Zinc-induced Free-radical Reactions of Aromatic α-Halogenoketones with Terminal Olefins

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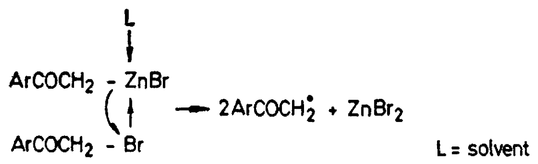
Summary Phenacyl bromide and its derivatives in the presence of zinc undergo coupling reactions to 1,4-diketones; free radicals, detected and identified by e.s.r. in the above reactions, also undergo anti-Markownikov additions with terminal olefins.

Treatment of α-monohalogenoketones with zinc affords enolates which can react with some electrophiles or give unsymmetrical furans by ionic self-condensation.[1] We found that a different self-condensation, leading to 1,4-diketones, occurs when phenacyl bromide [(I) 1 mol. equiv.] or its derivatives (Table 1) are heated in Me_2SO [2·5 ml for each mM of (I)] in a pressure bottle containing a stirred mixture of activated zinc dust or preferably Zn–Cu couple[2] (10 mol. equiv.), NaI, and collidine (1 mol. equiv. of each).

Table 1

$XC_6H_4COCH_2Br$	Reaction time (min)	Temp. (°C)	$(XC_6H_4COCH_2)_2$ Yield (%)	XC_6H_4Ac Yield (%)
(I; X=H)	30	90 (170)	32 (40)	22
(II; X=*p*-OMe)	60	170	25	31
(III; X=*p*-Br)	30	70	32	22

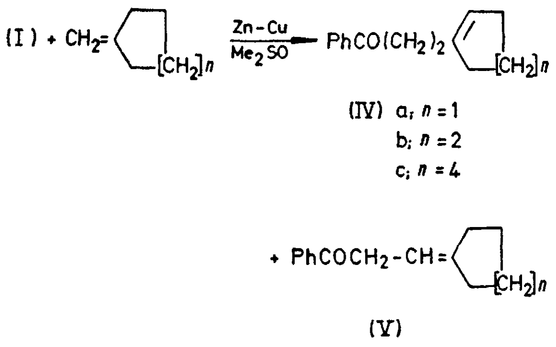
In the presence of styrene (0·5—3 mol equiv. at 90°) the yield of dibenzoylethane decreased to a constant 6—7% while $(PhCOCH_2CH_2CHPh)_2$ was isolated (5—10%, m.p. 235°, *m/e* 446, 326, 223).



Scheme

Use of an e.s.r. trapping technique[3] showed that the combination of short-lived free radicals can account for the formation of 1,2-diaroylethanes under the above reaction conditions: addition of phenyl-t-butylnitrone (0·14 mM) to the degassed reaction mixture containing (III) (0·75 mM) at room temperature† gave a spin adduct ($a_N = 14·3$G, $a_H = 5·0$G) which was not intensified on exposure to oxygen. Blank experiments eliminated the possibility of nucleophilic addition.[4] Use of Bu^tNO as a trap allowed the identification of the radicals: p-$BrC_6H_4COCH_2^{\bullet}$ ($a_N = 13·6$G, $a_H = 7·9$G) and p-$BrC_6H_4COCD_2^{\bullet}$ ($a_N = 14·0$G and $a_D = 1·2$G, triplet of quintets).

This novel zinc-induced homolytic cleavage[5] of an α-monohalogenoketone is attributed to co-ordination with an organometallic[6] followed by the intermolecular one-electron transfer process shown in the Scheme.



The potential synthetic value of these findings was shown in reactions with terminal olefins using methylenecycloalkanes and 1,1-diarylethylenes as substrates. Regio-

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† Compound (III) was used due to its greater reactivity.

specific addition of the phenacyl group occurred when a stirred mixture of the olefin (1 mol. equiv.), Zn–Cu couple[2]‡ (30 mol. equiv.), $NaHCO_3$ (10 mol. equiv.), and NaI (5 mol. equiv.) in Me_2SO (4 ml for each mM of olefin) was heated with an excess of (I) (5 mol. equiv.) in a nitrogen-flushed pressure bottle.

Table 2. Additions of (I) to olefins[a]

Olefin		Temp. (°C)	Products (%)[b]
Methylenecyclopentane	.. ..	60	43 (IVa); 5 (Va)
Methylenecyclohexane	.. ..	80	54 (IVb)
Methylenecyclo-octane	.. ..	60	50 (IVc); 6 (Vc)
17-Methyleneandrostan-3β-ol	..	60	55 (VI) and (VII)
1,1-Diphenylethylene	.. ..	140	56 (VIII)
1,1-Di-(*p*-methoxyphenyl)ethylene		140	54 (IX)

[a] Efficient (magnetic) stirring and dryness of reagents are essential. Reaction time was 1 h for all compounds and (I) was added to the reaction mixture under N_2 in two equal portions, at the start and after 30 min. Work-up (NH_4Cl) and chromatography afforded the products. [b] All isolated compounds were characterised by i.r., n.m.r., and mass spectroscopy. The side chain methylene groups of cycloalkenes exhibit an A_2B_2 pattern in n.m.r. and the use of a shift reagent, $Eu(fod)_3$, confirmed the location of the double bond.

Unsaturated adducts were formed from methylenecycloalkanes and (I) under relatively mild conditions (Table 2). The cycloalkenes (IV) were the only or major addition products, except with 17-methyleneandrostan-3β-ol, which afforded a 1:1 mixture of the $\Delta^{16,17}$ (VI) and $\Delta^{17,20}$ (VII)§ derivatives.

By contrast, reactions of (I) with diarylethylenes yielded only saturated addition products:

$$\text{(I)} + CH_2{=}CAr_2 \xrightarrow[\text{MeSO}_2]{\text{Zn–Cu}} PhCO(CH_2)_2CHAr_2$$

(VIII) Ar = Ph
(IX) Ar = p-$MeOC_6H_4$

The electrophilicity of the phenacyl species was supported by competitive experiments in which equimolar amounts of $Ph_2C{=}CH_2$ and $(p\text{-}MeOC_6H_4)_2C{=}CH_2$ were treated with (I): the molecular ratio of olefin recovery (2:1) showed a greater addition rate of the latter olefin.

Metal-induced additions of α-halogenoketones across unactivated and isolated double bonds have not been previously reported. The e.s.r. evidence and the regiospecificity of these new C–C bond formation reactions support a free radical mechanism, *via* a radical–adduct intermediate. The subsequent product-forming steps, at present under investigation, may occur directly (by hydrogen abstraction or chain transfer reaction) or *via* an organometallic complex[7] followed by heterolytic cleavage.

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‡ Use of activated zinc dust reduced the yields.

§ Only one $\Delta^{17,20}$ isomer was formed.

[1] *Cf.* T. A. Spencer, R. W. Britton, and D. S. Watt, *J. Amer. Chem. Soc.*, 1967, **89**, 5727.

[2] *Cf.* J. B. Lambert, F. R. Koeng, and J. W. Hamersma, *J. Org. Chem.*, 1971, **36**, 2946. The zinc dust is washed with 1% $CuSO_4$ solution and contains *ca.* 1% Cu.

[3] For a recent review see E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31.

[4] A. R. Forrester and S. P. Hepburn, *J. Chem. Soc.* (*C*), 1971, 701.

[5] In previously reported coupling reactions of aromatic α-halogenoketones to 1,4-diketones the intermediacy of transition-metal complexes has been suggested. *E.g.*, I. Hashimoto, N. Tsuruta, M. Ryang, and S. Tsutsumi, *J. Org. Chem.*, 1970, **35**, 3748; H. Alper and E. C. H. Keung, *ibid.*, 1972, **37**, 2566.

[6] In strongly co-ordinating solvents C–Zn bonding can be prevalent over O–Zn bonding, in analogy with organometallics formed from Zn and α-halogenoesters; see M. Gaudemar and M. Martin, *Compt. rend.*, 1968, **267C**, 1053.

[7] *E.g.*, J. K. Kochi in 'Free Radicals,' Wiley, New York, 1973, vol. 1, p. 591.