NMR ($CDCl_3$) δ 1.5–2.2 (m, 6 H, CH_2), 2.67 (s, 3 H, CH_3), 4.47 (s, 1 H, 1-CH), 7.0–7.4 (m, 5 H, aromatic).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.73; H, 7.40. Found: C, 72.72; H, 7.31.

Registry No.—**1a**, 64425-71-4; **1b**, 64425 72-5; **1c**, 64425-73-6; **1f**, 64425-74-7; **2a**, 64425-75-8; **2b**, 64425-76-9; **2c**, 64425-77-0; **2f**, 64425-78-1.

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Reduction of Aromatic Amides by Sodium in Liquid Ammonia

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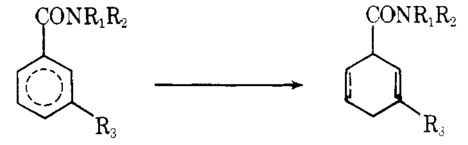
Because of reported variations for Birch reduction[1] of aromatic amides, we undertook a study of the reduction of benzamide (1), *m*-methoxybenzamide (2), *N*-methylbenzamide (3), and *N,N*-dimethylbenzamide (4).

We have found that some ring reduction of 1 to 1,4-dihydrobenzamide (5) occurs with sodium and either ethanol or *tert*-butyl alcohol while Kuehne and Lambert[2] report ring reduction with *tert*-butyl alcohol but not with ethanol. However we found *tert*-butyl alcohol more effective than ethanol with reduction proceeding well with 3.42 equiv of sodium regardless of whether the sodium or the *tert*-butyl alcohol was added last.[3]

In contrast ethanol gave poor and erratic results with the amount of **5** varying from reduction to reduction but never exceeding 50% when the procedure of adding sodium last was used. The crude product contained unreduced **1**, tetrahydro products, as well as **5** but not benzaldehyde or toluene. These latter two compounds were sought using GLC and were not found. Nor was any hydrobenzamide (**11**) found. Progressively increasing the sodium from 3.3 equiv to 5.0, 7.0, or 9.0 equiv progressively decreased the amount of unreduced **1**, increased the amount of tetrahydro products, but did not substantially increase **5**. This strongly suggests that **5** is an intermediate in the formation of the tetrahydroproducts. One experiment using 5.0 equiv of sodium plus an equimolar mixture of ethanol and *tert*-butyl alcohol gave no improvement over use of ethanol alone.

Also with *tert*-butyl alcohol, its addition last or sodium addition last made little or no difference. But in the case of ethanol, its addition last gave even less **5** than when sodium was added last.



1, R_1, R_2, R_3 = H
2, R_1, R_2 = H; R_3 = OCH_3
3, R_1, R_3 = H; R_2 = CH_3
4, R_3 = H; R_1, R_2 = CH_3

5, R_1, R_2, R_3 = H
6, R_1, R_2 = H; R_3 = OCH_3
7, R_1, R_3 = H; R_2 = CH_3

If no ammonium chloride was added to neutralize the alkoxide before work-up, then air oxidation of **5** to reform **1** occurred. A control experiment started with a solution of **5** in ammonia containing sodium ethoxide which was similarly exposed to air resulted in reformed **1**. Kuehne and Lambert[2] also report similar base-catalyzed air oxidations.

m-Methoxybenzamide (**2**) was reduced to 1,4-dihydro-3-methoxybenzamide (**6**) with 3.3 equiv of sodium and ethanol at −75 °C. At −33 °C more extensive reduction occurred yielding a mixture which was not separated. When 8.0 equiv of sodium at −33 °C was used, more extensive reduction resulted[4] in formation of 1,4,5,6-tetrahydro-3-methoxybenzyl alcohol (**8**). Kuehne and Lambert[2] report no reduction of **2** with 3.3 equiv of sodium and formation of **6** with 7.6 equiv of sodium.

While we can offer no firm explanation as to why our results[5] with **1** and **2** differ from those of Kuehne and Lambert,[2] it can be noted that the effects of many experimental variables on the Birch reduction are incompletely understood.[6]

Possibly more of their sodium was consumed in a side reaction. Thus reduction of **1** may have been too incomplete to be detected and reduction of **2** would have required more sodium. Such a side reaction might be sodium with alcohol and/or ammonia to produce hydrogen. Since their work, small amounts of colloidal iron, which commonly occur in commercial ammonia, have been reported to catalyze this reaction and affect Birch reductions.[6b–d]

An additional factor must be involved in the reduction of **1** with ethanol as more extensive reduction to tetrahydro products occurs. This consumes additional sodium but also requires formation of a conjugated diene as isolated double bonds are not reduced under these conditions. The conjugated diene could form if the more acidic ethanol is less specific in protonation of the anion intermediate than *tert*-butyl alcohol or by rapid rearrangement of initially formed unconjugated diene. The alkoxide produced in the reduction could catalyze this rearrangement and, as ethanol is reported[6b] to react faster than *tert*-butyl alcohol under these conditions, the more rapidly formed ethoxide could catalyze rearrangement faster than the more slowly formed *tert*-butoxide.

The following two experiments indicate the latter explanation is insufficient to explain the different results with ethanol and *tert*-butyl alcohol. Based on the report of Dryden[6b] that the presence of 0.5 or 1.0 ppm of iron increased the rate of the reaction of *tert*-butyl alcohol and sodium to that comparable to ethanol and sodium, we did a reduction using *tert*-butyl alcohol, adding 3.42 equiv of sodium last and having 1 ppm of iron present. There was a definite increase in the rate of disappearance of the sodium but **5** was still obtained in good yield and without any appreciable tetrahydro product. Another experiment using *tert*-butyl alcohol with 3.42 equiv of *tert*-butoxide initially present with 3.42 equiv of sodium

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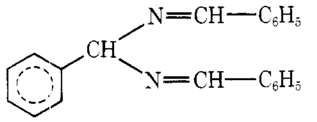
added last also yielded **5** in good yield without appreciable tetrahydro product. Possibly ethoxide catalyzes the double bond isomerization more rapidly than does *tert*-butoxide. Formation of more further reduced products with ethanol than with *tert*-butyl alcohol also occurs[6e] for reduction of anisoles and aromatic amines.

That ring reduction of **2** is easier than **1** is understandable as the methoxy group would stabilize the radical anion intermediate.[7] Anisole undergoes reduction more than three times faster than benzene.[8]

Reduction of *N*-methylbenzamide (**3**) resembled that of benzamide with ring reduction occurring with either ethanol or *tert*-butyl alcohol. With 5.0 equiv of sodium added last, ethanol gave some dihydro product (presumably 1,4-dihydro-*N*-methylbenzamide (**7**)), which was not successfully isolated, but mostly 1,4,5,6-tetrahydro-*N*-methylbenzamide (**9**), which was isolated and characterized. Use of *tert*-butyl alcohol added last and 3.42 equiv of sodium or use of ethanol and either 4.0 or 3.42 equiv of sodium added last yielded product which was largely the dihydro product and small amounts of starting material and tetrahydro product. Attempts to isolate the dihydro product by recrystallization were unsuccessful as the material underwent air oxidation back to **3** and some polymerization during these attempts. No presence of toluene or benzaldehyde was detected. No addition of NH_4Cl after reduction and before work-up resulted in increased **3** apparently reformed by air oxidation and little or no dihydro product.

The structure of **9** was assigned as NMR showed two vinyl hydrogens and the only other possibility with two vinyl hydrogens, 1,2,5,6-tetrahydro-*N*-methylbenzamide, was prepared and found not to be identical.

Unlike the other aromatic amides, *N*,*N*-dimethylbenzamide (**4**) underwent reduction of the amide group to form benzaldehyde (**10**) which was isolated as was hydrobenzamide (**11**), the condensation product of benzaldehyde and ammonia. The path for such a reduction has been proposed by Benkeser[9] for the related electrochemical reduction of amides and consists of stepwise addition of electrons and protons to the carbonyl group.



11

Although we found no toluene in the reduction of **4**, in principle it could form. Reduction of benzaldehyde to benzyl alcohol is to be expected[10] and benzyl alcohols are reduced to aromatic hydrocarbons under similar conditions.[6a,10]

Thus aromatic amides under Birch conditions follow a pattern of ring reduction if there is an amide hydrogen present and amide reduction if there is not. Presence of an amide hydrogen allows formation of an amide anion which protects the amide group from reduction.[2] When ring reduction occurs, it is in the 1,4 positions as with aromatic acids rather than in the 2,5 positions observed with most substituents. Thus aromatic amides with an amide hydrogen resemble aromatic acids and not aromatic amidines,[11] sulfonamides,[12] and sulfinic acids[13] which are reduced in the functional group and not in the ring.

Experimental Section[14]

Reduction of Benzamide (1). To a stirred, refluxing (−33 °C) mixture of 800 mL of NH_3, 200 mL of anhydrous *tert*-butyl alcohol, and 10.0 g (0.0826 mol) of **1** was added 6.3 g (0.274 g-atom, 3.32 equiv) of sodium in small pieces over a period of 10 min. After the deep blue color faded (15 min), 30 g of NH_4Cl was cautiously added and the ammonia was allowed to evaporate. The solid residue was dissolved in water and the organic material was extracted with four 250-mL portions of methylene chloride. The combined extracts were dried over $MgSO_4$. Evaporation of the solvent left 5.09 g (0.0413 mol, 50.0%) of solid, mp 137–143 °C, which NMR indicated was more than 90% 1,4-dihydrobenzamide (**5**) with possible small amounts of tetrahydro material and less than 10% of **1**. After two recrystallizations from benzene the mp was 152–153 °C [lit.[2] mp 154–155 °C]. Additional extracts could yield 3 to 4.5 g of less pure **5**.

After one reduction, 200 mL of ether was added and the ammonia was allowed to evaporate through two traps cooled in ice. GLC of the trapped liquid indicated no toluene. GLC of the ether layer indicated no toluene or benzaldehyde.

Reduction of 10.0 g (0.066 mol) of *m*-methoxybenzamide (**2**) was done as for **1** above but with 135 mL of absolute ethanol and a temperature (−75 °C) near dry ice. Seven extractions yielded 9.7 g (0.064 mol, 97%) of solid, mp 135–144 °C. Two recrystallizations from benzene and petroleum ether gave 3.25 g (32%) of 1,4-dihydro-3-methoxybenzamide (**6**), mp 161–163 °C [lit.[2] 158–160 °C].

Reduction of 10.0 g (0.074 mol) of *N*-methylbenzamide (**3**) was done as for **1** above but with 12 mL of absolute ethanol added last over 30 min. NMR of the 7.42 g of semisolid product, mp 72–74 °C, indicated small amounts of **3**, some 1,4,5,6-tetrahydro-*N*-methylbenzamide (**9**), but mostly material believed to be the expected 1,4-dihydro-*N*-methylbenzamide (**7**) (strong absorption at δ 5.8). Increasing the sodium to 5.0 equiv (8.51 g) yielded 9.23 g of viscous, brown liquid which NMR indicated was mostly **9**. GLC on 10 ft, 10% carbowax on 80/100 mesh firebrick treated with HMDS yielded sufficient **9**, mp 49–50 °C, for characterization: NMR ($CDCl_3$) δ 1.5–2.4 (complex m, 7 H, ring CH_2 and CH groups), 2.8 (d, 3 H, $NHCH_3$, J = 4.5 Hz), 2.7–3.2 (complex m, 1 H, -NH-), 5.5–6.2 (m, 2 H, vinyl H). Anal. Calcd for $C_8H_{13}ON$: C, 69.06; H, 9.35; N, 10.07; O, 11.51. Found: C, 69.07; H, 9.51; N, 10.07; O, 11.66.

Reduction of *N*,*N*-Dimethylbenzamide (4). From a procedure similar to that for **1** above, 10.0 g (0.0673 mol) of **4**, 5.11 g of sodium (0.222 g-atom, 3.3 equiv), and 9.0 mL of ethanol added last yielded 8.11 g of a viscous liquid which NMR indicated contained benzaldehyde, hydrobenzamide (**11**), and starting material. GLC confirmed the presence of benzaldehyde. From a similar reduction using 3.09 g (0.135 g-atom, 2.0 equiv) of sodium 0.42 g (0.0040 mol, 5.9% yield) of benzaldehyde was separated by means of sodium bisulite extractions and converted to 2,4-dinitrophenylhydrazone, mp 237–240 °C [lit.[15] 237 °C].

The **11** was identical to the authentic sample prepared from ammonia and benzaldehyde; after recrystallization four times from ethanol the mp was 103–104 °C [lit.[16] 102 °C]. Heating **11** produced 2,4,5-triphenylimidazole, mp 253–260 °C; after three recrystallizations from ethanol the mp was 274–275 °C [lit.[17] 276.5–277 °C]; picrate mp was 235–236 °C [lit.[18] mp 234 °C].

Whether ethanol or *tert*-butyl alcohol was used or whether the alcohol or the sodium was added last, the product was the same. Increasing the sodium to 5.0 or 10.0 equiv resulted in an uncharacterized, complicated mixture.

Acknowledgments. Appreciation is expressed to the Research Corp. for their support of the early stages of this investigation by a Frederick Gardner Cottrell grant, and to Dr. G. E. Pollard and the Shell Development Co., Modesto, Calif. for many of the NMR spectra.

Registry No.—**1**, 55-21-0; **2**, 5813-86-5; **3**, 613-93-4; **4**, 611-74-5; **5**, 64739-70-4; **6**, 64739-71-5; **7**, 64739-72-6; **9**, 64739-73-7; **10**, 100-52-7; **11**, 92-29-5; ammonia, 7664-41-7; sodium, 7440-23-5; 2,4,5-triphenylimidazole, 484-47-9.

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Stereochemistry of Grignard Additions to α-Keto Esters

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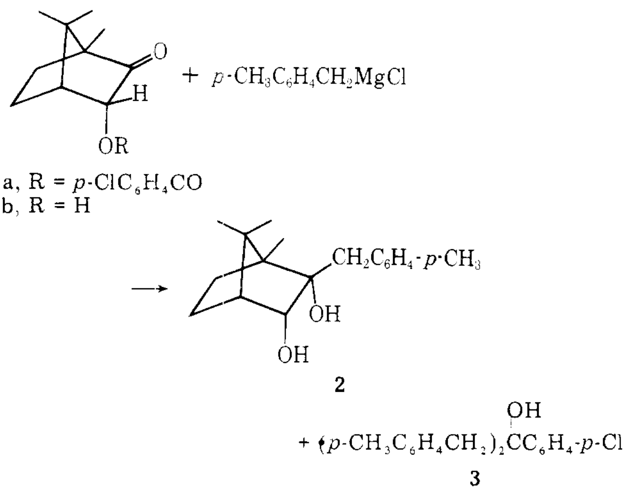
We have previously reported[1] unexpected stereospecificity in Grignard additions to α-keto esters in the bornane series and now wish to describe unexpected results obtained with a series of α-keto esters in the 2,2,5,5-tetramethyltetrahydrofuran series. In the earlier work, *cis*-2,3-dihydroxy-2- (or 3-) (*p*-methylbenzyl)bornanes were obtained from the four possible α-ketol *p*-chlorobenzoates even when this required the unusual exo attack of *p*-methylbenzylmagnesium chloride on the bornane system. For example, reaction of the *p*-chlorobenzoate **1a** of 3-*endo*-hydroxy-2-bornanone (**1b**) with the reagent afforded only 2,3-*cis,endo*-dihydroxy-2-*exo*-(*p*-methylbenzyl)bornane (**2**) and bis(*p*-methylbenzyl)-*p*-chlorophenylcarbinol (**3**).



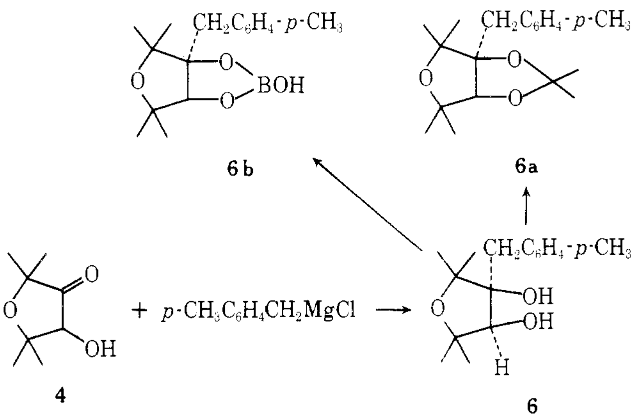
1a, R = p-ClC_6H_4CO
b, R = H

2

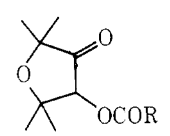
$$+\ (p\text{-}CH_3C_6H_4CH_2)_2\overset{OH}{C}C_6H_4\text{-}p\text{-}Cl$$

3

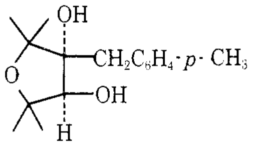
In the course of an investigation of photochemical reactions of the unusual α-diketone, 2,2,5,5-tetramethyltetrahydrofuran-3,4-dione,[2] with aldehydes, the corresponding α-ketol **4** and a number of its esters (**5a–d**) became available. In view of the earlier results, it appeared of interest to investigate their reactions with the Grignard reagent. Reaction of **4** with *p*-methylbenzylmagnesium chloride afforded the *cis*-diol **6** in nearly quantitative yield. The cis configuration was assigned on the basis of rapid cleavage with sodium periodate and formation of an acetonide (**6a**) and a borate ester (**6b**), both of which regenerated **6** upon hydrolysis. The *trans*-diol **7** was obtained together with **6** and **6b** upon sodium borohydride reduction of 3-hydroxy-3-(*p*-methylbenzyl)-2,2,5,5-tetramethyltetrahydrofuran-4-one[2] (**8**) or together with **6** from Grignard reactions of the esters **5a–d**. Pure **7** was isolated from its mixture with **6** by reaction of the mixture with acetone and anhydrous cupric sulfate, followed by chromatographic separation of **7** from **6a**. In addition to this failure to form an acetonide, the trans configuration of **7** was confirmed by its complete failure to form a borate ester or to react with sodium periodate under conditions comparable to those used successfully with **6**. Both **6** and **7** were oxidized to **8** under mild conditions.



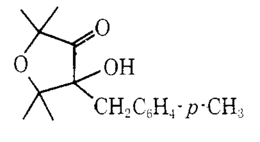
6b 6a 4 6



5a, R = p-$CH_3OC_6H_4$–
b, R = C_6H_5–
c, R = p-ClC_6H_4–
d, R = CH_3CH_2–



7



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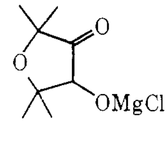

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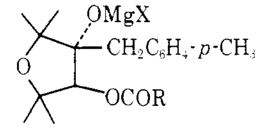

10

Gas chromatographic retention times of **6** and **7** differed markedly. It was thus readily possible to establish the stereochemistry of reaction of the esters **5a–d** with *p*-methylbenzylmagnesium chloride and to compare the results with the complete specificity observed in the bornane series and with **4**. Results of a series of experiments using a 3.5-fold excess of Grignard reagent are summarized in Table I. It is interesting

Table I. Reactions of Esters of 3-Hydroxy-2,2,5,5-tetramethyltetrahydrofuran-4-one (4) with *p*-Methylbenzylmagnesium Chloride[a]

Ester	Registry no.	*cis*-Diol 6,[b] %	*trans*-Diol 7,[b] %
p-Methoxybenzoate **5a**	64314-66-5	20	80
Benzoate **5b**	64314-67-6	25	75
p-Chlorobenzoate **5c**	64314-68-7	50	50
Propionate **5d**	64314-69-8	68	32

[a] Addition of ca. 0.08 M ester in ether to a 3.5-fold excess of ca. 0.34 M Grignard reagent in ether. [b] Determined by gas chromatographic analysis.