Carbonylation of Organomagnesium Compounds: Catalysis by Hexamethylphosphoric Triamide[1]

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Carbonylation of Grignard derivatives (RMgX), very slow in ether, is markedly accelerated when adding (or using neat) hexamethylphosphoric triamide (HMPT). Typically, uptake of CO is completed within a few minutes at room temperature and at *ca.* 30 atm. Product composition is dependent on R, solvent composition (RMgX : HMPT ratio), and on the presence of electrophiles such as 'extra' alkyl halide. Synthetically attractive methods for preparing several types of (hydroxy)ketone derivatives [(1), (4), and (5)] from primary alkyl halides are outlined. Other types of R(Mg)X mostly lead to acyloins RCH(OH)C(O)R. Evidence for the formation of RCOMgX, or equivalent(s), as 'first' intermediates is presented. The overall mechanism is discussed. Products, and effects of HMPT on rate and product composition, can satisfactorily be explained *via* nucleophilic addition and substitution steps, deprotonation, and reduction reactions, leading to Mg salts of enols as 'final' intermediates.

REACTIONS with carbon monoxide are important from a synthetic point of view, as useful, functionalized compounds can be produced from simple starting materials.[2] The importance of Grignard reagents in organic synthesis needs no emphasis. Reactions with carbonyl compounds such as ketones or esters have been studied in detail. Remarkably, *carbonylation* of 'RMgX' has thus far only been considered superficially.[3]

After preliminary work by Zelinsky,[4] Grignard,[5] and others,[6] Fischer and Stoffers were the first to describe both reaction conditions and product formation.[7] Ethereal solutions of primary derivatives (RCH_2MgX), when carbonylated for 3 h (60—160°; 50—180 atm. CO) consumed 0.5 mole of CO, giving alkenes $RCH_2CH=CHR$ (25—65%).[7-9] Tertiary alkyl and aryl compounds took up 1 mole of CO, yielding acyloins RCH(OH)C(O)R in good yield.[7] Secondary alkyl compounds gave a very complex reaction mixture.

The reaction of Grignard compounds with transition metal carbonyl derivatives sometimes led to acyloins in modest yields (up to 35%), but mostly resulted in a host

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[1] W. J. J. M. Sprangers, A. P. van Swieten, and R. Louw, (*a*) *Tetrahedron Letters*, 1974, 3377; (*b*) *Chimia*, 1976, **30**, 199.

[2] (*a*) J. Falbe, 'Carbon Monoxide in Organic Synthesis,' Springer–Verlag, Berlin, 1970; (*b*) C. W. Bird, 'Transition Metal Intermediates in Organic Synthesis,' Academic Press, London, 1966.

[3] M. S. Kharasch and O. Reinmuth, 'Grignard reactions of Nonmetallic Substances,' Prentice–Hall, New York, 1954.

[4] N. D. Zelinsky, *Zhur. Russ. fiz. Khim. obshchei*, 1904, **36**, 195, 336.

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[6] (*a*) Vinay, Thesis, Geneva, 1913, cited in ref. 12; (*b*) V. Jegorowa, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1319 (*Chem. Z.*, 1915, **1**, 1055).

[7] F. G. Fischer and O. Stoffers, *Annalen*, 1933, **500**, 253.

[8] Ya. T. Eidus, N. V. Elagina, and N. D. Zelinsky, *Bull. Acad. Sci., U.S.S.R.*, 1945, 672 (*Chem. Abs.*, 1948, **42**, 5838).

[9] K. V. Putztskii, Ya. T. Eidus, and K. G. Ryabova, *Bull. Acad. Sci., U.S.S.R., Chem. Science*, 1966, 1745.

of products, including aldehydes, ketones, and acyloins.[10–16]

We have recently reported that the reaction of Grignard compounds in ether with CO is speeded up considerably in the presence of hexamethylphosphoric triamide (HMPT). Then, uptake of CO by alkylmagnesium derivatives is often completed within 1—5 min at room temperature and ⩽35 atm.[1]

This paper deals with the effect of changing reaction conditions (especially solvent composition) on rates and products. The mechanism is discussed, taking into account the results of experiments designed at elucidating reaction intermediates such as acylmagnesium derivatives.

RESULTS AND DISCUSSION

(a) *Effect of HMPT on Rates and Product Formation.*—Upon transferring a standard Grignard solution, prepared from EtBr in ethyl ether to an autoclave (1 l), and pressurizing with CO (500 lb in^{-2}), pressure decreased slowly with stirring; the uptake is *ca.* 0.9 equiv. in 1.6 h. After work-up the main component (1b), constituting *ca.* 50% by wt. of the product mixture, accounts for 8% of initial EtBr only. Carbonylation in the presence of 0.7—1 equiv. of HMPT, however, leads to both enhanced rates and much better yields. The exothermic reaction is over within 2 min (uptake 1 equiv. of CO); compound (1b) now is formed in 36% overall yield, and constitutes *ca.* 90% w/w of the isolated crude material. In Table 1 the effect of variation of the EtMgBr : HMPT ratio is outlined.

TABLE 1

Carbonylation of ethereal EtMgBr [a]; effect of HMPT

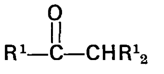
HMPT [b] (equiv.)	CO [b] absorbed (equiv.)	(1b) (%) (by g.l.c.)
0	0.9	8
0.7	0.8	41
1.0	0.8	36
1.1	1.1	25
1.25	1.2	20
3 [c]	1.5	0 [c]

[a] 20°, 500 lb in^{-2} of CO. [b] mole per mole of initial EtBr. [c] In neat HMPT; formation of a large variety of other products, including Et_2CHOH, Et_2CO, (2b), EtCOCOEt, (4b), and (5b); total yield 40%.

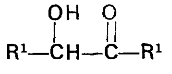
As for other solvents, we have briefly studied carbonylation of Pr^{n}MgBr in iso-octane and THF, with and without one equiv. of HMPT. There was no increase in the (low) yield or selectivity to (1c) due to HMPT, however.

Although carbonylation in neat HMPT is also very rapid a large number of products are formed (see footnote *c*, Table 1). It appears that 0.7—1 equiv. of HMPT is about the right proportion from a synthetic point of view.

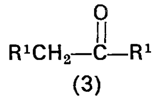
Product composition appears to depend on the method of preparation of the Grignard solution. If it is made in ether and the solvent subsequently replaced by HMPT, (4b) and (5b) are not formed. When the Grignard system is made directly in HMPT, however, (4b) and (5b) do arise, probably due to residual EtBr [see also section (b)]. At atmospheric pressure, the rate of absorption of CO is very slow; pressurizing appears to be necessary in order to obtain useful rates. At *ca.* 500 lb in^{-2} (initial pressure) primary alkyl derivatives react most rapidly (within 1—2 min); secondary and tertiary analogues are somewhat slower (⩽5 min). Aryl and aralkyl derivatives usually take 3—4 h before CO absorption is completed.


$R^1\overset{O}{\overset{\|}{C}}CHR^1_2$

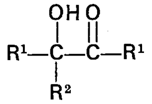
(1)

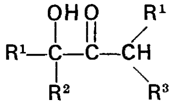

$R^1\overset{OH}{\overset{|}{C}H}\overset{O}{\overset{\|}{C}}R^1$

(2)


$R^1CH_2\overset{O}{\overset{\|}{C}}R^1$

(3)


(4)


(5)

a, $R^1 = Me$
b, $R^1 = R^2 = Et$, $R^3 = Me$
c, $R^1 = Pr^n$
d, $R^1 = Bu^n$, $R^2 = Et$, $R^3 = Me$
e, $R^1 = R^2 = Bu^n$, $R^3 = Pr^n$
f, $R^1 = n\text{-}C_7H_{15}$
g, $R^1 = Cl[CH_2]_4$
h, $R^1 = Pr^i$
k, $R^1 = Bu^s$
l, $R^1 = Bu^t$
m, $R^1 = t\text{-}C_5H_{11}$
n, $R^1 = Ph$
p, $R^1 = PhCH_2$

In Table 2 a product survey is given for various substrates, under ' standard ' conditions (500 lb in^{-2} of CO, 1 mol of HMPT per mol of organomagnesium derivative) at room temperature. Under these circumstances, primary derivatives form ketones (1). There appear to be no other products formed of comparable complexity (volatility). Isolation is therefore possible by a simple distillation. Secondary derivatives lead to mixtures including (2) and (3). Tertiary alkyl, aryl, and aralkyl compounds yield acyloins (2) as the predominant carbonylated product. Both bromides and chlorides can be employed. With tertiary and secondary chlorides overall yields appear to be better than with the corresponding bromides. This is probably due to better conversions into Grignard compounds for chlorides in these cases.[3]

(b) *Systems involving Additional Alkyl Halide.*—As mentioned above, larger proportions of HMPT (or, using neat HMPT as a solvent) lead to very complex products. This situation holds for carbonylation of Grignard solutions *per se*. Markedly different results are obtained when an additional equivalent of alkyl halide is present. Em-

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[10] M. Ryang and S. Tsutsumi, *Bull. Chem. Soc. Japan*, 1961, **34**, 1341.

[11] H. O. Jones (*a*) *Chem. News*, 1904, **90**, 144; (*b*) *Chem.-Ztg.*, 1904, **11**, 1111.

[12] W. L. Gilliland and A. A. Blanchard, *J. Amer. Chem. Soc.*, 1926, **48**, 410.

[13] A. Job and R. Reich, *Compt. rend. C*, 1923, **177**, 1438 (*Chem. Abs.*, 1925, **19**, 1851.

[14] A. Job and A. Cassal, *Compt. rend. C*, 1926, **183**, 58 (*Chem. Abs.*, 1926, **20**, 2999).

[15] A. Job and A. Cassal, *Bull. Soc. chim. France*, 1927, 814.

[16] M. Ryang, K. Yoshida, and S. Tsutsumi, *Chem. Abs.*, 1966, **65**, 15422a.

ploying ethereal R^1MgX with 3 equiv.* of HMPT and 1 equiv. of R^2X, acyloin (4) is found to be the main product together with (5). When using neat HMPT, however, the (5) : (4) product ratio is markedly enhanced, resulting in a useful preparative method for acyloins of type (3) (Table 3). Most of the derivatives types (1), (4), and (3), described above, are novel compounds. Especially for mixed analogues alternative synthetic methods would entail multistep procedures. Although yields and selectivities are modest, the simple (essentially one-step) procedures, and the relatively easy isolation techniques, would make carbonylation of Grignard compounds an attractive method for preparing (1), (4), and (5).

Table 2

Carbonylation of ethereal RMgX with 1 equiv. of HMPT

R	X	Main product(s)	Yield (%) [a]	Further products (%)
Me	I	(1a)	N.d.	$CH_3{\cdot}CO{\cdot}CH_3$ [b]
Et	Br	(1b)	36 (36)	
Pr^n	Br	(1c)	56 (56)	
Pr^n	Cl	(1c)	31	
$n\text{-}C_7H_{15}$	Br	(1f)	46 (35)	
$Cl[CH_2]_4$	Br [c]	(1g)	N.d.	
Pr^i	Br	(2h)	26 (18)	$Pr^i{}_2CHOH$ (7)
Pr^i	Cl	(2h)	30	$Pr^i{}_2CHOH$ [b]
Bu^s	Br	(2k)	16	butane + butene (4 : 1);[b]
		(3k)	10	$Bu^sCH{=}C(Me)Et$ (22)
Bu^s	Cl	(2k)	16	Bu^sOH (4);[d]
		(3k)	4	$Bu_sCH{=}C(Me)Et$ (24)
Bu^t	Br	(2l)	17	
	Cl	(2l)	40	
$t\text{-}C_5H_{11}$	Br	(2m)	20	$EtC(Me_2)C(Me_2)\text{-}Et$ (20); $(t\text{-}C_5H_5)_2CHOH$ [c]
Ph	Br	(2n)	22	Ph_2CHOH (15)
$PhCH_2$	Br	(2p)	N.d. (17)	Bibenzyl (69)

[a] Yields are based on starting compound RX; data in parentheses refer to isolated materials. [b] Not analysed quantitatively. [c] This Grignard compound was made in THF [17] and the solvent replaced by ether. [d] Due to blank reaction of RMgX with HMPT (see Experimental section).

Table 3

Carbonylation of $R^1MgBr + R^2Br + 3$ HMPT

R^1	R^2	Solvent [a]	Products (% yield by g.l.c.)
Et	Et	e	(4b) (10); (5b) (0)
Et	Et	n	(4b) (10); (5b) (54) [b]
Bu^n	Et	e	(4d) (35); (5d) (15)
Bu^n	Et	n	(4d) (20); (5d) (25)
Bu^n	Bu^n	e	(4e) (35); (5e) (10)
Bu^n	Bu^n	n	(4e) (20); (5e) (33)

[a] n = neat HMPT; e = additional ether. [b] Also identified: Et_2CHOH, Et_2CO, $EtCH(OH)COEt$, and $EtCOCOEt$.

(c) *Search for Intermediates*.—It is beyond doubt that the reaction of Grignard compounds with CO consists of a rather large number of consecutive (and/or parallel) steps. An equally large variety of intermediates, probably with widely different concentrations (stability, lifetime) is to be expected. In order to get insight into the overall mechanism a number of experiments aiming at identification of likely intermediates has been performed.

Acylmagnesium derivatives. As a first step, insertion of CO to give acylmagnesium compounds (A) can be envisaged. Measurable concentrations should be converted into aldehydes upon hydrolysis. We have not been able to detect aldehydes in carbonylation products of aliphatic systems. Presumably, further reactions of (A) (with CO and/or RMgX) are too rapid. However, carbonylation of phenylmagnesium bromide, at low temperatures (0 to −5°; 35 atm of CO), leading to 5% conversion after 21 h, followed by hydrolysis, led to benzaldehyde in *ca.* 20% yield, as determined by g.l.c. on two different columns. Under these conditions, $PhC(O)MgBr$, or equivalent(s) thereof, is relatively stable. Whitesides *et al.* found no evidence for benzoyl-lithium in the reaction of phenyl-lithium with CO.[18]

That an analogous intermediate (A) is also formed in aliphatic systems could be demonstrated as follows. Carbonylation of Bu^nMgBr in neat HMPT, in the presence of 2 equiv. of $NaBH_4$ (7 atm. of CO; room temperature) led to 6% n-pentanol; this reaction may be compared with that of carbonylation of organoboranes in the presence of $NaBH_4$.[19]

'Final' intermediates. Very likely, before hydrolysis, hydroxy-ketones are present in the reaction mixture as their magnesium enolates. These derivatives may well be capable of reacting with *e.g.* (starting) Grignard compounds, and thus lead to even more complex molecules. In order to test this hypothesis, a carbonylation product of Bu^sMgCl (see Table 2) was additionally stirred for 15 h with 2 equiv. of EtMgBr plus 2 equiv. of HMPT † in ether prior to hydrolysis. After work up, a new product, $Bu^sCH(Et)C(O)Bu^s$ (6), was isolated in *ca.* 2% yield. Compound (6) is an analogue of (1k) which, *inter alia*, is not observed in the product of carbonylation of Bu^s-$MgCl$; this difference may be due to steric reasons [see section (d)].

As a further example the effect of the addition of 2 equiv. of Bu^sMgBr plus 2 equiv of HMPT † to a similar carbonylation product of Bu^sMgCl can be given. The yield of (2k) was lowered from 16 to 8%, (3k) amounting to 12 rather than 4%. Primary Grignard compounds, upon hydrolysis, lead to ketones (1). That the 'final' intermediate is the corresponding enolate is shown by the formation of enol ester when stirring the reaction mixture

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* In systems with 1 equiv. of HMPT per mole of R^1MgX additional R^1X has no effect on the product composition; apparently, the (carbonylated) Grignard compound is not sufficiently activated.

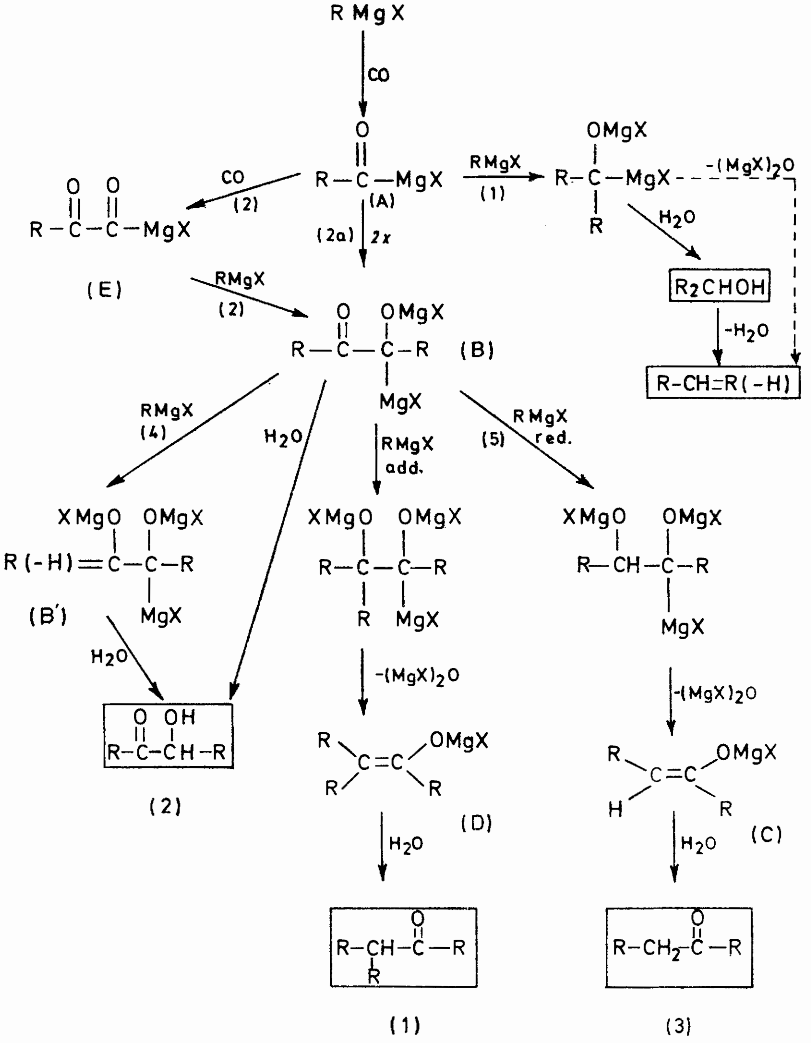
† Without additional HMPT the 'extra' Grignard derivative exerted no effect. Presumably its reactivity is too low in that case.

[17] M. Noel, J. C. Combret, Y. Leroux, and H. Normant, *Compt. rend. C*, 1969, **268**, 1152.

[18] L. S. Trzupek, T. L. Newirth, E. G. Kelly, N. E. Sbarbati, and G. M. Whitesides, *J. Amer. Chem. Soc.*, 1973, **95**, 8118.

[19] H. C. Brown, *Acc. Chem. Res.*, 1969, **2**, 65.

with acetic anhydride prior to hydrolysis. Thus, Pr^nMgBr, after carbonylation in ether–HMPT, and subsequent reaction with 4 equiv. of Ac_2O, led to $Pr^n_2C=C(Pr^n)$-OCOMe (7) (22%), together with 9% (1c). Addition of 2 equiv. of EtBr after completion of the carbonylation did not lead to enol ether; apparently, the corresponding S_N2 process is too slow.[20] Treatment with dimethyl sulphate was shown by g.l.c. to give another product at the expense of (1c), presumably the methyl ether (*O*-alkylation).



Scheme 1

(d) *Mechanistic Considerations.*—Supposing the first step to be nucleophilic addition of RMgX to CO, yielding RCOMgX (A) as a first intermediate, the large rate increase caused by one equiv. of HMPT can be understood on the basis of C–Mg bond polarization, making R more carbanion-like.[21] In systems with HMPT as a (co)solvent, a bulk dipolar aprotic solvent effect may also obtain, resulting in enhanced (free?) carbanion reactivity.[22]

From (A) on, several parallel pathways can be envisaged as the second step, *viz.* further addition of CO or RMgX, reduction, and/or enolization by RMgX. The mode of reaction of Grignard reagents with carbonyl functions is dependent on the nature of the alkyl group, the halide atom, the carbonyl derivative, and the solvent.[3,23-30] A large number of products is therefore expected. A full description of all individual steps, also taking into

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[20] B. J. Wakefield, *Chem. and Ind.*, 1972, 450.

[21] J. Ducom, *Bull. Soc. chim. France*, (*a*) 1971, 3518; (*b*) p. 3523; (*c*) J. Ducom and B. Denise, *J. Organometallic Chem.*, 1971, **26**, 305.

[22] A. J. Parker (*a*) *Quart. Rev.*, 1962, **16**, 163; (*b*) *Adv. Org. Chem.*, 1965, **5**, 1.

[23] D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, 1962, **27**, 1.

[24] R. Hamelin. *Bull. Soc. chim. France*, 1963, 1411.

[25] J. Fauvarque and J-F. Fauvarque, *Compt. rend. C*, 1966, **263**, 488.

[26] A. Kirrmann and J. Rabesiaka, *Bull. Soc. chim. France*, 1967, 2370.

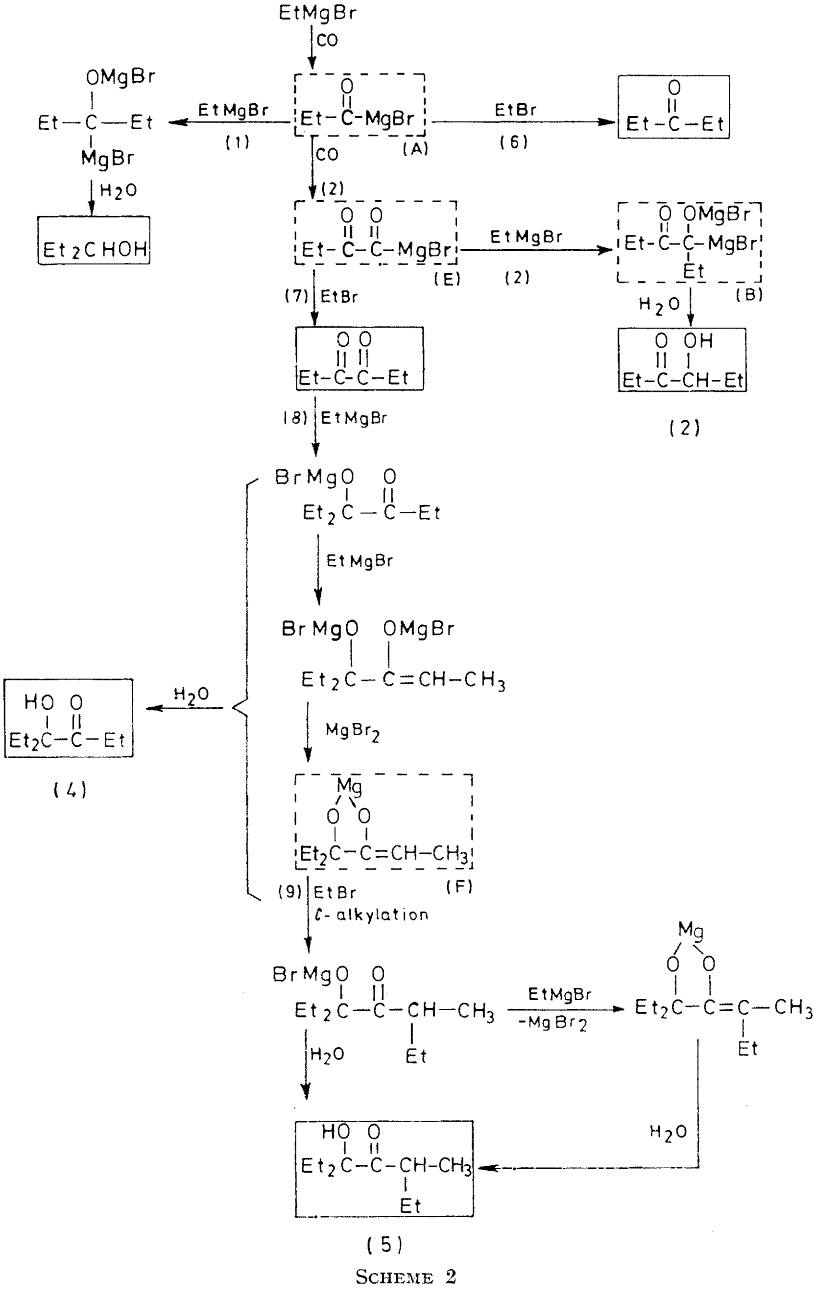
[27] J. Rabesiaka, *Bull. Soc. chim. France*, 1968, 2493.

[28] J. Koppel and A. Tuulmets, *Org. Reactivity*, 1970, **4**, 1186.

[29] G. Emptoz, F. Huet, and A. Jubier, *Compt. rend. C*, 1971, **273**, 1543.

[30] J. Fauvarque and J. Ducom, *Compt. rend. C*, 1971, **273**, 268.

account the character of R, cannot be given; we prefer to discuss the overall mechanism on the basis of a reaction scheme that has been reduced to a bare minimum (Scheme 1). Intermediate (A) may add another RMgX (route 1) to give secondary alochol R_2CHOH and/or the corresponding alkene(s). This process appears to be unimportant for primary R in systems with ⩽1 equiv. of HMPT, as these products are not observed. Apparently, insertion of a second mole of CO to give (E) [step (2)] and subsequent addition of another RMgX to give (B) is the preferred route. If this pathway obtains, the addition to the CO group next to MgX is understood when accepting that the MgX group, solvated by HMPT,[31] is a stronger electron donor than ethyl. Formally, this carbonyl group carries the negative charge of the acyl anion; this group would give stronger co-ordination with the magnesium atom of entering RMgX.[32,33]



SCHEME 2

Alternatively, (A) may dimerize to give (B) ' directly ' [step (2a)] supposedly *via* a carbenoid analogue RCOMgX. With primary R further addition of RMgX [step (3)] and

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[31] (*a*) H. F. Ebel and R. Schneider, *Angew. Chem.*, 1965, **77**, 914; (*b*) H. F. Ebel and B. O. Wagner, *Chem. Ber.*, 1971, **104**, 320.

[32] E. C. Ashby, J. Laemmle, and H. M. Neuman, *Acc. Chem. Res.*, 1974, **7**, 272.

[33] C. E. Enteman, jun., and J. R. Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 2900.

formation of the ' final ' intermediate (D) is straightforward. Hydrolysis of (D) leads to ketone (1), whereas treatment with acetic anhydride gives enol acetate (7).

With secondary derivatives, addition to RMgX to (B) will be less easy due to steric hindrance (Mg is co-ordinated with HMPT). Part of RMgX may be ' lost ' *via* deprotonation of (B) [route (4)] to give RH and (B′). Both (B) and (B′) will lead to product (2). Furthermore, reduction of (B), to yield (C) [step (5)] can be envisaged; after hydrolysis ketone (3) is isolated. Such a reduction leads to net addition of ' HMgX ' to the carbonyl group of (B), leaving alkene R–H. The small amount of ROMgX which is formed from RMgX and MHPT (see Table 2, footnote *d*) does not appear to be involved in a Meerwein–Ponndorf–Verley type of reduction. In a model experiment addition of 10% of ROH before carbonylation did not lead to an increased (3) : (2) ratio.

Addition of ' extra ' RMgX after carbonylation leads to increased (3) : (2) ratios; this is understood on the basis of (B) as a relatively stable intermediate and competitive conversion [steps (4) and (5)].

With tertiary alkyl (and aryl) derivatives, (B) appears to be the important final intermediate, further reactions (3)—(5) being too slow, or impossible.

In systems of (primary) derivatives RMgX containing additional alkyl halide, in HMPT as a (co)solvent, (4) and (5) are formed as main products. In Scheme 2 the appropriate pathways are shown, exemplified for R = Et. The formation of side products (see Table 3) is also outlined. Reactions (1) and (2) (*cf.* Scheme 1) lead to Et_2CHOH and EtC(O)CH(OH)Et, respectively. The small proportion of Et_2CO can be explained *via* nucleophilic acylation of EtBr by (A) [step (6)]. The major pathway (7) involves an analogous acylation of EtBr by (E) to give EtCOCOEt, which, in turn will react with EtMgBr [step (8)]. Additional metallation is likely, giving (F) as a relatively stable intermediate. Further *C*-alkylation (9) is to be expected.[25,34] Subsequent hydrolysis leads to (5), non-alkylated (F) giving (4). As step (9) will be faster in neat HMPT than in ether–HMPT it can be understood that the (5) : (4) ratio is higher in the former case. In mixed systems, crossed products will result. Thus, when carbonylating Bu^nMgBr–EtBr–HMPT reaction (7) will yield $Bu^nCOCOEt$. Further addition of Bu^nMgBr then appears to occur on the less hindered site, the final products being (4e) and (5e) (Table 3).

The Schemes adequately explain the overall processes for these (mostly aliphatic) derivatives. All steps with RMgX or RX can be described as (semi)ionic reactions, involving ion pairs.* It is not excluded, however, that in some cases one-electron-transfer takes place,[39] not only as a minor, or unimportant side reaction, but even leading to radical anion precursors for (part of) the products. Distinction between the two important alternatives: electron pair donation and two successive rapid one-electron transfers, is, generally speaking, far from easy, or will even be impossible.[40]

EXPERIMENTAL

Methods.— G.l.c. analyses were carried out on Becker F-410 Multigraph or F and M 5750 instruments (both flame ionization detection); columns: Carbowax TPA (20% on Chromosorb WAW 80—100 mesh, 2 m × 1/8 in; 0.7 atm.), SE-30 or OV-17 (10%; other conditions as before); temperature programme 80—180° at 10° min^{-1}. Preparative g.l.c. was carried out on a Hupe–Busch APG 402 FID with a Carbowax TPA column (20% on Chromosorb WAW; 40—50 mesh; 7.5 m × 10 mm; 150—180°). Yields were determined with the aid of an internal standard (4-chlorobenzonitrile or methyl 4-phenylbenzoate). N.m.r. spectra were recorded for $CHCl_3$ solutions on JEOL JNM-MH-60 or JEOL-C-60H spectrometers. I.r. spectra were taken on a Beckman IR 10 apparatus, mass spectra on an A.E.I. MS902 or A.E.I. MS20 spectrometer (70 eV), the latter coupled with a F and M 5750 gas chromatograph *via* an A.E.I. glass membrane separator.

Materials.—HMPT (Servo; Delden, Holland or Fluka) was refluxed over calcium hydride (48 h) under reduced pressure, distilled twice from CaH_2, and stored (molecular sieves 5 Å) in the dark. Ether, THF, and iso-octane were sodium-dried. Grignard reagents were prepared under nitrogen from freshly distilled organic halides, available as high-grade commercial products. For ether systems the method of Kharasch *et al.*[3] was used, for iso-octane that of Zakharkin.[41] Mono-Grignard reagents from α,ω-dihalogenoalkanes were prepared by the method of ref. 17, modified by keeping the concentration of dihalogenoalkane and the amount of Mg low by adding both reagents portionwise. Reagents prepared from bromides were used immediately, those of chlorides were stirred overnight prior to carbonylation.

The appropriate amount of HMPT was added slowly with vigorous stirring and cooling; in appropriate cases the ether is stripped off *in vacuo*. With 1 equiv. of HMPT in ether primary and secondary RMgX yield solutions, tertiary derivatives giving suspensions. In neat HMPT or in THF–HMPT solutions were obtained, iso-octane–HMPT giving suspensions.

Typical Examples of Carbonylation.—With 1 *equiv. of HMPT*: *n-heptylmagnesium bromide.* A solution (*ca.* 350 cm^3) of $C_7H_{15}MgBr$ (0.4 mol) in ether with HMPT (0.4 mol) was transferred to an autoclave (1 l; type AE AFP-1005; stainless steel SA 182–F316), flushed with dry nitrogen, and closed. From a sampling cylinder (type Hoke 8HD1000; stainless steel), in which CO was stored over ' Soda Asbestos ' (B.D.H.) to eliminate traces of CO_2 and water, the autoclave was pressurized with CO (500 lb in^{-2}). On vigorous

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* Free radicals do play a part in the formation of Grignard compounds from RX and Mg.[35-38]

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stirring the temperature rose from 25 to 45° in 2 min. After 30 min the pressure was diminished to 370 lb in^{-1} at 25°; this corresponds to an uptake of 0.28 mole of CO. After 20 h of stirring (pressure remaining at 370 lb in^{-2}) CO was blown off, the autoclave opened, 1N aqueous HCl (200 cm^3) added, and stirred in the autoclave. The mixture was extracted with ether (3—5 times). After drying over $CaCl_2$ the ether was removed. The resulting oil was purified by chromatography with pentane over neutral alumina giving (1f) (15.5 g, 35%).

Carbonylation of ethylmagnesium bromide in neat HMPT. EtMgBr (0.2 mol) in neat HMPT (0.6 mol) was transferred to an autoclave (1 l; flushed with dry nitrogen) and EtBr (0.2 mol) added. The autoclave was pressurized with CO (500 lb in^{-2}). Upon stirring, the temperature rapidly rose to 35° and the pressure fell to *ca.* 350 lb in^{-2} at 20° (corresponding to an uptake of 0.18 mole of CO). After work up [addition of 1N-hydrochloric acid (100 cm^3), four extractions with ether, drying over $CaCl_2$, and evaporation *in vacuo*] an oil (15.8 g) was obtained. Compounds (4b) and (5b) were obtained by preparative g.l.c. After distillation (Vb) (2.3 g, 14%), b.p. 76° at 500 mmHg (spinning band; 40 theoretical plates) was isolated.

For reactions at *ca.* 0° the autoclave was cooled by a pump cryostat *via* its cooling circuit, before CO was admitted. Reagents used for additional interaction, such as EtBr, acetic anhydride, or ' extra ' amounts of RMgX, were added after carbonylation and removal of the remaining CO from the autoclave; the apparatus was closed again and stirred for $\geqslant$15 h. The product mixture was worked up as before. Experiments at atmospheric pressure were carried out in a three-necked bottle, with magnetic stirring; CO was admitted after evacuation.

Blank reaction of RMgX *with HMPT* (cf. *footnote* d, *Table* 2). In a nitrogen atmosphere, RMgX was reacted with 2 equiv. of HMPT in ether at room temperature; Bu^{s}MgCl led to 8% Bu^{s}OH after work up after 18 h; n-C_5H_{11}MgBr gave 12% pentanol (15 min), 16% after 30 min, 16% after 18 h; n-C_8H_{17}MgBr led to 11% n-octanol in 18 h. HMPT being the only reasonable source for oxygen, ROMgX presumably arises *via* biphilic addition of RMgX to the P=O bond, elimination of ROMgX being possible due to the strong Mg–O bond formed. Radical anions may, alternatively, be involved. An endeavour to ' oxidise ' $(Me_2N)_3P$ with n-C_8H_{17}MgBr in ether failed; no HMPT was formed at room temperature after 48 h.

Products were identified by comparing g.l.c. retention times on two different columns with those of authentic samples. In most cases pure materials isolated from another run were employed (also for determining yields). Simple derivatives, such as (1a) were available as high grade commercial products. Compound (4b) was prepared according to Speck and Bost,[42] hexane-3,4-dione according to Inhoffen,[43] and compound (2b) by the method of Snell.[44]

Physical Properties of (*Novel*) *Carbonylation Products*.— Physical data for (1)—(7) were in accord with their structures. Data for ^{1}H or ^{13}C n.m.r., i.r., mass spectra, elementary analyses, and n_D are available from the authors on request.

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