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Mechanical Activation of Magnesium Turnings for the Preparation of Reactive Grignard Reagents

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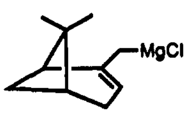
Preactivation of magnesium by dry stirring in an inert atmosphere is highly beneficial for the clean synthesis of reactive allylic or benzylic organomagnesium chlorides. This procedure routinely produces 0.4 M solutions of the Grignard reagent in diethyl ether free from coupling products. The purity may be directly assayed by ^{13}C NMR spectroscopy. Using spin saturation transfer techniques, the rate constant for interconversion of the enantiomers of (1-phenyl-2-methylpropyl)magnesium chloride in Et_2O at 25 °C was shown to be $<0.2\ s^{-1}$. Electron microscopy has been used to define the surface changes occurring during the dry stirring of magnesium turnings.

Introduction

Two specific problems limit the ease of synthesis of Grignard reagents. The first is that unreactive halides can react very sluggishly with magnesium, leading to low yields and/or incomplete conversion. The second, which is a particular difficulty with reactive allylic or benzylic halides, relates to the ease of formation of coupled product by direct reaction between the halide and reagent. These constraints have led to the development of a range of methods designed to provide more active and reactive forms of metallic magnesium.

The reaction of organohalides with magnesium requires electron transfer from the metal surface to halide,[1] which leads to formation of an organic radical R•. The carbon–magnesium bond is formed by reaction of this radical with the metal surface; recombination with halide ion then produces the R–MgX entity. In many cases, the initial step is limited by diffusion control,[2] and consequently the available surface area of active magnesium is a critical factor. This is important when the Grignard reagent reacts rapidly with its precursor, so that RMgX is in competition with the Mg surface for the organic halide.

Reactive magnesium powder can be prepared by Rieke's method in which magnesium halides are reduced in situ by metallic potassium.[3] The resulting finely divided black powder can be especially useful in the synthesis of Grignard reagents where the halide reacts only sluggishly.[4] An alternative approach to the synthesis of highly dispersed magnesium requires the evaporative sublimination of high purity metal in vacuo with condensation into a solvent slurry at −196 °C.[5] Using magnesium prepared in this way, reagent 1 can be synthesized in 60% yield, although its synthesis proved impossible by conventional techniques.[6]



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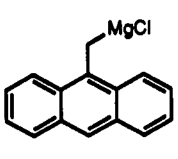

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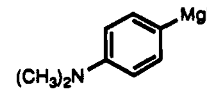

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The availability of magnesium anthracene provided a major advance for the synthesis of reactive Grignard reagents.[7] This orange, thf-soluble adduct, whose X-ray crystal structure has been determined, is especially effective for the preparation of benzylmagnesium halides, some of which (e.g. 2) are otherwise difficult to synthesize.[8] The reagent is easily prepared, but formation of 1 mol of anthracene for each mode of Grignard reagent consumed when the stoichoimetric reagent is used presents a drawback.

Commercial unactivated magnesium turnings may be activated by sonication.[9] This method has been employed to initiate sluggish Grignard reactions in ether and appears to be critically dependent on the water content of the ethereal solution. It is suggested that the function of ultrasound is to disperse surface-bound water from the metal, since there is an induction period which increases dramatically with increasing water content.[10] Sonication is the preferred technique for effecting the Barbier variation, in which the carbonyl compound and organohalide are introduced concomitantly and the Grignard reagent is then intercepted as fast as it is formed.[11]

There have been scattered reports in the literature of magnesium activation through stirring the solid in an inert atmosphere. The method is exemplified by the synthesis of 3 which frustrated attempts at its preparation by con-

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[1] For recent studies on the mechanism of Grignard reagent formation, see: Root, K. S.; Hill, C. L.; Lawrence, L. M.; Whitesides, G. M. *J. Am. Chem. Soc.* 1989, *101*, 5405 and references therein. Walborsky, H. M.; Rachon, J. *J. Am. Chem. Sox.* 1989, *111*, 1896. Garst, J. F.; Swift, B. L. *J. Am. Chem. Soc.* 1989, *111*, 241.

[2] Garst, J. F.; Deutch, J. M.; Whitesides, G. M. *J. Am. Chem. Soc.* 1986, *108*, 2490.

[3] Rieke, R. D.; Hudnall, P. M. *J. Am. Chem. Soc.* 1972, *94*, 7178. Rieke, R. D.; Bales, S. E. *J. Chem. Soc., Chem. Commun.* 1973, 879. Rieke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* 1974, *96*, 1775. Rieke, R. D.; Li P. T.-Z.; Burns, T. P.; Uhm, S. T. *J. Org. Chem.* 1981, *46*, 4323.

[4] Rieke, R. D.; Bales, S. E.; Hudnall, P. M.; Burns, T. P.; Poindexter, G. S.; *Organic Syntheses*, Wiley New York, 1988; Collect Vol. VI, p 845.

[5] Kündig, E. P.; Perret, C. *Helv. Chim. Acta* 1981, *64*, 2606.

[6] Oppolzer, W.; Kündig, E. P.; Bishop, P. M.; Perret, C. *Tetrahedron Lett.* 1982, *23*, 3901.

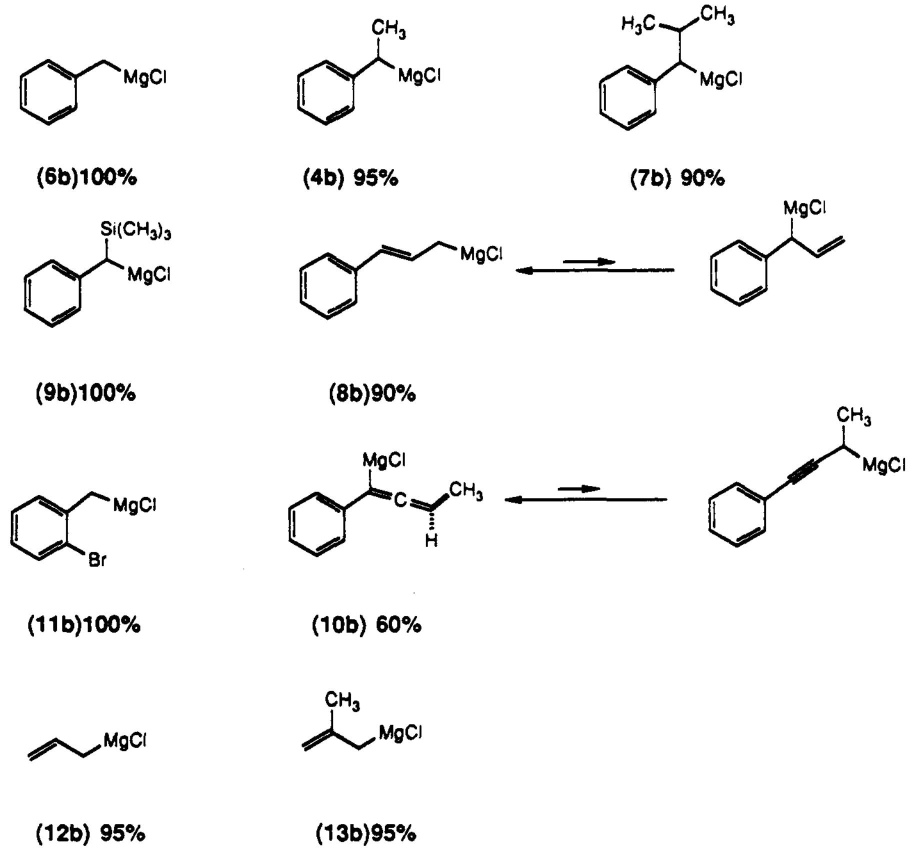
[7] Bogdanovic, B.; Liao, S.-T.; Schwickardi, M.; Sikorsky, P.; Spliethoff, B. *Angew. Chem., Int. Ed., Engl.* 1980, *19*, 818. Bodganovic, B.; Janke, N.; Krüger, C.; Mynott, R.; Schlichte, K.; Westeppe, U. *Angew. Chem., Int. Ed. Engl.* 1985, *24*, 960.

[8] Raston, C. L.; Salem, G. *J. Chem. Soc., Chem. Commun.* 1984, 1702. Gallagher, M. J.; Harvey, S.; Raston, C. L.; Sue, R. E. *J. Chem. Soc., Chem. Commun.* 1988, 289. Harvey, S.; Raston, C. L. *J. Chem. Soc., Chem. Commun.* 1988, 652. Nicoletti, T. M.; Raston, C. L.; Sargent, M. V. *J. Chem. Soc., Chem. Commun.* 1988, 1491. Harvey, S.; Junk, P. C.; Raston, C. L.; Salem, G. *J. Org. Chem.* 1988, *53*, 3134. See: de Boer, H. J. R.; Akkerman, O. S.; Bickelhaupt, F. *J. Organomet. Chem.* 1987, *321*, 291, for a more conventional approach to 2.

[9] Lorimer, J. P.; Mason, T. J. *Chem. Soc. Rev.* 1987, *16*, 239. Lindley, J.; Mason, T. J. *Chem. Soc. Rev.* 1987, *16*, 275. Luche, J.-L.; Damiano, J.-C. *J. Am. Chem. Soc.* 1980, *102*, 7926.

[10] Sprich, J. D.; Levandos, G. S. *Inorg. Chim. Acta* 1982, *76*, 1241.

[11] Ishikawa, N,; Koh, M. G.; Kitazume, T.; Choi, S. K. *J. Fluorine Chem.* 1984, *24*, 419. For related Li chemistry, see: De Sousa-Barbosa, J. C.; Pétrier, C.; Luche, J. L. *J. Org. Chem.* 1988, *53*, 1212.



(6b)100% **(4b)** 95% **(7b)** 90% **(9b)**100% **(8b)**90% **(11b)**100% **(10b)** 60% **(12b)** 95% **(13b)**95%

Figure 1. *Grignard reagents prepared by the "dry-stir" method.*

ventional techniques.[12] The development of this method has proved very effective in synthesis of several allyl- and benzylmagnesium halides. We report its application, together with solution NMR studies on the reagents produced, and electron microscopy of the surface to determine the changes induced.

Results and Discussion

Preparative Aspects. The incentive for this work came from studies on asymmetric cross-coupling.[13] Many authors who have studied this reaction with nickel or palladium complex catalysts have examined the coupling of (α-phenylethyl)magnesium chloride (**4b**) with vinyl bromides. This particular Grignard reagent is notoriously difficult to obtain pure, being contaminated by up to 40% of (R^*R^*)- and (R^*S^*)-1,2-dimethyl-1,2-diphenylethane (**5**), the homocoupling product. We experienced this problem, but because a major objective of the work was to probe the mechanism of asymmetric cross-coupling, a pure reagent was required. Neither sonication or the use of different grades of magnesium powder provided a satisfactory solution.

In order to test the dry stirring procedure, a batch of commercial magnesium turnings (Fison's) was mechanically stirred with a Teflon bar in a wide-bore Schlenk tube under a nitrogen atmosphere for 15 h. This led to gross changes in the appearance of the magnesium. The particle size was reduced, the color was much darker gray-black, and a magnesium mirror had been deposited on the lower walls of the Schlenk tube. At this stage the metal was covered with dry Et_2O, maintaining the inert atmosphere. A solution of freshly distilled α-phenethyl chloride (**4a**) in Et_2O was added dropwise to the center of the vortex of the stirred magnesium slurry held at 0 °C over a period of 3–4 h. The quantity of magnesium constituted a 5-fold excess over the halide. In this way a clear solution was maintained. This contrasts with the normal appearance of the reaction mixture during preparation of **4b**, when substantial precipitation of $MgCl_2$ is formed as a result of homocoupling, leading to cloudiness and eventually a white precipitate.

After addition was complete, the Grignard solution was filtered throug a frit under positive nitrogen pressure and made up to a standard volume with dry Et_2O in a second Schlenk tube. The purity was then established in one of two ways: by titration against 0.1 M HCl or by direct ^{13}C observation. For the latter, an aliquot of the Grignard solution was transfered under argon to an 8.4-mm NMR tube sealed with a septum, and the spectrum was recorded on a Bruker AM 250 with CD_3OD lock solvent in a coincentric 10-mm tube. If the procedure described above is followed carefully, the Grignard reagent **4b** is produced free from impurities detectable by ^{13}C NMR, including the coupled product **5**.

It was established that the nitrogen atmosphere can be replaced by argon without affecting the activation process. This demonstrates that surface Mg nitrides do not play a part.

The successful application of dry-stir activation to the synthesis of **4b** encouraged us to carry out a series of experiments in which allyl or benzyl chlorides were converted

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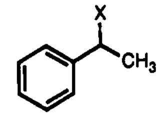
[12] Mendel, A. *J. Organomet. Chem.* **1966**, *6*, 97. Among earlier studies on the mechanical activation of magnesium, see: Gilman, H.; Meyers, C. *J. Am. Chem. Soc.* **1923**, *45*, 159. Fuson, R. C.; Hammann, W. C.; Jones, P. R. *J. Am. Chem. Soc.* **1957**, *79*, 928. Similarly with aluminum: Wittenberg, D. *Liebigs Ann. Chem.* **1962**, *654*, 23.

[13] Hayashi, T.; Konishi, M.; Okamoto, Y.; Kabeta, K.; Kumada, M. *J. Org. Chem.* **1986**, *51*, 3772. Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, K.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195. Cross, G. A.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1987**, 1746. Vriesma, B. K.; Lemaine, M.; Buter, J.; Kellogg, R. M. *J. Org. Chem.* **1986**, *51*, 5169. Consiglio, C.; Piccolo, O.; Roncetti, L. *Tetrahedron* **1986**, *42*, 2043 and earlier references contained therein.

Table I. ^{13}C **Chemical Shifts of Benzylic Grignard Reagents and Their Halide Precursors**

reagent	C-X	C-α	C-β	C-γ	aromatic
4a	58.7	26.4			(126.6, 128.7) o, m, 128.3 p, 142.4 i
4b	30.3	18.8			118.6 p, 124.1 o, 129.6 m, 160.9 i
6a	70.8	36.6	20.0	19.5	(ca. 128 o, m, p), 141.3 i
6b	51.0	32.6	28.9	26.2	119.4 p, 125.9 o, 129.8 m, 157.9 i
7a	46.2				(128.5–128.9) o, m, p, 137.7 i
7b	22.8				116.5 p, 123.9 o, 128.2 m, 155.6 i
8a	45.4	125.0	134.3		(126.9–128.9) o, m, p, 136.1 i
8b	24.8	142.6	109.9		121.6 p, 123.2 o, 127.9 m {128 i}
9a	52.9	(−3.8)			126.7 p, 127.0, 128.3 o, m, 140.4 i
9b	28.6	(1.4)			118.1 p, 125.9 o, 128.2 m, 153.0 i
10a	44.5	26.4	104.8	84.0	128.4 m, 128.9 p, 131.9 o
10b	67.3	15.4	145.8	145.8	123.4 o, 127.5, 128.0 m, p
11a	46.1				124.3 (C-Br), 128–133, 136.9 i
11b	25.7				117.9 (C-Br), 125–132

into the corresponding Grignard reagents indicated in Figure 1. When analyzed by ^{13}C NMR, the products were free of impurities produced by C–C coupling. Among the benzylmagnesium chlorides prepared, the synthesis of **6b** was straightforward, while the formation of **7b** had to be carried out with careful control of the rate of addition in order to avoid coupling side products. Cinnamylmagnesium chloride[14] (**8b**) can be synthesized very cleanly by the present techniques, although reaction of the chloride **8a** with dispersed Mg had been reported to yield little or no Grignard reagent.[6] Synthesis of the α-silylated reagent **9b**, widely utilized in asymmetric cross-coupling,[13] was straightforward, although in this case the reagent can be prepared in high yield by standard procedures.



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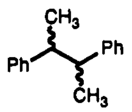

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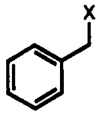

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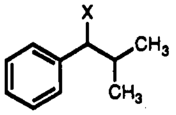

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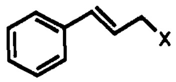

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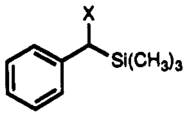

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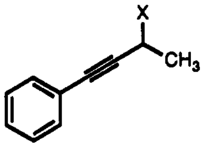

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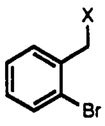

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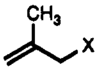

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a X= Cl ; **b** X = MgCl

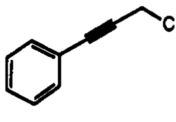
The propargyl halide **10a** can be converted into a Grignard reagent **10b** in 63% yield by the dry-stir technique. Previously, this reagent had been prepared only by recourse to a cyclic reactor, using amalgamated magnesium.[15] The impurities observed in the ^{13}C spectrum were acetylene **14** and allene **15** rather than homocoupling products; possibly the propargyl radical formed initially is capable of H atom abstraction from solvent.

Finally, the method was used to prepare allyl- and methallylmagnesium chlorides **12b** and **13b**, whose ^{13}C spectra were consistent with the expected dynamic η^1-η^1 allyl structure.[16]

Table II. ^{13}C **Chemical Shifts of Allylic Grignard Reagents and Their Halide Precursors**

reagent	C-X	C-α	C-β	C-Me
12a	45.1	134.0	119.5	
12b	58.5	148.5		
13a	40.5	141.5	115.0	19.6
13b	57.9	109.9		26.6

Analysis of ^{13}C **Spectra.** Chemical shifts for the Grignard reagents and their halide precursors are recorded in Tables I and II. Consider first the benzyl derivatives. The only X-ray crystal structure of a benzylmagnesium reagent is that of **16**. There are two distinct environments for the benzyl group (terminal and Mg–Li bridging) both with a covalent C–Mg bond.[17] This covalent structure is likely to prevail for benzylmagnesium chlorides in Et_2O solution, where there is strong precedent[18] for the chloro-bridged dimer structure **17**.



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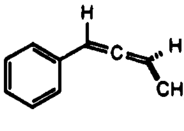

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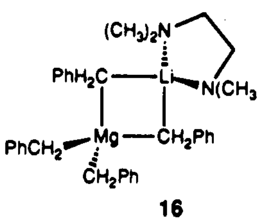

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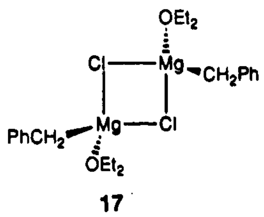

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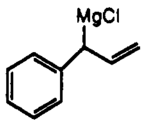

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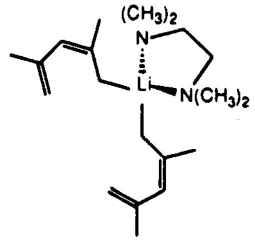

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Several consistent trends are apparent in the series. C(ipso) is deshielded relative to chloride precursors, but C(ortho) and C(para) are shielded, the latter up to 12 ppm. This is consistent with the delocalization of significant negative charge into the ring. Both side chain carbons C_α

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[14] E.g.: Highcock, W. J.; Mills, R. M.; Spencer, J. L.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1986**, 821.

[15] Cochran, J. C.; Kuivila, H. G. *Organometallics* **1982**, *1*, 97.

[16] Marsch, M.; Harms, K.; Massa, W.; Boche, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 696 and references therein.

[17] Schubert, B.; Weiss, E. *Chem. Ber.* **1984**, *117*, 366.

[18] Lindsell, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 1, Chapter 4 p 155ff.

and C-X are shielded, the latter by about 25 ppm, relative to the precursor chloride.

The reagents with α-methylbenzyl (**4b**) and α-isopropylbenzyl groups (**7b**) exhibit broadened signals for C-Mg and C-X carbons. Other benzylmagnesium chloride ^{13}C NMR spectra are comparatively sharp. This indicates that some dynamic process is occurring in the former cases. One possibility is that dimeric complexes of R^*R^* and R^*S^* stereochemistry are in moderately rapid equilibrium on the NMR timescale and have slightly different ^{13}C shifts for those carbon atoms responsive to magnesium. The structure of such chiral organometallic species in solution will be investigated further.

For cinnamylmagnesium chloride[14] (**8b**) two possible η^1-allyl structures exist, and the ^{13}C NMR helps distinguish between them. The observed ^{13}C chemical shift of CH_2 in **9b** is 24.8 ppm. The change on going from RCl to RMgCl is simlar to the benzylic cases so that the methylene must be the *predominant* site for magnesium bonding. There may well be a small amount of the alternative benzylic isomer **18** in rapid equilibrium since the degenerate process in η^1-allylmagnesium chloride is fast on the NMR time scale. For comparison, the X-ray structure of reagent **19** reveals a conjugated dienyl rather than a cross-conjugated dienyl structure.[19]

The situation with regard to allenyl $\rightleftharpoons$ propargyl equilibrium in compound (**10**) is more complex. Grignard reagents have been prepared from both allenyl and propargyl halides and used widely in synthesis,[20] the regiochemical course of reaction does not appear to depend on which halide tautomer is used, since allenic or acetylenic products can be formed and the true structure of the reagents formed is unclear. In the present case, key ^{13}C signals of **10b** are very close to the CH_3 and CH_2 peaks of diethyl ether. However, there are high-field signals at 15.4 ppm (CH_3) and 66.5 ppm and none evident in the 80–100 ppm region (excepting a little **14** formed as a byproduct). This evidence favors the allenyl structure, since the observed chemical shift changes at C-X and C_α on going from **10a** to **10b** are both in the wrong direction for the propargyl isomer.

Finally, the selective synthesis of a benzylic Grignard reagent **11b** from *o*-bromobenzyl chloride has been demonstrated; this had previously been achieved with the magnesium anthracene reagent.[8]

The Racemization of Chiral Benzylic Grignard Reagents. Earlier studies of Roberts and Whitesides[21] had eludicated the mechanism of racemization of α-chiral Grignard reagents. For the primary case this is rapid on the NMR timescale, although secondary Grignard reagents are configurationally stable for hours at ambient temperature in favorable cases.[22] There appears to be a lack of quantitative data on the recemization of secondary benzylic Grignard reagents, and since this is a crucial parameter in symmetric cross-coupling[13] we attempted to gain some further information.

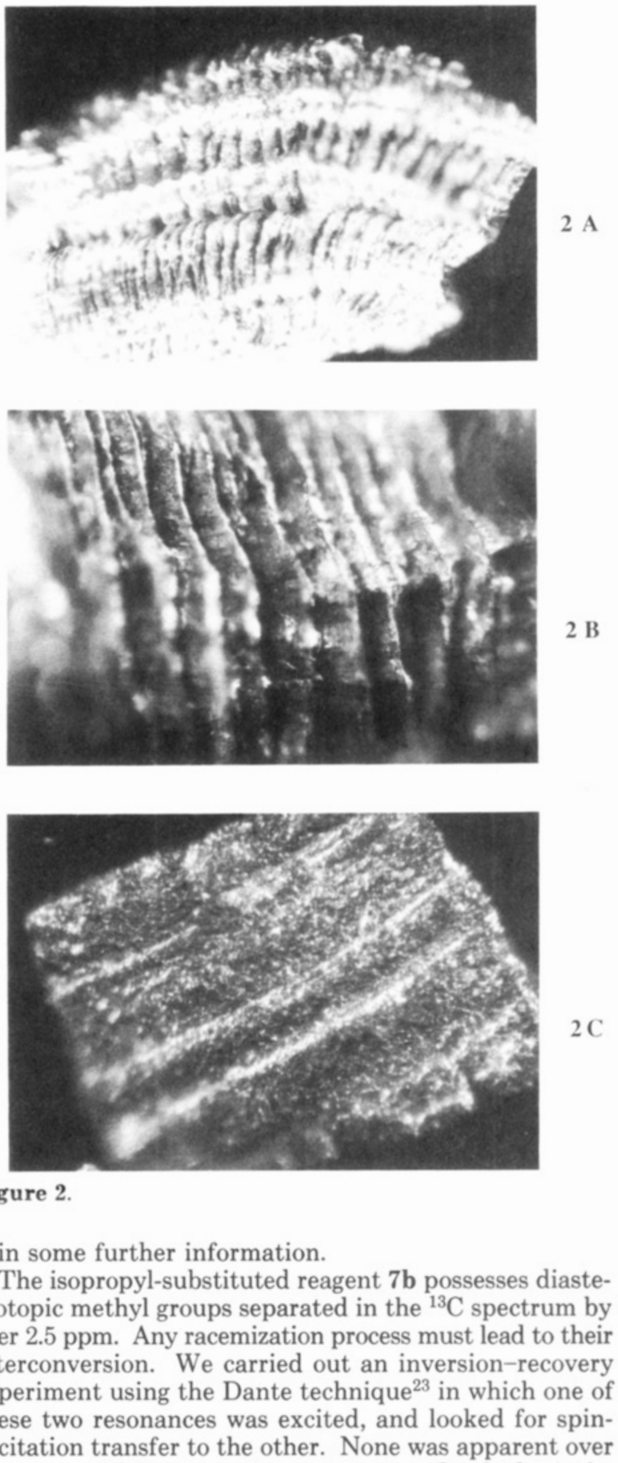

Figure 2.

The isopropyl-substituted reagent **7b** possesses diastereotopic methyl groups separated in the ^{13}C spectrum by over 2.5 ppm. Any racemization process must lead to their interconversion. We carried out an inversion–recovery experiment using the Dante technique[23] in which one of these two resonances was excited, and looked for spin-excitation transfer to the other. None was apparent over the range of delay times from 0.1 to 20 s. On the basis the rate constant for interconversion of R and S enantiomers of **7b** is $<0.02\ s^{-1}$ at 25 °C, much slower than the primary Grignard reagents studied by Roberts and Whitesides.[20] If this is sustained under the conditions of catalytic cross-coupling, then kinetic resolution of the Grignard reagent may make an important contribution to the ultimate optical yield. It has been recognized as a possible source of irreproducibility by Kellogg and co-workers,[24] who use an excess of Grignard reagent for this reason.

Structural Changes in Dry-Stirred Magnesium. A darkening and reduction of particle size on stirring mag-

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(19) Yasuda, H.; Yamauchi, M.; Nakamura, A.; Sei, T.; Kai, Y.; Yasuoko, M.; Kasai, N. *Bull Chem. Soc. Jpn.* **1980**, *53*, 1089.

(20) For recent examples: Epifani, E.; Florio, S.; Ingrosso, G.; Sgarra, R.; Stasi, F. *Tetrahedron* **1987**, *43* 2769. Lehrich, F.; Hopf, H. *Tetrahedron Lett.* **1987**, *28*, 2697. Marshall, J. A.; Crooks, S. L.; de Hoff, B. S. *J. Org. Chem.* **1988**, *53*, 1616.

(21) Whitesides, G. M.; Witanowski, M.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 2854. Whitesides, G. M.; Roberts, *J. Am. Chem. Soc.* **1965**, *87*, 4878. Fraenkel, G.; Cottrell, C. E.; Dix, D. T. *J. Am. Chem. Soc.* **1971**, *93*, 1704.

(22) Jensen, F. R.; Nakamaye, K. L. *J. Am. Chem. Soc.* **1966**, *88*, 3437. Davies, A. G.; Roberts, B. P. *J. Chem. Soc. B* **1969**, 317. San Filippo, J., Jr.; Nicoletti, J. W. *J. Org. Chem.* **1977**, *42*, 1940. Cf: Walborsky, H. M.; Young, A. E. *J. Am. Chem. Soc.* **1964**, *86*, 3288. Walborsky, H. M.; Impastato, F. J.; Young, A. E. *J. Am. Chem. Soc.* **1964**, *86*, 3283. Pechhold, E.; Adams, D. G.; Fraenkel, G. *J. Org. Chem.* **1971**, *36*, 1368.

(23) Morris, G. A.; Freeman, R. A. *J. Magn. Reson.* **1978**, *29*, 433.

(24) Cross, G.; Vriesma, B. K.; Boven, G.; Kellogg, R. M.; van Bolhuis, F.; *J. Organomet. Chem.* **1989**, *370*. 357.

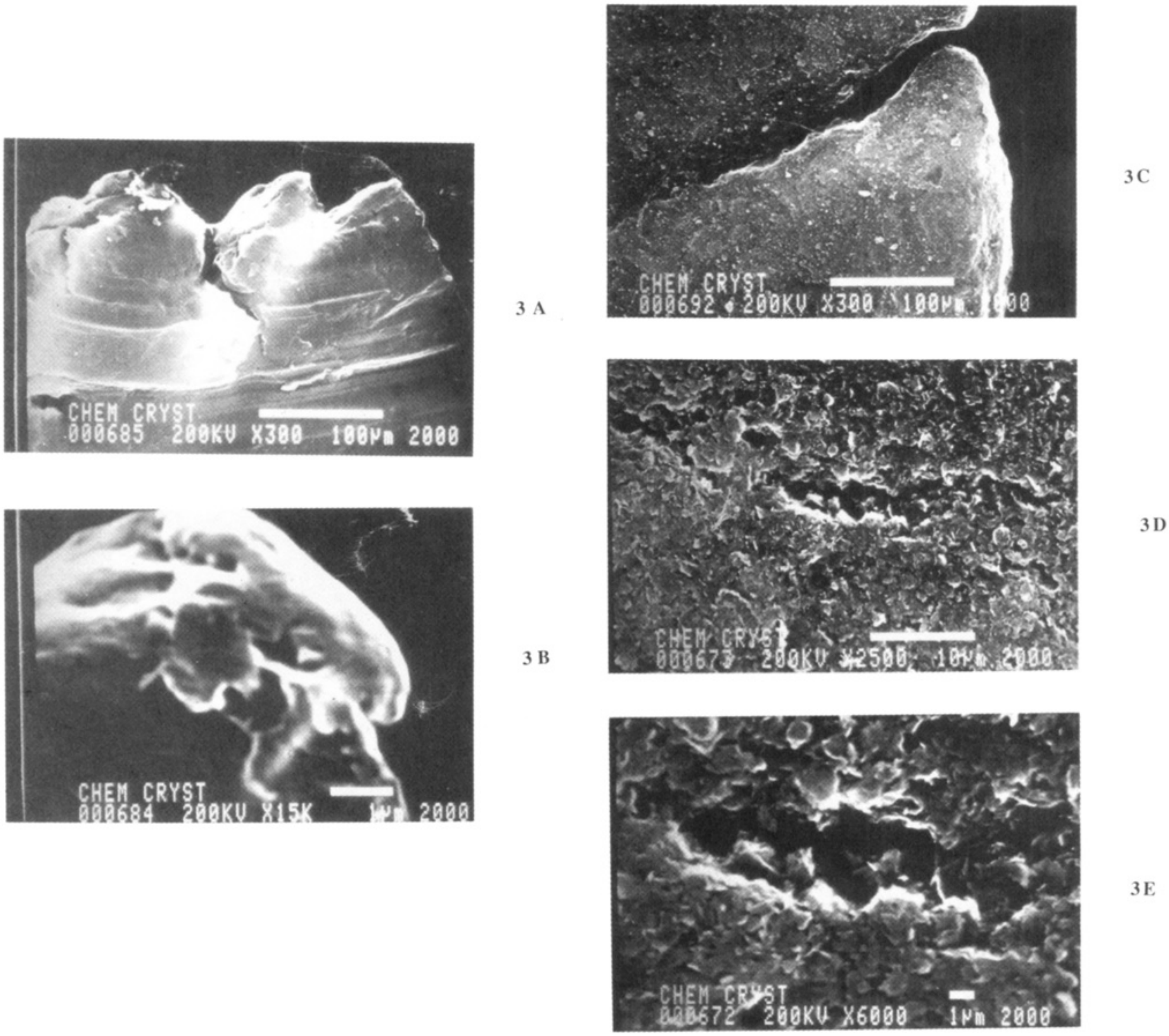

Figure 3.

nesium turnings under the conditions described are evident on casual observation. Our initial attempts to examine the process in greater detail involved optical microscopy and the changes seen are displayed in Figure 2. The magnesium turnings employed have a ridged structure with the ridges orthogonal to the long axis of the turning (2A). On protracted stirring under argon or nitrogen, considerable darkening occurs and black flecks are apparent in the grain structure (2B). Smaller particles produced by cleavage down the ridges can be observed (2C).

More detail is revealed by electron microscopy. Consider first untreated magnesium at low magnification (Figure 3A). At higher magnification the degree of detail is limited by the high reflectivity of the Mg surface (3B). Much more detail can be obtained on observation of dry-stirred magnesium turnings, which are considerably rougher. Observation at a magnification of 300× reveals the roughness of the surface and the accretion of small particles (<1 μm) is clearly apparent (3C). The breakdown of structure and particulation are very apparent in electron micrographs taken at magnifications of 2500 and 6000, respectively (3D,E).

We conclude from this investigation that magnesium turnings are mechanically unstable. Vigorous stirring under an inert atmosphere causes fragmentation and then further cleavage to form microcrystalline magnesium particles which adhere to the surface. These processes enhance the surface area of oxide-free magnesium when the dry-stir procedure is performed under an inert atmosphere.

Experimental Section

The halides **6a**, **8a**, **12a**, and **13a** were commercial materials distilled before use. Compound **4a** was prepared from the corresponding alcohol (Aldrich) by reaction with $SOCl_2$ ($CHCl_3$, room temperature), bp 74 °C (10 mmHg) (lit.[25] bp 91–2 °C (15 mmHg)). Compound **7a** was similarly prepared bp 48–50 °C (0.3 mmHg) (lit.[26] bp 36–4 °C (0.5 mmHg)), as was **11a**, bp 73–74 °C (0.2 mmHg) (lit.[27] bp 110–1 °C (15 mmHg)). The α-chlorosilane **9a** was synthesized by chlorination of benzyltrimethylsilane,[28] bp 100–101 °C (0.6 mmHg) (lit.[28] bp 190 °C (760 mmHg)). 3-Chloro-1-phenyl-1-butyne (**10b**) was synthesized as described

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(25) Moye, C. J. *Aust. J. Chem.* **1967**, *20*, 779.

(26) Baddeley, G.; Chadwick, J.; Taylor, H. T. *J. Chem. Soc.* **1954**, 2405.

(27) Parham, W. E.; Jones, L. D.; Sayed, Y. A. *J. Org. Chem.* **1976**, *41*, 1184.

(28) Sommer, L. H.; Bailey, D. L.; Strong, W. A.; Whitmore, F. C. *J. Am. Chem. Soc.* **1946**, *68*, 1881.

earlier,[15] bp 41 °C (0.1 mmHg) (lit.[15] bp 75–76.5 °C (0.25 mmHg)). Magnesium turnings were purchased from Fisons, Birmingham, England. ^{13}C NMR were recorded on a Bruker AM 250 spectrometer operating at 63.86 MHz in a septum-sealed 8.4-mm tube contained in a 10-mm tube with CD_3OD in the annular space. Electron microscopy was carried out with JEOL JEM 200FX instrument in SM mode operating at 2000 KV with a spot size of 5000A.

The following procedure is typical for the synthesis of benzylic Grignard reagents. Magnesium metal turnings (16 g) were transferred to a Schlenk tube (ca. 300-mL capacity, 60 mm o.d.) together with a Teflon-coated stirrer bar (50 mm). The system was sealed with a 250-mL pressure-equalized dropping funnel and purged with purified N_2. Vigorous mechanical stirring was carried out for 2 day. After this time much of the magnesium was finely divided and dark gray in color. Sufficient Et_2O (freshly distilled off sodium benzophenone ketyl) was run in to cover the magnesium. The solution was cooled to 0 °C under a nitrogen atmosphere, and a solution of 1-chloro-1-phenylethane (**4a**) (13.2 g, 0.1 mol) in dry Et_2O (150 cm^3) was added dropwise to the center of the vortex created by the stirrer. The addition was complete after 3.5 h, and stirring was then continued at 0 °C for a further 2.5 h. The clear solution was filtered by cannula into another Schlenk tube of the same dimensions and made up to 250 cm^3. The stock solution was titrated as 0.38 M (95%, including transfer losses) against 0.1 M HCl and phenolphthalein, and stored at 0 °C prior to use. Samples prepared and stored in this was have a shelf life of at least several weeks. [NB. The activated magnesium may be pyrophoric and create a flare which is hazardous to the eyes if exposed to air. This has never occurred with our samples even when deliberately brought into contact with the air. Nevertheless, due caution should always be observed in the handling of activated magnesium.]

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Unsymmetrical Oxidative Cleavage of Cyclic Ketones. Conversion to ω-Ethoxycarbonyl Aldoximes under Alkaline Conditions[1]

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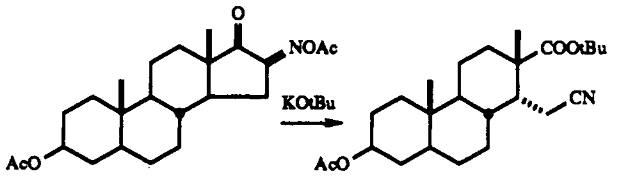
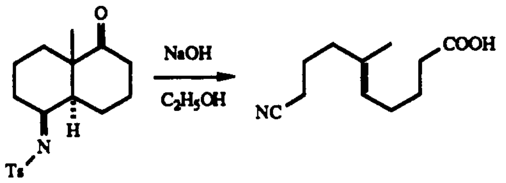
A useful procedure for effecting the direct unsymmetrical cleavage of an enolizable cyclic ketone to an oximino ester has been developed. The process begins by deprotonation with LDA and is followed by the addition of ethyl nitrite in THF at low temperature. Rapid reaction customarily ensues with resultant overall nitrosolysis. Of particular importance is the facile application of this procedure to substrate ketones that are otherwise sensitive to acidic environments. This feature is exemplified in particular in the case of *syn*- and *anti*-sesquinorbornenones **34** and **35**, access to which is described for the first time. Since the entire process is executed in a single flask, the methodology is very convenient to implement in practice.

To the extent that predictable regiochemistry results, the oxidative cleavage of ketones to oximino esters (**1** → **2**) holds considerable synthetic interest since such a process results in the simultaneous conversion of adjoining carbonyl and methylene groups into two differently oxidized terminal carbon atoms. While the Baeyer–Villiger[2] and Beckmann rearrangements[3] constitute chemical operations that result in functional group transmutations of a similar type, the oxidation level of the methylene center is only nominally affected by these changes, and additional steps are required to arrive at an aldehyde or aldehyde equivalent. A few exceptions typified by the behavior of **3**[4] and **5**[5] (both reactions can be classified as Grob fragmentations[6]) are known that lead to cyano carboxylates.

1 **2**



3 **4**



5 **6**

In actuality, the feasibility of the transform **1** → **2** has been intensively scrutinized by Rogić and co-workers for reaction conditions that are quite acidic.[7] For example, they found that exposure of cyclohexanone to nitrosyl

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[1] Part 53 of the series Isodicyclopentadiones and Related Molecules. For part 52, see: Sivik, M. R.; Rogers, R. D.; Paquette, L. A. *J. Organomet. Chem.*, in press. Part 51: Paquette, L. A.; Bauer, W.; Sivik, M. R.; Buhl, M.; Feigel, M.; Schleyer, P. v. *J. Am. Chem. Soc.*, in press.

[2] (a) Hassall, C. H. *Org. React.* **1957**, *9*, 53. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697. (c) Bentley, P. H. *Chem. Soc. Rev.* **1973**, *2*, 29. (d) Plesnicar, B. In *Oxidation in Organic Chemistry, Part C*; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; pp 254–262.

[3] (a) Gawley, R. E. *Org. React.* **1988**, *35*, 1. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 1283.

[4] Kohen, F. *Chem. Ind.* (*London*) **1966**, 1378.

[5] (a) Eisele, W.; Grob, C. A.; Renk, E.; von Tschammer, H. *Helv. Chim. Acta* **1968**, *51*, 816. (b) Grob, C. A.; von Tschammer, H. *Ibid.* **1968**, *51*, 1082. (c) Artz, K. G.; Grob, C. A. *Ibid.* **1968**, *51*, 807.

[6] Becker, K. B.; Grob, C. A. In *Chem. Double-Bond Functional Groups*, John Wiley: Chichester, England, 1977; Vol. 2, pp 653–723.

[7] (a) Rogić, M. M.; Van Peppen, J. F.; Klein, K. P.; Demmin, T. R. *J. Org. Chem.* **1974**, *39*, 3424. (b) Rogić, M. M.; Vitrone, J.; Swerdloff, M. D. *J. Am. Chem. Soc.* **1975**, *97*, 3848. (c) Rogić, M. M.; Tetenbaum, M. T.; Swerdloff, M. D. *J. Org. Chem.* **1977**, *42*, 2748. (d) Rogić, M. M.; Vitrone, J.; Swerdloff, M. D. *J. Am. Chem. Soc.* **1977**, *99*, 1156.

0022-3263/91/1956-0703$02.50/0