37.0 (C2 + C12), 35.3 (C8), 35.0 (C10), 27.8 (C21), 27.6 (C16), 26.5 (C7), 25.4 (C6), 23.5 (C15), 22.6 (C19), 20.7 (C11), 12.1 (C18), 9.3 (C22).

3b: ^{13}C NMR δ 211.8 (C3), 174.4 (C20), 82.3 (C17), 53.6 (C9), 50.5 (C14), 46.5 (C5), 44.6 (C4), 42.6 (C13), 38.4 (C1), 38.0 (C2), 36.8 (C12), 35.6 (C10), 35.1 (C8), 31.2 (C7), 28.7 (C6), 27.7 (C21), 27.6 (C16), 23.5 (C15), 20.8 (C11), 12.1 (C18), 11.4 (C19), 9.3 (C22).

Catalyst Preparation. To a solution of $Cu(NO_3)_2{\cdot}3H_2O$ (16 g) in 150 mL of H_2O was added 30% NH_4OH till dissolution of the hydroxide initially formed. To the clear solution was added 20 g of alumina (Riedel-De-Haen), pH 4.5, surface area 200 m^2/g, particle size 70–290 mesh. The suspension was stirred for 10 min and diluted, very slowly, to 2-L volume, stirred for 30 min, and filtered. The solid was dried at 120 °C for 4 h and heated in air at 350 °C for 6 h.

The catalyst was pretreated at 270 °C with H_2 at atmospheric pressure (prereduced catalyst: Cu/Al_2O_3) according to the procedure previously reported for copper chromite,[20] before its use in the hydrogenation reaction. Cu/Al_2O_3 obtained in this way has a copper content of 7–8%, determined by atomic absorption, surface area before the reduction treatment 220–250 m^2/g (BET method[33]), specific Cu(0) area after pretreatment 20–30 m^2/g (N_2O decomposition[34]).

Hydrogenation Procedure. The steroid (0.2 mmol) was dissolved in toluene (6 mL) and the solution heated to 60 °C and then transferred, under H_2, into the reaction vessel where the catalyst (150 mg) had been previously pretreated. The final charge of H_2 was adjusted to 1 atm with a mercury leveling bulb, stirring was begun, and H_2 uptake was measured through a mercury sealed gas buret.

To monitor the product distribution versus H_2 uptake (Figure 1), 20-μL samples were withdrawn from the reacting solution through a viton septum and analyzed by GC. The number of equivalents of hydrogen was calculated on the basis of the molar amount of H_2 consumed by each molecule, e.g., [(74% 4-en-3-one $\times$ 1H_2) + (17% **a** $\times$ 2H_2) + (4% 1-en-3-one $\times$ 1H_2) + (5% **b** $\times$ 2H_2)] = 122% H_2 consumed = 1.2 equiv.

As 5β and 5α stereoisomers give well-separated GC peaks and significative differences in mass spectra, their formation can be monitored during reaction by GC and/or GC–MS. After absorption of 1 or 2 equiv of H_2 (GC monitoring) on a 0.5-g-scale experiment, the reaction mixture was eluted on silica with ethyl ether/hexane or toluene/hexane and the products were identified.

The equatorial:axial ratio was determined inside the separated fractions by digitonide precipitation,[35] GC quantitative determination after silyl derivative formation,[36] and CAD-MIKE spectroscopy following the procedure already described.[37]

Catalytic Hydrogenation of 5. Compound **5** (60 mg, 0.2 mmol) was dissolved in dioxane (6 mL) and the solution added, under H_2, to (a) 5% Pd/C (50 mg) previously dried at 50 °C for 20 min or (b) 1% Pd/Al_2O_3 (150 mg) previously kept under H_2 flow at 200 °C for 5 minutes, in a reaction vessel connected to a gas buret. The reaction mixture was stirred at 25 °C under 1 atm of H_2; after consumption of 1 equiv of H_2 (volumetric), the mixture was analyzed by GC.

Hydrogenation of 5 in the Presence of $RuCl_2(PPh_3)_3$. Steroid **5** (500 mg, 1.8 mmol), $RuCl_2(PPh_3)_3$ (51 mg, 0.05 mmol), NEt_3 (5 mg, 0.05 mmol), and anhydrous benzene (10 mL) were placed in a bomb equipped with a Teflon liner and magnetic stirrer. The bomb was filled with hydrogen (130 atm) and heated at 50 °C, and stirring was begun. After 10 h the reaction was stopped and the benzene solution was passed through alumina to separate the catalyst. Analysis by GC gave the results collected in Table II.

Registry No. 1, 63-05-8; **1a**, 1229-12-5; **1b**, 846-46-8; **3c** (equatorial), 53-42-9; **1c** (axial), 571-31-3; **1d**, 481-29-8; **2**, 57-83-0; **2a**, 128-23-4; **2b**, 566-65-4; **2c**, 128-20-1; **2d**, 516-55-2; **3**, 57-85-2; **3a**, 18179-14-1; **3b**, 855-22-1; **4**, 601-57-0; **4a**, 601-53-6; **4b**, 566-88-1; **4c**, 516-92-7; **4d**, 80-97-7; **5**, 897-06-3; **6**, 57-88-5; **7**, 979-02-2; 5-pregnen-3β-ol-20-one acetate, 1778-02-5.

Supplementary Material Available: ^{13}C NMR spectra of compounds **3a**, **3b** and pregnenolone acetate (hydrogenation product of compound **7**) and listing of ^{13}C NMR data for the other hydrogenated products (9 pages). Ordering information is given on any current masthead page.

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Reformatsky and Luche Reaction in the Absence of Solvent

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Reformatsky (eq 1) and Luche reactions (eq 2) with Zn provide more economical C–C bond formation methods than Grignard reactions with more expensive Mg metal.

$$R^1R^2C{=}O + BrCH_2COOR^3 \xrightarrow{Zn} R^1R^2C(OH)CH_2COOR^3 \quad (1)$$

$$R^1R^2C{=}O + BrCH_2CH{=}CH_2 \xrightarrow{Zn} R^1R^2C(OH)CH_2CH{=}CH_2 \quad (2)$$

$$\underset{1}{ArCHO} + \underset{2}{BrCH_2COOEt} \xrightarrow[NH_4Cl]{Zn} \underset{3}{ArCH(OH)CH_2COOEt}$$

In addition, we found that Reformatsky and Luche reactions proceed efficiently in the absence of solvent, although Grignard reactions under similar conditions are not very efficient and give more reduction product than the normal carbonyl addition product.[1] The nonsolvent Reformatsky and Luche reactions can be carried out by a very simple procedure and give products in higher yield than with solvent.

In general, the nonsolvent reaction was carried out by mixing aldehyde or ketone, organic bromo compound, and Zn–NH_4Cl in an agate mortar and pestle and by keeping the mixture at room temperature for several hours.

Treatment of the aromatic aldehydes (**1a–e**) with ethyl bromoacetate (**2**) and Zn–NH_4Cl gave the corresponding Reformatsky reaction products (**3a–e**) in the yields shown in Table I. The yield, for example, of **3a** obtained in the nonsolvent reaction (91%) is much better than that obtained by the reaction in dry benzene–ether solution (61–64%).[2] The nonsolvent Reformatsky reaction, which does not require the use of an anhydrous solvent, is thus advantageous.

Synthesis of homoallylic alcohols by the Luche reaction[3] can also be carried out efficiently in the absence of solvent. Treatment of aldehydes (**1a**, **1e**, **5**, **6**) or ketones (**7**, **8**) with 3-bromopropene (**4**) and Zn–NH_4Cl in the absence of solvent gave the corresponding Luche reaction products (**9–14**) in the yields shown in Table II. It has been reported that the Luche reaction of **8** with **4** in water[4] and

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Table I. Reaction Time and Yield of the Product 3 in the Reformatsky Reactions of 1 and 2 in the Absence of Solvent

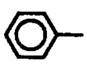
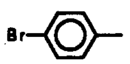
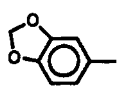
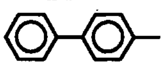
1	Ar	reaction time (h)	yield (%) of 3
a		2	91
b		3	94
c		3	94
d		3	83
e		3	80

Table II. Reaction Time and Yield of the Luche Reaction of Aldehydes and Ketones with 4 in the Absence of Solvent

aldehyde or ketone	reaction time (h)	product	
			yield (%)
1a	4	9	99
1e	4	10	87
5	1	11	83
6	1	12	98
7	2	13	89
8	2	14	90

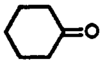
DMF[5] at room temperature gives 14 in 82 and 99% yields, respectively. However, the nonsolvent reaction procedure is much simpler and does not require removal of solvent.

$BrCH_2CH{=}CH_2$ **4**

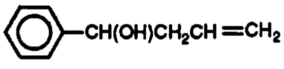
$CH_3CH_2CH_2CH_2CH_2CHO$ **5**

trans-$CH_3CH{=}CHCHO$ **6**

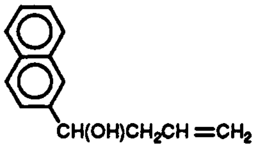
$CH_3CH_2CH_2CH_2COCH_3$ **7**



8



9

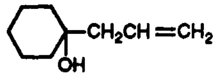


10

$CH_3CH_2CH_2CH_2CH_2CH(OH)CH_2CH{=}CH_2$ **11**

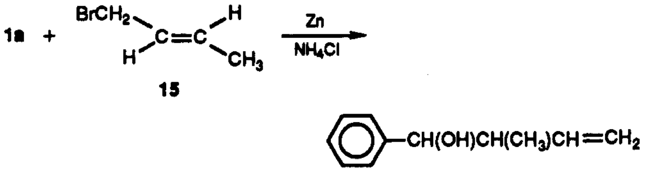
trans-$CH_3CH{=}CHCH(OH)CH_2CH{=}CH_2$ **12**

$CH_3CH_2CH_2CH_2C(CH_3)(OH)CH_2CH{=}CH_2$ **13**



14

The steric course of the Luche reaction in the absence of solvent is slightly different from that in solution. Thus, while the Luche reaction of 1a and 1-bromo-2-butene (15) in THF gives 16 in 90% yield in a 57:43 erythro–threo ratio,[4] the same reaction in the absence of solvent gives 16 in 98% yield in a 43:57 erythro–threo ratio.



In the Luche reaction in solution, NH_4Cl plays an important role and the yield of the reaction product increases dramatically upon its addition.[3] The role of NH_4Cl in the Luche reaction in solution has been postulated to be the activation of Zn.[3] In the case of the nonsolvent Luche reaction, however, NH_4Cl is not very important. The nonsolvent reaction of 8 and 4 in the absence of NH_4Cl, for example, gave 14 in 76% yield. Interestingly, when the reaction is carried out in an NH_3 atmosphere, the yield of 14 increased to 84%. However, Zn–NaCl[6] and Zn–$ZnCl_2$ reagents,[7,8] which are very effective for the reduction of activated olefins and ketones and coupling of aromatic aldehydes and ketones to pinacol, respectively, were not effective for the Luche reaction in the absence of solvent.

Experimental Section

General Procedure for the Reformatsky Reaction in the Absence of Solvent. A mixture of aromatic ketone (1; 5.1 mmol), ethyl bromoacetate (2; 2.56 g, 15.3 mmol), Zn powder (5 g), and NH_4Cl (2 g) was thoroughly ground in an agate mortar and pestle, and the mixture was kept at room temperature for 2–3 h. The reaction product was mixed with aqueous NH_4Cl and extracted with ether. The ether solution was washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent and volatile ketone in vacuo gave the product 3 in pure form in the yields shown in Table I. The purity of 3 was determined by HPLC and ^1H NMR spectroscopy.

General Procedure for the Luche Reaction in the Absence of Solvent. A mixture of aldehyde (**1a**, **1e**, **5**, **6**) or ketone (**7**, **8**) (5.1 mmol), allyl bromide (**4**; 3.09 g, 25.5 mmol), Zn powder (5 g), and NH_4Cl (2 g) was ground in an agate mortar and pestle, and the mixture was kept at room temperature for 1–4 h. The product was mixed with aqueous NH_4Cl and extracted with ether. The ether solution was washed with water and dried over anhydrous $MgSO_4$. The solvent and volatile material were removed in vacuo to give the corresponding Luche reaction product in pure state in the yields shown in Table II. The purity of the Luche reaction product was determined by HPLC and ^1H NMR spectroscopy.

Luche Reaction of 1a and 15. A mixture of **1a** (0.54 g, 5.1 mmol), 1-bromo-2-butene (**15**; 1.38 g, 10.2 mmol), Zn powder (5 g), and NH_4Cl (2 g) was treated as in the previous text to give the Luche reaction product **16** (0.81 g, 98% yield). The threo–erythro ratio of **16** was determined to be 57:43 by ^1H NMR spectroscopy.[9]

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