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CARBONYLATION OF GRIGNARD COMPOUNDS IN ETHER - HMPT MIXTURES; A SIMPLE, ONE-STEP SYNTHESIS OF KETONES $RC(O)CHR_2$ FROM PRIMARY ALKYL DERIVATIVES RMgX

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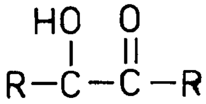
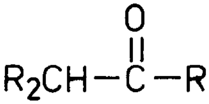
Whereas the carbonylation of several classes of organometallics (e.g. trialkylboranes [1], or transition metal-olefin complexes [2]) is of considerable synthetic utility, the reaction of Grignard compounds with carbonmonoxide has thus far been of little value [3,4]. Ethereal RMgX slowly absorbs CO at 150° and 100 atm [5], resulting in a complex mixture of products containing R_2CHOH, the corresponding alkene(s) and ketoin I [6] as main components.


$R-CH(OH)-C(=O)-R$

(I)


$R_2CH-C(=O)-R$

(II)

This reaction has been described for various types of R, viz. Et, nPr, nBu, n-Heptyl, i-Amyl, t-Bu and C_6H_5 [3,4,5].

We have now found that the addition of hexamethylphosphoric acid triamide (HMPT) to the solvent greatly enhances the rate of carbonylation: with 1 mole of HMPT per mole of RMgX, the system readily absorbs CO even at room temperature and atmospheric pressure. Using an autoclave (30 atm) the reaction is often completed within one minute.

With tertiary alkyl derivatives (R = t-Bu or t-Pent) ketoins I are produced without formation of side products of comparable volatility.

Primary compounds, however, yield ketones II; isolation is again achieved without difficulty, as there are little or no carbonylated side products [7].

Typically, 0,4 mole of HMPT was slowly added to a Grignard solution prepared from 1-n-heptylbromide (0.4 mole) in 0.25 l of dry ether; the resulting solution was transferred to a 1 l autoclave and pressurized with CO (500 psi). On vigorous stirring the temperature rose from 25 to 45°C in 2 minutes. After 30 min. the pressure was diminished to 370 psi at 25° C; this corresponds to an uptake of 0.28 mole of CO. Work up (addition of 200 cc of 1 N HCl, extraction with ether) led to II (R = 1-n heptyl) in 35% yield (after chromatography with pentane over neutral alumina; V.P.C. yield 46%) [7]; $n_D^{20.5}$ = 1.4483.

n-Propylbromide (0.8 mole) also led to II (R = nPr), 25.5 g (56%) after distillation; b.p. 90°/15 mm, n_D^{20} = 1.4263. Similar results were obtained with ethylbromide, yielding 36% of II (R = Et), b.p. 35°/14mm, $n_D^{20.6}$ = 1.4138. All products mentioned, being novel compounds, had spectral properties - NMR (+LIS), IR, MS - in accord with structure II.

Comparable results were obtained for alkylchlorides. Hence, the present reaction constitutes a simple, one-step procedure for the preparation of ketones II from primary alkyl derivatives[8].

Thus far, secondary alkyl derivatives invariably have led to product mixtures containing a.o. alkenes R - CH = R(-H), ketoins I and ketones RCH_2-CO - R.

Type and quantity of additive may strongly influence the reaction. Albeit that in neat HMPT (HMPT/RX molar ratio ca 3) rates of CO absorption are equally high, product compositions are altered. For example, EtMgBr then leads to a complex mixture including Et_2CO, $EtC(O)C(OH)Et_2$ and $Et_2C(OH)C(O) - CH(CH_3)Et$.

The effect of other additives is now being investigated together with mechanistic features.

NOTES AND REFERENCES

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2. G.P.Chiusoli, Acc. Chem. Res. 6, 422, (1973)
3. Ya.T.Eidus, N.V.Elagina and N.D.Zelinskii, Bull. Acad. Sci. USSR, chem.sect. 672, (1945)
4. K.V.Puzitskii, Ya.T.Eidus and K.G.Ryabova, Ibid. 1745, (1966)
5. F.G.Fischer and O.Stoffers, Annalen 500, 253, (1933)
6. Ketoins I can also be prepared by means of carbonylation of organozinc compounds, cf. M.W.Rathke and H.Yu, J.Org.Chem. 37, 1732, (1972)
7. Yields are based on starting alkylhalide and are therefore not corrected for e.g. Wurtz-coupling occurring after addition of HMPT or for formation of alkene.
8. Carbonylation of butyl- or phenyllithium in hexane also leads to type II products, cf. P.Jutzi and F-W Schröder, J. of Organomet. Chem., 24, 1, (1970)