Chematek

IN THE PURSUIT OF PROGRESS

/SYNHYDRID® AND PIPERHYDRIDE®: SAFE, SECURE, RELIABLE REDUCING AGENTS

CONTENTS

/INTRODUCTION

The first batch of Sodium dihydrido-bis (2-methoxyethoxo) aluminate (SDMA) Synhydrid® was initially synthesised in 1971 (in academic settings). Since then, Synhydrid® has been used in organic reductions because of its versatility and physicochemical properties. Synhydrid® belongs to the family of hydrides and is soluble in organic solvents, particularly aromatics and ethers. It is distinctive as a reducing agent because it is safer during handling and manipulation than traditional reducing agents like $LiAlH_4$ and DIBAL-H. Synhydrid® exhibits superior chemoselectivity to $LiAlH_4$ and therefore an effective replacement, which can also led to superior yields.

The following equation can summarise the commonly adopted synthesis:

$$Na + Al + H_2 + 2\ CH_3OCH_2CH_2OH \longrightarrow NaAlH_2(OCH_2CH_2OCH_3)_2\ (1)$$ [1]

Sodium and aluminium elements are used in the reaction with 2-methoxyethanol in toluene as a solvent to give SDMA as a product. The product is obtained in toluene solution up to 70% wt. concentrations in toluene. This concentration confers the optimal viscosity for handling and safe manipulation under an inert atmosphere to the solution. Moreover, SDMA does not self-ignite when exposed to moisture. As a result, Synhydrid® possesses unique properties that may confer stability and ease of manipulation in both lab and commercial-scale reactions.

The physicochemical properties of Synhydrid® set the basis for its versatility in organic transformations. Synhydrid® is a colourless viscous liquid that becomes a glassy amorphous solid at temperatures below 0°C.

The solubility of Synhydrid® is surprisingly high in ethers (Et_2O) and aromatic hydrocarbons (o-xylene, m-xylene, p-xylene, mesitylene) and may increase depending upon the reaction temperatures.[1] Synhydrid® is also a stable reducing agent at a very high range of temperatures, as slight decomposition occurs only at temperatures above 170°C.[1] In solution, disproportionation reaction leading to $NaAlH_4$ and $NaAlH(OCH_2CH_2OCH_3)_3$ and probably also to $NaAl(OCH_2CH_2OCH_3)_4$ was observed by IR spectra and by ^{27}Al-NMR for polar ethers (1,2-dimethoxyethane and THF), whereas in benzene SDMA behaves as a separate compound.[2]

Its intermediate stability results from the opposite effects: the general low stability of dihydro-bis(alcoxo)aluminates, $NaAlH_2(OR)_2$, and the stabilising effect by solvation of the Na atom and the oxygen in β-position of the alcoxy group (Figure 1).

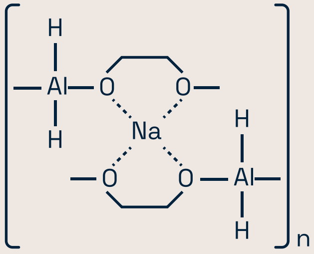

Figure 1: Proposed intramolecular solvation unit of SDMA

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[1] Časenský B., Macháček J., Vít J.: Chem. Abstr. 74, 89, 240 (1971)

[2] Fusek J., Hanousek, F.: Collect. Czech. Chem. Commun. 42, 967 (1977)

Synhydrid® safe handling is also confirmed by the lack of self-ignition when exposed to moisture or in contact with water. The reagent should be used and treated like a 1st class combustible. However, due to its properties, the manipulation in organic reactions may need not be carried out strictly inertly, as Synhydrid® can be poured rapidly without causing any self-ignition risk under air.

After the reaction goes to competition, the excess Synhydrid® present in the reaction mixture can be easily quenched by adding water and carefully handling the exothermic reaction (the heat of hydrolysis is 86.66 kJ/mole).[3] The evolution of hydrogen must be continuously replaced by nitrogen gas flux.

Because of these properties and safe handling, Synhydrid® can be used as a reagent for selection among nucleophilic reducing agents, such as $LiAlH_4$ and $NaBH_4$.

In addition, its solubility in organic solvents, lack of self-ignition during hydrolysis or exposure to moisture, and ease of manipulation even under a “not strict” inert atmosphere make Synhydrid® the preferred options in organic transformations involving reductions of organic substrates dissolved in organic solvents.

Reaction work-up is also safe as the hydrogen evolution is slow at low temperatures and safely assisted by slow nitrogen gas replacement reflux.

COMPARISONS WITH OTHER REDUCING AGENTS

Synhydrid® can be used instead of Lithium Aluminum Hydride (LAH) and sodium borohydride ($NaBH_4$), thus avoiding the problems associated with the use of pyrophoric chemicals (Figure 2).

LAH, for example, may cause a high exothermic reaction with hydrogen gas evolution upon mechanical stimulation.

LAH is sold in solid pellets for industrial applications to reduce contact with air and moisture.

Nevertheless, the salt can auto-ignite at 25 °C and undergo decomposition, releasing hydrogen gas. The following scheme may summarise the reactions.

$$\boxed{LiAlH_4 + 2H_2O \longrightarrow 4H_2 + LiAlO_2 \ (2)}$$

$$\boxed{LiAlH_4 + 4H_2O \longrightarrow LiOH + Al(OH)_3 + 4H_2}$$

Lithium aluminium hydride LAH explosions from powders or pellets are hazardous, especially when subjected to mechanical pressure and grinding.

For this reason, LAH is listed among the highly reactive hazardous chemicals in academic and industrial research labs and provides standard operating procedures SOP for handling and storing the chemical.

In addition, LAH is poorly soluble in common organic solvents and is for sale for lab-scale reactions as a solution in THF or ether.[4]

To achieve complete conversion, LAH is expected to be used also as a diluted solution in THF or as a suspension.

Once the reaction completes, the aluminium salts precipitate with aqueous quenching and must be filtered, causing a loss of product material during the filtration step.

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[3] Institute of Inorganic Syntheses, Czechoslovak Academy of Sciences: Sodium dihydrido-bis(2-methoxyethoxo)aluminate (leaflet) 1986

[4] Merlic, C. Ferber C, Schröder I., ACS Chem. Health Saf. 29, 4, 362 (2022)

Another commonly used reducing agent is sodium borohydride $NaBH_4$. Sodium borohydride $NaBH_4$ is used in industrial plants as solid or as 12-20% wt aq. NaOH solution. Gradual decomposition of the product with concomitant slow releasing of hydrogen occurs when $NaBH_4$ is in contact with moisture or water, as expressed by the formula below:

$$\boxed{NaBH_4 + 2H_2O \longrightarrow NaBO_2 + 4H_2}$$

$NaBH_4$ usually converts ketones and aldehydes in quantitative yield to the corresponding alcohols. The reaction is known to be highly exothermic, about -150 kcal/mol, thus raising critical safety concerns.[5]

To overcome the limitations of $NaBH_4$ and $LiAlH_4$ reducing agents, Synhydrid® is used as a viscous, dense liquid toluene solution in a high concentration of 70% wt.

The solution does not precipitate even when heated, and aluminium compounds can be easily eliminated through an aqueous acidic or basic work-up. Synhydrid® is chemoselective and can also be modified to achieve partial reductions of various functional groups, thus enhancing its versatility as a reducing agent.

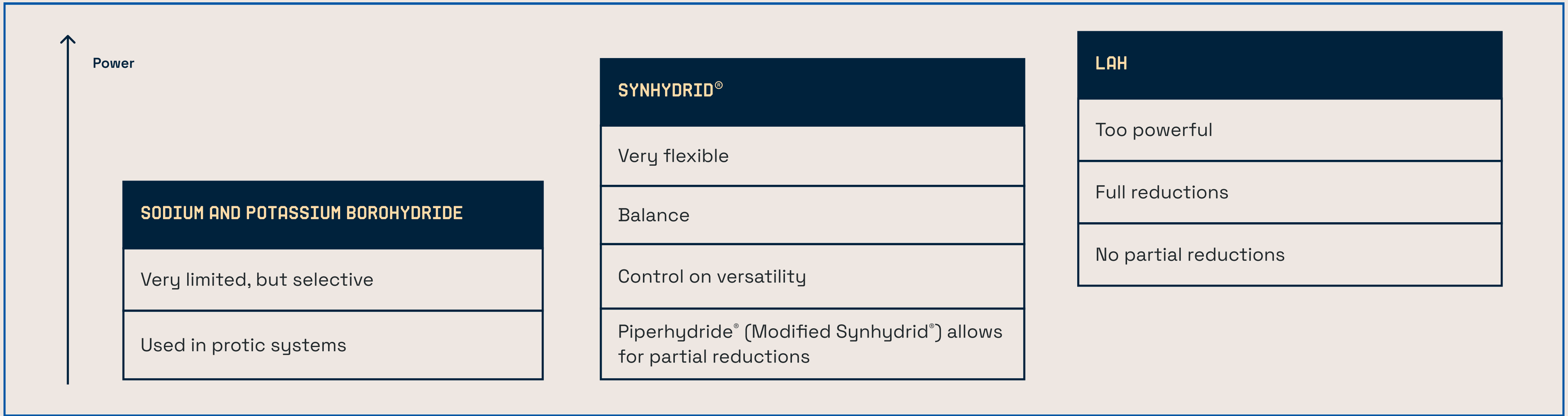

Figure 2: Comparison between Synhydrid® and common reducing agents, $NaBH_4$ and $LiAlH_4$

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[5] Duggan, PJ; Johnson, AA.; Rogers, RL. Institution of Chemical Symposium Series, 134, 553, (1994)

/REACTIONS OF SYNHYDRID®

A summary of the reactions performed by Synhydrid® can be found in Figure 3, which is reported below.

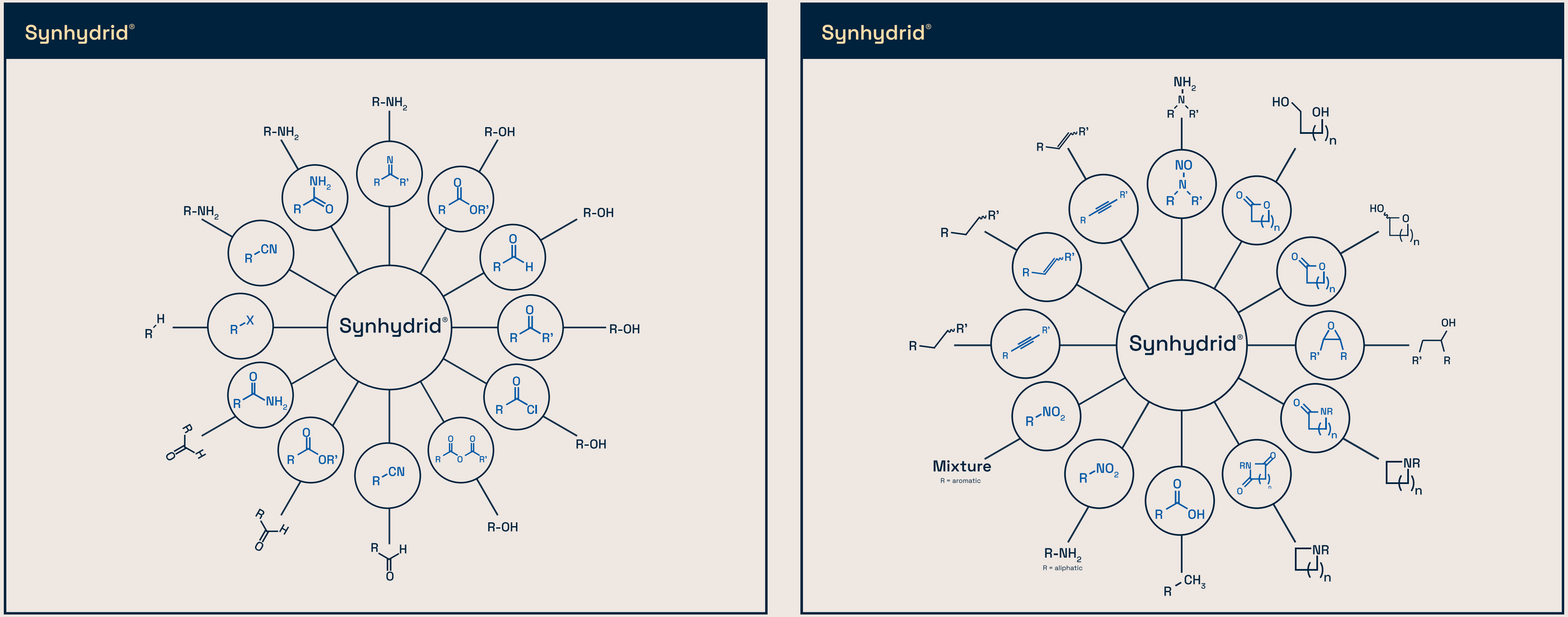

Figure 3: Common functional group interconversion performed by Synhydrid®

Carboxylic acids, esters, acyl chlorides, anhydrides, ketones, and aldehydes are efficiently converted into the corresponding alcohol. Partial reductions of carboxylic esters, nitriles, and amide using Synhydrid® at low temperatures are instead leading to aldehydes.

Amines can be synthesised by reducing amide, nitriles, imines, azido compounds, nitro compounds, oximes, lactams, and imides. Depending on the reaction conditions, lactones reduce to diols or lactols.

Synhydrid® also applies to the reductive ring opening of epoxides and the reduction of saturated substrates (alkenes and alkynes).[6] Despite its utility, the presence of other functional groups or moieties on the substrate molecule influences the reactivity of Synhydrid®.

Failure to account for these additional functionalities may result in unintended side reactions, impeding the desired synthetic pathways. A few of the most common interconversions will be detailed in the following sections.

REDUCTION OF ALDEHYDES AND KETONES

Main transformations in organic chemistry, including reactions with aldehydes, take advantage of the use of Synhydrid® as it is soluble in common organic solvents, and just 0.5 equivalents are necessary to complete the reaction (Figure 4). Aliphatic aldehydes react almost quantitatively with Synhydrid® in a very short time (5-10 minutes).

Aromatic aldehydes can be reduced by Synhydrid® at higher temperatures (e.g. 80°C) in high yields, giving the corresponding benzyl alcohols.

Synhydrid® shows efficient usage for the reduction of ketones to the secondary alcohols in quantitative yields with 0.5 equivalents of Synhydrid® per mole of ketone (Figure 5).

Only sterically hindered ketones do not afford the desired product as the nucleophilic reducing agent Synhydrid® reacts mainly with the hydroxy group of the enol adduct. α,β-unsaturated ketones can selectively be reduced. The unsaturated alcohols were efficiently produced to synthesise commercially essential intermediates like those involved in the stereospecific synthesis of estrone.[7]

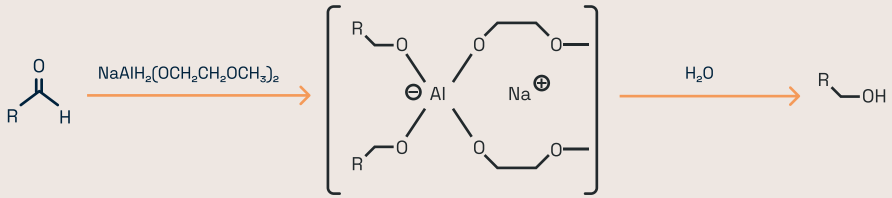

Figure 4: Reduction of aldehydes by Synhydrid®

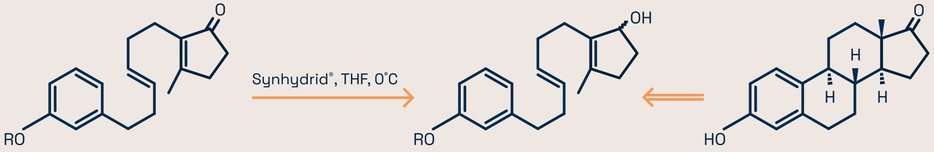

Figure 5: Reduction reaction involved in the stereospecific synthesis of estrone

[7] Bartlett P. A., Johnson W. S.: J. Am. Chem. Soc. 95, 7501 (1973)

REDUCTION OF ESTERS TO ALCOHOLS

Esters of aromatic and aliphatic carboxylic acids can be easily reduced with Synhydrid® to the corresponding alcohol, with a reducing ability comparable to $LiAlH_4$. The reaction usually requires a slight excess of hydride (10-20%) to achieve high yields. Figure 6 shows its application in the synthesis of the sex pheromone of the horse Chestnut Leaf Miner (Cameraria Ohidella).[8]

The reaction of Synhydrid® is also very chemoselective as it does not interfere with other functional groups that hydride ions can reduce. The following example shows that Synhydrid® does not attach the thiazole functional group despite the presence of hydride ions in the solution; when DIBAL-H was employed, side-product reactions were observed (Figure 7).[9]

Similarly, potent reducing agents like LAH and $NaBH_4$ reduce imines and esters together, while with Synhydrid®, the reduction of esters to primary alcohol can be performed chemoselectively in the presence of imines and oximes (Figure 8).[10]

Reduction of the ester functionality to give the desired alcohol is present in the reduction step of several crucial active pharmaceutical ingredients like Tolterodine®, an antimuscarinic medication used to treat urinary incontinence (Figure 9).[11]

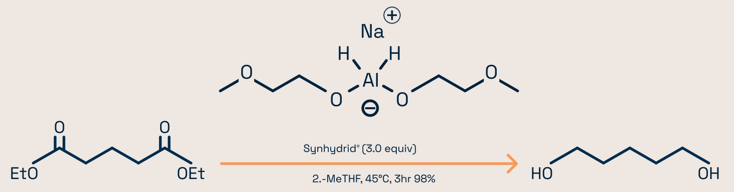

Figure 6: Reduction of diester to diol

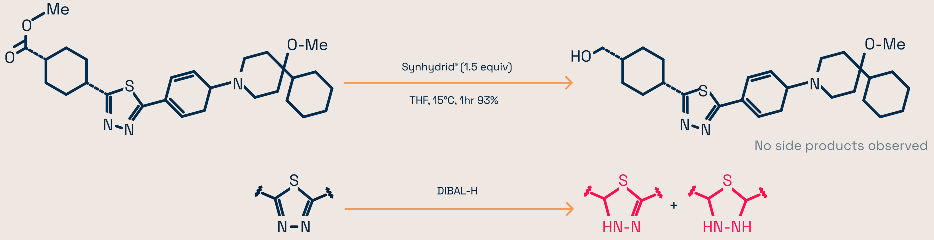

Figure 7: Comparison of Synhydrid® with DIBAL-H in the reduction of an ester

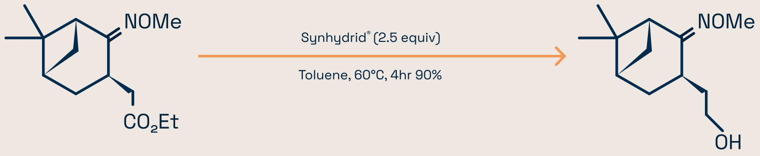

Figure 8: Chemoselective reduction of esters to alcohols in the presence of oximes

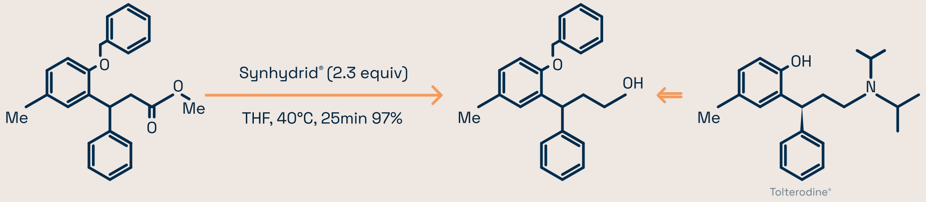

Figure 9: Reduction of the ester by Synhydrid® in the synthesis of Tolterodine®

[8] Chorreau P., Guerret O., Guillonneau L., Gayon E., Leféure G.: Org. Process Res. Dev., 24, 7, 1335 (2020)

[9] Yoshida S., Ohigashi A., Morinaga Y., Hashimoto N., Takahashi T., Ieda S., Okada, M.: Org. Process. Res. Dev., 17, 10, 1252 (2013)

[10] Hida T., Mitsumori S., Honma, T., Hiramatsu, Y. Hashizume H., Okada T., Kakinuma M., Kawata K., Oda K., Hasegawa A., Toshiaki M., Hideo N. Org. Process Res. Dev. 13, 6, 1413 (2009).

[11] Srinivas K., Srinivasan N., Reddy K. S., Ramakrishna M., Reddy C. R., Arunagiri M., Kumari R. L., Venkataraman S., Mathad V. T.: Org. Process. Dev. 9 (3), 314 (2005)

REDUCTION OF ALKYNES AND ALKENES

Alkynes can be reduced to the corresponding alkene in a stereoselective manner: the stereoselective reduction of propargyl alcohol is an example. [12]

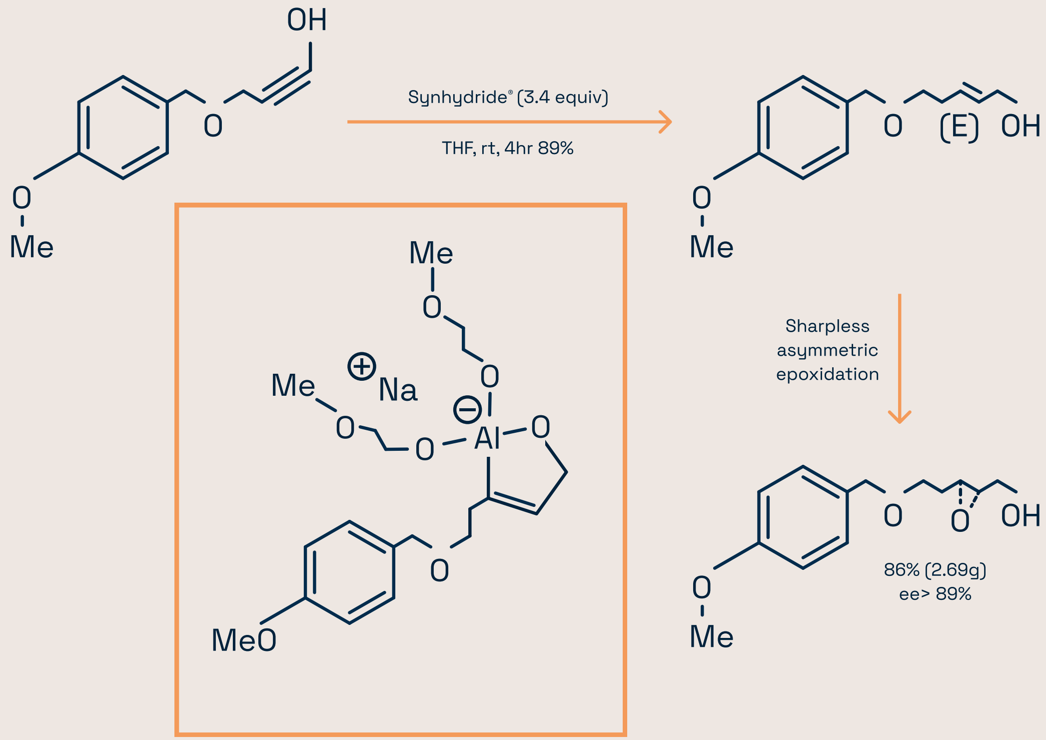

Figure 10: Stereoselective reduction of alkyne function to trans alcohol (E) configuration

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[12] Tang M., Pyne S. G.: J. Org. Chem. 68, 7818 (2003)

The product is supposed to be a cyclic intermediate adduct with aluminium that drives the formation of the E-alkene, which is then used in a Sharpless epoxidation to give an enantiopure material.
Eldecalcitol, a drug compound used for the treatment of osteoporosis in Japan, uses Synhydrid® in its large-scale synthesis (Figure 11).[13]

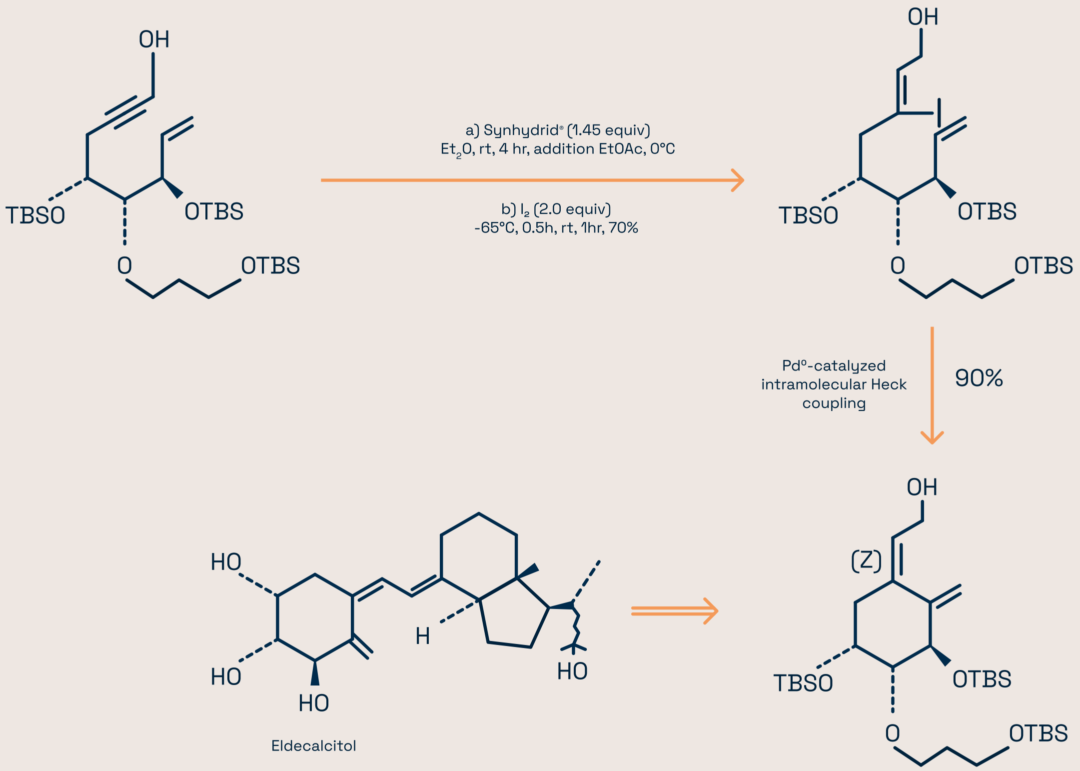

Figure 11: Stereoselective reduction of alkyne function to (E) olefins followed by intramolecular Heck-cyclization.

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[13] Moon H. W., Lee S. J., Park S. H., Jung S. G., Jung I. A, Seol C. H., Kim S. W., Lee S. M., Gangganna B., Park S., Lee K.-Y., Oh C.-Y., Song J., Jung J., Heo J. S., Lee K. H., Kim H. S., Lee W. T., Baek, A., Shin H. Org. Process Res. Dev. 25, 1, 98 (2021)

REDUCTION OF AMIDES

Amides are easily reduced to the corresponding amine by SDMA according to the following equation:

$$R_1CONR_2 + NaAlH_2(OCH_2CH_2OCH_3)_2 \rightarrow R_1CH_2NR_2 + NaAlO(OCH_2CH_2OCH_3)_2 \quad (7)$$

Examples are taken from the work of Sun et al., where the reduction of the amide is obtained in excellent yield using Synhydrid® with respect to commercially available reducing agents like lithium aluminium hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$) with or without the presence of additives (Figure 12; Table 1).[14] The reaction was performed in toluene and converted completely at 60 °C, obtaining the product with 95% HPLC purity after basic work-up.

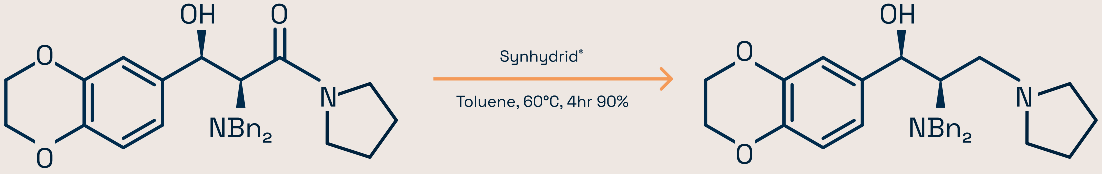

Figure 12: Carbonyl reduction of amide function to secondary amine

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[14] Sun, G. Jian, W. Luo, Z. Sun, T. Li, C. Zhang, J., Wang, Z. Org. Process Res. Dev. 23, 6, 1204 (2019)

ENTRY	REAGENT	ADDITIVE	SOLVENT	STARTING MATERIAL (AREA %)	PRODUCT (AREA %)
1	$LiAlH_4$ (3.0 equiv)	None	THF	ND	74
2	$NaBH_4$ (6.5 equiv)	TFA (3.0 equi)	THF	52	34
3	$NaBH_4$ (10 equiv)	$TiCl_4$ (5.0 equiv)	DME	82	ND
4	$NaBH_4$ (20 equiv)	$AlCl_3$ (10 equiv)	THF	47	16
5	$NaBH_4$ (20 equiv)	LiCl (20 equiv)	THF	4	ND
6	$NaBH_4$ (20 equiv)	I_2 (10 equiv)	THF	78	11
7	Synhydrid® (5.0 equiv)	None	Toluene	ND	86

Table 1: Screening of amide-reducing agents for the carbonyl reduction of amide function to secondary amine. Reactions were performed with 0.3 mmol of amide, reducing agents, and additives in 10 mL of solvent at 70°C. HPLC detected areas %

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[14] Sun, G. Jian, W. Luo, Z. Sun, T. Li, C. Zhang, J., Wang, Z. Org. Process Res. Dev. 23, 6, 1204 (2019)

REDUCTION OF NITRILES

Reduction of Nitriles to Amines

Reducing nitrile to the corresponding amine with Synhydrid® is strongly dependent on the nitrile's structure and often requires a 100% excess of the reducing agent. In contrast to $LiAlH_4$, nitriles containing hydrogen(s) in the α-carbon position are usually poorly reduced by Synhydrid®, as the formation of polymerisation products complicates the reaction.[15] An example of amine obtained in modest yield is represented in Figure 13.[16]

On the other hand, aromatic nitriles without hydrogen in the α-carbon position can be reduced to the corresponding benzylamines in high yields. It is reported in the literature that the reduction of benzonitrile with 100% excess of Synhydrid® in toluene at reflux yields 81% benzonitrile and similar reductions of o- and m-tolunitriles give up to respectively 95% of 2-methylbenzylamine and 91% 3-methylbenzylamine.[16c]

Reduction of Nitriles to Aldehydes

Partial reduction of nitriles to the corresponding aldehydes use Synhydrid®. The interconversion of nitrile to aldehyde, as exemplified in the synthesis of Platensimycin, an antibiotic effective against many resistant bacteria (Figure 14), is an example.[17]

Reductions of aromatic nitriles to aldehydes with Synhydrid® usually proceed in high yield, as exemplified in Figure 15.[18]

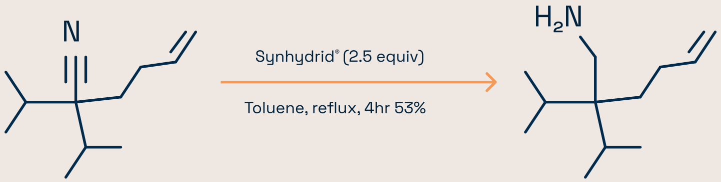

Figure 13: Partial reduction of an aliphatic nitrile to a primary amine

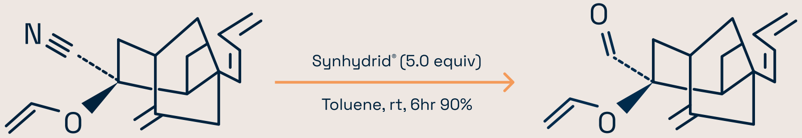

Figure 14: Reduction of an aliphatic nitrile to aldehyde for the synthesis of Platensimycin

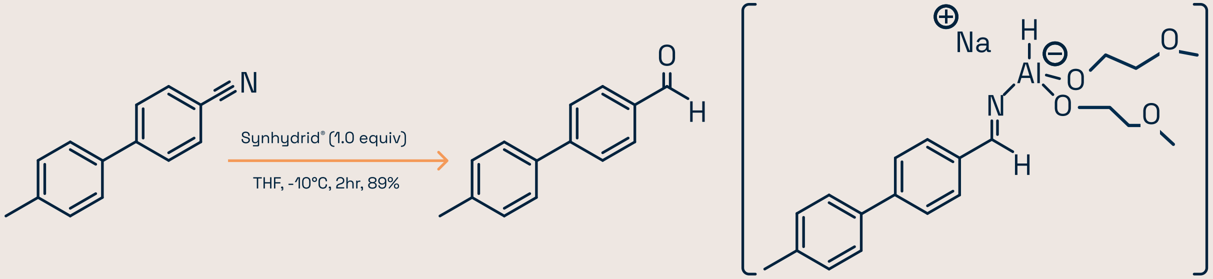

Figure 15 Reduction of aromatic nitrile to aldehyde

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[15] a) Bažant V., Čampka M., Černý M., Chvalovský V., Kochloefl K., Kraus M., Málek J.: Tetrahedron Lett. 3303 (1968); b) Kříž O., Časenský B., Štrouf O.: Ibid 38, 2076 (1973); c) Černý M., Málek J., Čapka M., Chvalovský V.: Ibid 34, 1033 (1969).

[16] Langhals H., Rausher M. DE 2007/102005060074.

[17] Nicolaou K. C., Stepan A. F., Lister T., Li A., Montero A., Tria g. S., Turner C. I., Tang Y., Wang J., Denton R. M., Edmonds D. J., Nicolaou K. C.: J. Am. Chem. Soc. 130, 13110 (2008)

[18] Ikemoto T., Ito T., Hashimoto H., Kawarasaki T., Nishiguchi A., Mitsudera H., Wakimasu M., Tomimatsu K. Org. Proc. Res. Dev. 4, 6, 520-525 (2000)

/PIPERHYDRIDE® AND OTHER AMINE/ALCOHOL-MODIFIED SYNHYDRID®

As mentioned, aldehydes can be obtained by partially reducing carboxylic esters, nitriles, and amide using Synhydrid® at low temperatures.

Alternatively, alcohol or amine-modified Synhydrid® has been employed to achieve selectively the interconversions mentioned above: in particular, modified Synhydrid® with N-methylpiperazine and morpholine has been reported for the synthesis of aldehydes, while conversion of lactones to lactols can be achieved using alcohol-modified reagents (e.g., EtOH, i-PrOH, 2,2,2-trifluoroethanol; Figure 16).[19]

Modified Synhydrid® is usually synthesised in toluene, adding 1 equivalent of additive (alcohol or amine) to 1 equivalent of Synhydrid®. Chematek S.p.A commercialises modified Synhydrid® containing N-methylpiperazine as Piperhydride®, it is becoming a valuable alternative to DIBAL-H for partial functional group reductions.

Piperhydride® applied to partial reductions has the indisputable advantage of avoiding cryogenic temperature conditions and giving high yields, together with the safety advantages of the non-pyrophoric nature of Synhydrid®. The following sections show a few functional group interconversions.

LACTONE TO LACTOL REDUCTION

One class of reactions that particularly employs modified Synhydrid® is the partial reduction of lactones to lactols. The synthesis of Sofosbuvir, a drug used for treating hepatitis C shows an example of the higher reactivity of modified Synhydrid® versus the standard reducing agents (Figure 17, Table 2).[20]

The reaction is conducted in DCM at a temperature of -10 °C with high selectivity: ring opening and debenzylation are not detected with modified Synhydrid®, while they are present as side-reactions when the experiment is conducted using DIBAL in THF at -20°C.

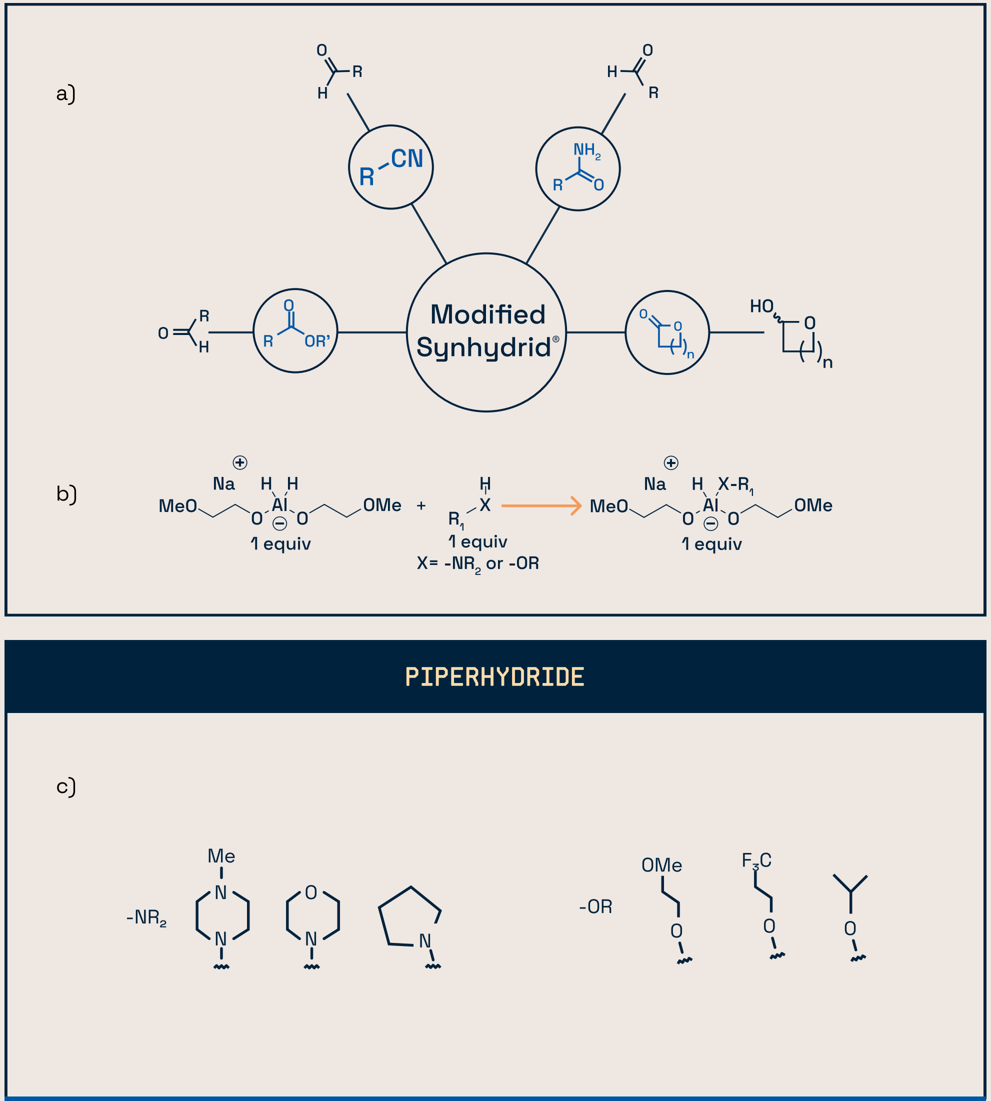

Figure 16 a) Reduction of different functional groups by Modified Synhydrid®. B and c) Modification of Synhydrid® with ligands of choice. Chematek is selling Modified Synhydrid®, which contains N-methylpiperazine as a ligand, Piperhydride®.

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[19] An K. et al. Bull. Korean. Chem. Soc. 35, 2169 (2014)

[20] N. C. Chaudhuri N. C., Moussa, A., Stewart, A., Wang, J., Storer, R. Org. Process Res. Dev. 9, 457 (2005)

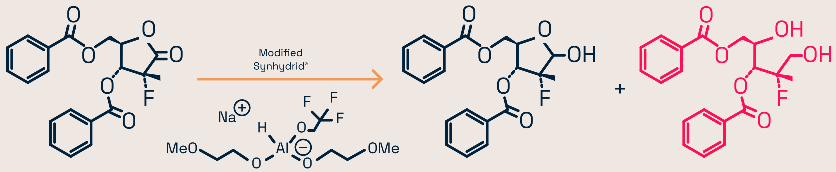

Figure 17: Reduction of an aliphatic nitrile to aldehyde for the synthesis of Platensimycin

REDUCING AGENT	ADDITION	SOLVENT	TEMP	TIME	YIELD
Synhydrid®/ Modified Synhydrid®	**Reverse[a]**	**DCM**	**-10°C**	**1h**	**76%**
TBLAH	Reverse[a]	THF	-10°C -15°C	3h	63%
DIBAL	Reverse[a]	THF	-78°C	6h	Poor conversion
DIBAL	Reverse[a]	THF	-20°C	0.5h	Degradation; lactone opening and debenzylation

Table 2: Comparison of Synhydrid® and common reducing agents in the lactone reduction step of Sofosbuvir shown in Figure 17. A reverse addition refers to the procedure where the reducing agent is added to the organic compound (see Section on Experimental setup)

ESTER TO ALDEHYDE REDUCTION

The partial reduction of ester to aldehyde, a common functional group interconversion in the API synthesis, uses Modified Synhydrid®. Tertiary aromatic amines bearing esters groups are also reduced to aldehydes by modified Synhydrid®, which reduces the esters' functions (Figure 18)[21]. An in situ equimolar ratio of Synhydrid® and N-methylpiperazine is used to obtain the modified Synhydrid®.

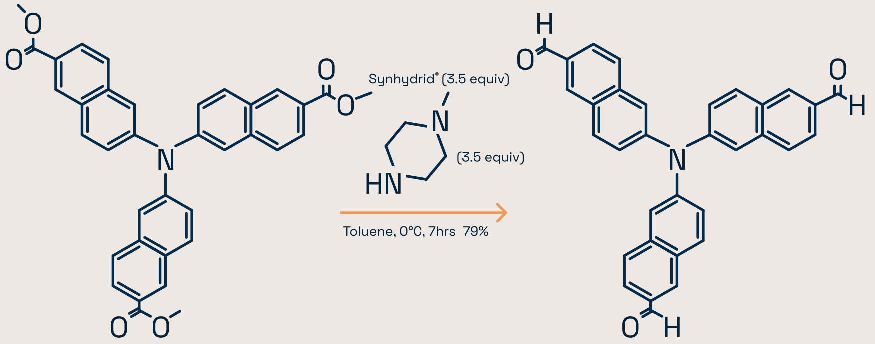

Figure 18: Reduction of ester functionality of a tertiary aromatic amine giving tri-aldehyde function in toluene

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[21] Bordeau G., Lartia R., Metge G., Fiorini-Debuisschert C., Charra F., Teulade-Fichou M.-P. J. Am. Chem. Soc. 130, 50, 16836 (2008)

/DILACTAMATE

Synhydrid® is used in polymerisation reactions, with notable applications including its role in the conversion of 6-caprolactam.[22] For polyamide and styrene polymerisation, Chematek offers Dilactamate (Sodium dicaprolactamato-bis (2-methoxyethoxo)aluminate—Figure 19), which is supplied in a toluene solution. The compound finds utility in anionic polymerisation and co-polymerisation processes involving lactams.

Chematek also offers Dilactamate S, an initiator specifically designed to delay the crystallisation phase during the polymerisation of lactams.

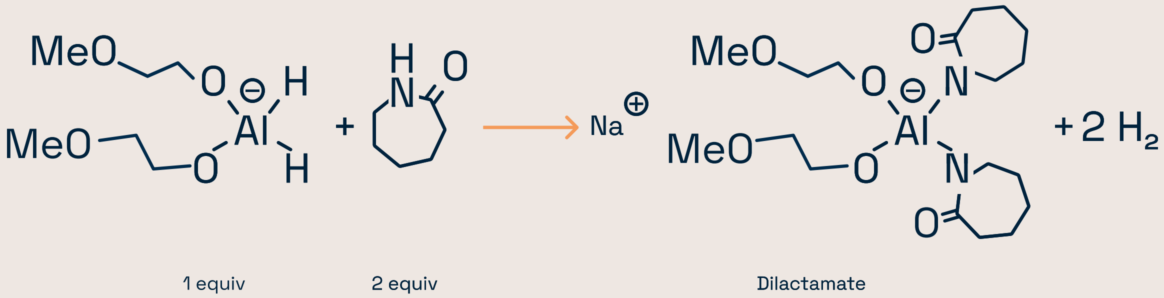

Figure 19: Synthesis of Dilactamate

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[22] Štěrbáček, Z., Votrubec, J., Černy, M., Kubánek, V. (1986). Polycaprolactam (Patent No. CS 226091B1). Czech.

/EXPERIMENTAL SETUP

The reaction conditions influence the outcome of the reaction. There are two procedures that the operator can proceed with:

STANDARD PROCEDURE

The compound to be reduced is added dropwise into a diluted solution of Synhydrid®. An excess of Synhydrid® is maintained throughout the experiment.

INVERSE PROCEDURE

Synhydrid® is added dropwise into a solution of the compound. This way, an excess of the compound to be reduced is maintained during the entire experiment, which is usually carried out at low temperatures. Due to mild reaction conditions, this procedure is generally recommended to avoid side reactions.

Another possibility for influencing the product of reductions is the choice of solvent. In most cases, the selection of solvent depends on the solubility of reactants, intermediates, and products, but for stereochemical reasons, it is recommended to take the polarity of the solvent into account.

The product is obtained as sodium alcoxyaluminate, which is easily hydrolysed.
Either acidic, neutral, or alkaline hydrolysis can be employed. The most frequently used acid hydrolysis is when sulfuric or hydrochloric acid is diluted.

/HANDLING & SAFETY

SAFE HANDLING OF SYNHYDRID®

- Follow standard industrial safety precautions.
- Wear protective clothing:
    - Solvent-resistant gloves
    - Safety goggles or face shield
    - If ventilation is poor, use a respirator with an organic vapor filter or a self-contained breathing apparatus.

HANDLING INSTRUCTIONS

- **When opening a drum:**
    - Flush the space above the solution with dry nitrogen.
    - Reseal before returning to storage.
- Use oxygen monitoring in vessels where hydrogen generation is possible.
- Maintain oxygen levels below 5% in the nitrogen atmosphere for safety.

STORAGE GUIDELINES

- Store in original, perfectly sealed containers.
- Keep in a cool, dry area for flammables.
- **Keep away from:**
    - Water
    - Acids
    - Oxidizing agents
    - Ignition sources

PACKAGING & AVAILABILITY

- Available in drums and safety containers.
- Other sizes including 450KG and 2,500KG are available

EMERGENCY PROCEDURES

- **In case of fire:**
    - Use dry chemical extinguishers (snow or powder) or inert gas (nitrogen).
    - Do not use water, halocarbon, or foam extinguishers, as they can support the fire.
- **For spills:**
    - Cover the spill with dry materials (sand or dolomite).
    - Transfer to a dry metal container.
    - Dispose of according to local regulations.

SAFETY & FIRST AID

1

First aid for skin contact with Synhydrid® (which may cause burns) consists of immediately flushing the contaminated site with plenty of water for at least 15 minutes. Contaminated clothing and shoes must also be removed, and hair must be washed. The injured person should be removed into fresh air.

2

In case of ingestion (which causes severe burns to the mouth, throat, and gastrointestinal tract), never induce vomiting. Rinse the mouth with water, then give about 0.5L of lukewarm water with 10 tablets of charcoal to drink. Call the physician immediately.

3

In case of inhalation (severely irritating to mucous membranes and respiratory tracts), remove to fresh air. If breathing is difficult, give oxygen. If not breathing, provide artificial respiration. Seek medical attention.

4

In case of eye contact (which may cause severe damage to the cornea), immediately flush your eyes with plenty of water for at least 15 minutes. In both cases, seek medical attention.

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