$CH_2$, $J_{trans}=$ 17.1 Hz, $J_{cis}=10.3$ Hz, $J_{gem}=7.3$ Hz); 6.44 (1H, d, C(1′)H, $J_{1'-2'}=12.7$ Hz); 6.87 (2H, m, Har); 7.15 (2H, m, Har). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 45.2; 75.4; 116.7; 119.4; 120.2; 124.7; 125.2; 128.7; 129.5; 133.0; 138.1; 152.5. FTIR ($CaF_2$) $\nu_{max}$: 3528, 3306, 3076, 3010, 2978, 2928 2849, 1838, 1698, 1640, 1604, 1586, 1576, 1502, 1450, 1414, 1364, 1228, 1170. GC–MS *m*/*z* (% base peak): 41 (70), 77 (12), 91 (46), 103 (46), 115 (12), 147 (100), 171 (22), 189 (22), 230 (1). HRMS (IE) calcd for $C_{15}H_{18}O_2$: 230.1307, found: 230.1310. ***cis*-3-(2-Allyl-2-hydroxy-pent-4-enyl)-cyclopentanol (3)**: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ (ppm): 1.19–2.04 (9H, C(1)OH, C(2)$H_2$, C(3)H, C(4)$H_2$, C(5)$H_2$, C(2′)OH); 1.62 (2H, d, C(1′)$H_2$, $J_{1'-3}=6.4$ Hz); 2.24 (4H, d, C(3′)$H_2$, $C\underline{H}_2$-CH=$CH_2$, $J_{3'-4'}=6.8$ Hz); 4.29 (1H, m, C(1)H); 5.12 (4H, m, C(5′)$H_2$, $CH_2$-CH=$C\underline{H}_2$); 5.85 (2H, m, C(4′)H, $CH_2$-CH=$C\underline{H}_2$). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 32.1; 34.0; 35.4; 43.9, 44.0; 44.3; 45.6; 73.4; 73.9; 118.8; 133.9. FTIR ($CaF_2$) $\nu_{max}$: 3369, 3075, 3006, 2930, 2858, 1832, 1711, 1640, 1441, 1420, 1295. GC–MS (IC-$NH_3$) *m*/*z* (% base peak): 151 (26), 175 (55), 192 (18), 193 (100), 210 (11), 211 (8). HRMS (IE) calcd for $C_{13}H_{22}O_2$–$H_2O$: 192.1514, found: 192.1509. **4-Allyl-hepta-2,6-diene-1,4-diol (4)**: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ (ppm): 2.31 (1H, br s, OH); 2.32 (4H, d, C(5)$H_2$, $C\underline{H}_2$-CH=$CH_2$, $J_{5-6}=7.3$ Hz); 3.37 (1H, br s, OH); 4.25 (2H, dd, C(1)$H_2$, $J_{1-2}=5.9$ Hz, $^4J_{1-3}=1.5$ Hz); 5.11 (4H, m, C(7)$H_2$, $CH_2$-CH=$C\underline{H}_2$); 5.44 (1H, dd, C(3)H, $J_{3-2}=12.2$ Hz, $^4J_{3-1}=1.5$ Hz); 5.68 (1H, dt, C(2)H, $J_{2-3}=12.2$ Hz, $J_{2-1}=5.9$ Hz); 5.83 (2H, m, C(6)H, $CH_2$-C$\underline{H}$=$CH_2$). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 45.9, 58.8, 75.1, 118.8, 129.3, 133.3, 136.1. FTIR (NaCl) $\nu_{max}$: 3354, 3076, 3012, 2997, 2928, 1640, 1438, 1219, 1028, 997, 916. GC–MS (IE) *m*/*z* (% base peak): 41 (100), 53 (33), 57 (26), 79 (50), 81 (47), 85 (94), 109 (37), 127 (42). HRMS (IE) calcd for $C_{10}H_{16}O_2$–$H_2O$: 150.1045, found: 150.1044. **2-(3-Heptyl-3-hydroxydecyl)-phenol (5)**: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ (ppm): 0.97 (6H, t, C(10′)$H_3$, $C\underline{H}_3$-$nC_6H_{13}$, $J_{10'-9'}=6.8$ Hz); 1.35 (20H, m, C(5′)$H_2$, C(6′)$H_2$, C(7′)$H_2$, C(8′)$H_2$, C(9′)$H_2$, $CH_2$-$(C\underline{H}_2)_5$-$CH_3$); 1.40 (4H, m, C(4′)$H_2$, C(3′)OH-$C\underline{H}_2$-$C_6H_{13}$); 1.82 (2H, m, C(2′)$H_2$); 2.74 (2H, m, C(1′)$H_2$); 2.94 (1H, br s, C(3′)OH); 6.32 (2H, m, Har); 7.14 (2H, m, Har); 7.88 (1H, br s, C(1)OH). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 14.0; 22.6; 23.6; 24.1; 29.2; 30.1; 31.8; 38.7; 39.2; 75.6; 116.1; 120.2; 127.1; 129.0; 129.9; 153.9. FTIR ($CaF_2$) $\nu_{max}$: 3306, 3032, 2929, 2857, 1924, 1889, 1776, 1594, 1584, 1490, 1457, 1378, 1242. GC–MS (IE) *m*/*z* (% base peak): 41 (27), 43 (28), 77 (10), 107 (100), 133 (8), 231 (70), 249 (10), 330 (4). HRMS (IE) calcd for $C_{23}H_{40}O_2$–$H_2O$: 330.2923, found: 330.2918. **3-(Tetrahydrofuran-2-yl)-decane-1,3-diol (6)**: $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ (ppm): 0.88 (3H, t, C(10)$H_3$, $J_{10-9}=8.8$ Hz); 1.28 (10H, m, C(5)$H_2$, C(6)$H_2$, C(7)$H_2$, C(8)$H_2$, C(9)$H_2$); 2.03–1.37 (8H, m, C(2)$H_2$, C(4)$H_2$, C(3′)$H_2$, C(4′)$H_2$); 2.38 (1H, s, C(3)OH); 3.10 (1H, s, C(1)OH); 3.82 (5H, m, C(1)$H_2$, C(2′)H, C(5′)$H_2$). $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ (ppm): 14.0; 22.5; 23.9; 25.6; 26.1; 29.2; 30.2; 31.7; 35.3; 36.8; 58.9; 68.4; 75.8; 82.8. FTIR (NaCl), $\nu_{max}$: 3386; 2926; 2856; 1464; 1378; 1288; 1186; 1130; 1070; 927; 877; 733. GC–MS (IE) *m*/*z* (% base peak): 41 (82), 43 (83), 55 (48), 57 (95), 70 (15), 71 (86), 83 (12), 97 (21), 101 (8), 127 (55), 145 (16), 155 (27), 173 (100), 174 (11), 199 (9). HRMS (IE): calcd for $C_{14}H_{28}O_3$–$H_2O$: 226, 1933; found: 226, 1934.
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