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In Grignard Reagent Formation from Cyclopropyl Bromide in Diethyl Ether, Trapping by DCPH Is Consistent with Diffusing Cyclopropyl Radical Intermediates

John F. Garst* and Ferenc Ungváry[‡]

Department of Chemistry, The University of Georgia, Athens, Georgia 30602

garst@chem.uga.edu

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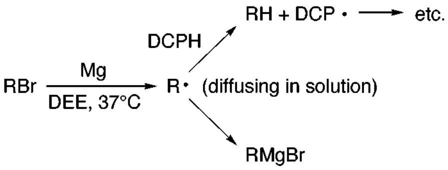
ABSTRACT



For reactions of magnesium with cyclopropyl bromide in diethyl ether, added DCPH decreases the yield of cyclopropylmagnesium bromide by as much as 75%, while solvent-derived products disappear and cyclopropylcyclohexylphosphine and tetracyclohexyldiphosphine appear. These changes reflect trapping of diffusing intermediate cyclopropyl radicals.

In Grignard reagent formation from magnesium metal and a cyclopropyl or typical alkyl halide RX in an appropriate solvent SH (often diethyl ether, DEE), "Grignard" radicals $R^{\bullet}$ are intermediates.[1−3] The A and D models are contradictory descriptions of their behavior. In the A model Grignard radicals remain adsorbed at the magnesium surface Mg_Z,[4] while in the D model they diffuse in solution near Mg_Z.[5] Considerable evidence supports the D model, including kinetic analyses of competitive product formation[6−8] and, for typical alkyl halides, radical trapping by TMPO (tetramethylpiperidine-*N*-oxyl) and DCPH (dicyclohexylphosphine).[9−11] In addition, for cyclopropyl bromide, RBr, the D model predicts correctly and the A model predicts incorrectly the effects of solvent deuteration on product distributions.[12]

In contrast, it has been reported that the extent to which DCPD (DCPH-*P*-*d*) traps cyclopropyl Grignard radicals is only ∼4%.[13] This has been cited as being among the strongest pieces of evidence for the A model; the D model predicts more trapping.[14]

[‡] Department of Organic Chemistry, University of Veszprém and Research Group for Petrochemistry of the Hungarian Academy of Sciences, 8200 Veszprém, Hungary.

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Several observations can be made in response.[3] (1) The analytical techniques used in the DCPD work are suspect. RD (cyclopropane-d_1) was determined by PFT ^{1}H NMR spectroscopy after transfer to a cold trap. The reaction mixture was then quenched with D_2O, and RMgBr (cyclopropylmagnesium bromide) was determined as RD by the same method. Losses could have occurred during the transfers to cold traps, and there is evidence that insufficient delays between pulses were used in the NMR spectroscopy. (2) The low yield of RMgBr, 6% (reported but not discussed in the original work),[13] is not consistent with the conclusion that that there is only 4% trapping of Grignard radicals. (3) The trapping of $R^\bullet$ by DCPH involves more complex chemistry than simple hydrogen-atom transfer. Cyclopropylcyclohexylphosphine (RCPH) is a significant product.[3] (4) A primary isotope effect on D/H-atom transfer could reduce the extent of trapping from DCPH to DCPD. (5) Other data indicate that ca. 20% of cyclopropyl Grignard radicals attack the solvent DEE.[3,8] Comparing this with the reported 4% extent of trapping by DCPD, one must conclude that DEE is a better cyclopropyl radical trap than DCPD, which is not plausible.

These considerations led us to determine the effect of DCPH on the yield (RMgBr) by a time-honored method, successive carbonation, methylation, and gas chromatography. (Attempts to titrate RMgBr by the Eastham method[15] gave dubious results; there were unusual color changes and precipitates.) Reactions of magnesium with cyclopropyl bromide (initially 0.2 M) in DEE containing $MgBr_2$ (initially 0.12 M), octane (internal standard for GC analysis), and DCPH (initially 0.0−0.6 M) occurred, as described previously,[8,16] under nitrogen at 37 °C. Excess dry CO_2 was admitted, followed (after carbonation was complete) by dry CH_2N_2. Subsequent GC analyses for methyl cyclopropanecarboxylate used the internal standard, calibrated response factors, and model mixtures. Yields of RCPH, RS (1-cyclopropyl-1-ethoxyethane), and SS (2,3-diethoxybutane), all of which were synthesized independently, were also determined by GC. Tetracyclohexyldiphosphine was detected but not determined reliably (apparent yields were 5−8 mol per 100 mol RBr consumed).

As $[DCPH]_0$ increases RMgBr decreases, RS and SS become undetectable, and RCPH increases (Table 1).

Although it is not clear how RCPH arises, we find it is also formed in substantial yields when cyclopropyl radicals are generated in DEE by the photolysis of di(cyclopropanecarboxylyl) peroxide.[17] It is clearly a product of cyclopropyl radical trapping, and its formation does not require the presence of Mg, RBr, or RMgBr.

Table 1. Effects of DCPH on Yields from Reactions of Magnesium with Cyclopropyl Bromide in Diethyl Ether[a]

$[DCPH]_0$ (M)	RMgBr	RS	SS	RCPH
0	40	2.1	3.0	0
0.20	23			12
0.60	11	0.0	0.0	19

[a] Yields are given as moles of product formed per 100 mol of cycloproyl bromide consumed. Initial concentration of cyclopropyl bromide: 0.20 M. Initial concentration of magnesium bromide: 0.12 M. Temperature: 37 °C.

DCPH does not react with octylmagnesium bromide in THF.[11] The lack of gas (cyclopropane) evolution when DCPH is added to a solution of preformed RMgBr in DEE, the finding (by GC) of all of the added DCPH after 10 and 140 min of reflux at 37 °C, and the persistence of RMgBr in the presence of excess DCPH all show that DCPH does not react with RMgBr in our experiments.

RS, SS, RCPH, and tetracyclohexyldiphosphine are products of radical reactions. If $R^\bullet$ were trapped by DCPH, then in its presence RMgBr would decrease, RS and SS would approach zero, RCPH would appear and increase, and tetracyclohexyldiphosphine would appear. All of this is observed. The disappearance of products CpS and SS in the presence of DCPH shows that it is a better cyclopropyl radical trap than solvent DEE, as expected.

At 0.6 M, DCPH decreases RMgBr by nearly 75%, to a value of 11 mol per 100 mol RBr consumed. As they diffuse in solution, a very large fraction of cyclopropyl Grignard radicals can be trapped.

Could something other than $R^\bullet$ be trapped by DCPH? For Grignard reactions of aryl and vinyl bromides (and cyclopropyl bromides to a lesser extent), there is evidence of non-$R^\bullet$ or extremely short-lived-$R^\bullet$ pathways,[18,19] and for aryl bromides there is evidence of possible carbanion intermediates R^-.[20,21] In the present case, R^- trapping would not explain observed variations in yields of RS, SS, RCPH, and tetracyclohexyldiphosphine. It is conceivable, however, that an anion-radical $RX^{-\bullet}$ could undergo reactions that are usually, as here, assigned to $R^\bullet$.[22−24]

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