Bimolecular reactions of alkyl halides and acylgermanes: formation of ketones, diketones, and other products by radical–radical reaction

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Abstract

Reactions of alkyl halides (R^1X) with acyltriphenylgermanes ($R^2COGePh_3$) under radical conditions provide mixtures of ketones (R^1COR^2), diketones (R^2COCOR^2), alkanes (R^1H) and alkenes. These products arise from radical–radical reactions, and the results suggest that bimolecular addition reactions of alkyl radicals to acylgermanes are too slow to propagate radical chains.

Keywords: Germanium; Alkyl halides; Ketones; Radical reactions; Acylgermanes

1. Introduction

Irradiation of δ- and ε-halo acyltriphenylgermanes provides cyclic ketones along with concomitant elimination of triphenylgermyl halide [1]. For example, acylgermane 1 forms cyclopentanone and triphenylgermyl iodide, and this transformation is thought to occur by the mechanism outlined in Scheme 1. Acylgermanes react under photolytic conditions with homolytic (Norrish Type I) bond cleavage creating an acyl and a germyl radical [2,3]. This initiates a chain whose propagation steps are: (1) iodine abstraction, (2) cyclization of the resulting alkyl radical to the carbonyl carbon of the acylgermane, and (3) elimination of the chain-carrying triphenylgermyl radical. The rate constant of the cyclization at 80 °C ($k_c = 7 \times 10^6 \ \text{s}^{-1}$) [3] is high compared with the 5-exo cyclization of related aldehydes ($k_c = 9 \times 10^5 \ \text{s}^{-1}$) and ketones ($k_c < 10^3 \ \text{s}^{-1}$) [4].

The surprisingly high reactivity of acylgermanes in radical cyclizations suggests that bimolecular additions of radicals might also occur. Were this reaction to be sufficiently rapid, it would be possible to add alkyl halides to acyl germanes by the route outlined in Eq. (1). This would provide a strategic option for the acylation of alkyl halides, a common transformation that now

almost always involves conversion of the halide to an organometallic intermediate and subsequent reaction with an acyl electrophile. There is even some evidence in the literature that might, when viewed in a favorable light, suggest that radicals add bimolecularly to acylgermanes [5] or stannanes [6]. [Photolysis of acetyltriph-

Initiation step

**Propagation steps**
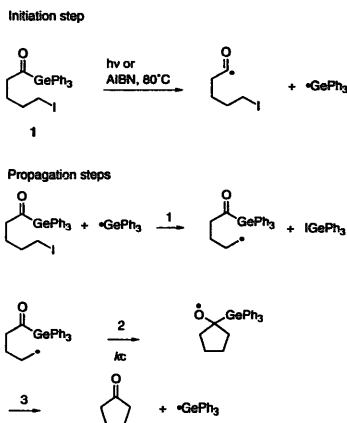
Scheme 1.

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enylgermane in the presence of styrene provides a mixture of products, some of which clearly derive from radical–radical reactions. However, the major product of the reaction, [CH$_3$COCH(Ph)CH$_2$GePh$_3$] is produced in a yield above the statistical level. This can be formulated to arise by a radical chain involving addition of a benzyl radical to an acylgermane. This chain was not postulated in the original paper, and our results suggest that it is improbable. The reaction of TolCOSnMe$_3$ with ^{t}BuI is reported to give tolyl *tert*-butyl ketone in an unspecified yield.] We report herein that the reactions of alkyl halides with acylgermanes do indeed produce ketones. Unfortunately, a number of other types of product are also produced, suggesting that radical–radical reactions are occurring and that bimolecular additions of alkyl radicals to acylgermanes are not fast enough to propagate chains (for other non-chain radical reactions of acylgermanes see Ref. [7]).

$$R-X \; + \; R^1 \overset{O}{\underset{}{\|}} GePh_3 \longrightarrow R^1 \overset{O}{\underset{}{\|}} R \; + \; Ph_3GeX \qquad (1)$$

2. Results and discussion

To investigate bimolecular reactions, we allowed representative 1°-, 2°-, and 3°-alkyl halides to react with acetyl- and benzoyl-triphenylgermane (2 and 3). The acylgermanes were prepared as described by Kiyooka and Miyauchi by reaction of triphenylgermyllithium with the corresponding ester in THF at 0 °C [8]. [Acylgermane 3 was also prepared by reaction of the germyllithium with benzaldehyde followed by oxidation with diisopropylazodicarboxylate in 72% yield.] The bimolecular radical reactions were carried out in sealed NMR tubes with benzene-d_6 as the solvent. The products were identified by comparing ^{1}H NMR spectra of
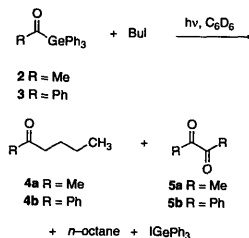
the reaction mixtures with spectra of authentic samples. The product ratios were determined by integration of the crude ^{1}H NMR spectra. These ratios were confirmed in a few experiments by GC-MS analysis (for details see Section 3). The absolute yields were calculated based on the total amount of aromatic protons as a standard. This is a rather crude standard, so yields are not highly accurate. The volatility of many products precluded the determination of isolated yields.

In contrast to the intramolecular reactions [1], it was not possible to initiate the bimolecular radical reactions of iodobutane (BuI) with 2 and 3 under thermal conditions (10% AIBN, 10% HGePh$_3$ or HSnPh$_3$, 80 °C). The starting materials remained unchanged. However, conversion did occur when the mixtures were irradiated, and the results of a series of experiments are shown in Scheme 2 and Table 1. The reaction of acylgermane 2 with the iodobutane provided about 20% of the butylketone 4a along with α-diketone 5a, octane, and triphenylgermanium iodide after 1 h irradiation with a Hg lamp (entry 2). Varying the amount of the alkyl iodide (compare entries 1–3) or changing the source of irradiation (Hg lamp/sunlamp, compare entry 2 with entries 4 and 5) had no effect on the product ratio (although the sunlamp reactions were slower). Generally similar results were obtained in two experiments with acylgermane 3 (entries 6, 7).


2 R = Me
3 R = Ph

4a R = Me   **5a R = Me**
4b R = Ph   **5b R = Ph**

+ *n*-octane + IGePh$_3$

Scheme 2.

Table 1
Bimolecular addition of iodobutane to acylgermanes 2 and 3

Entry	[RCOGePh$_3$]	Iodide (equiv.)	Conditions	Ketone 4a,b	Diketone 5a,b	*n*-Octane [a]
1 [b]	0.1 M 2	0.8	1 h [Hg, 400 W]	21%	19%	9%
2	0.1 M 2	1.0	1 h [Hg, 400 W]	21%	17%	19%
3	0.1 M 2	2.3	1 h [Hg, 400 W]	20%	19%	19%
4	0.1 M 2	1.3	2 h [sunlamp]	22%	21%	21%
5 [c]	0.1 M 2	1.6	5 h [sunlamp]	12%	14%	13%
6	0.1 M 3	1.1	1 h [Hg, 400 W]	20%	n.d.	10%
7	0.2 M 3	1.5	5 h [sunlamp]	15%	n.d.	8%

[a] Calculated by subtracting the integration of ketones 4 and 5 from the total alkane region.
[b] 25% acylgermane 2 remained.
[c] 47% acylgermane 2 remained.

Scheme 3.

Scheme 4.
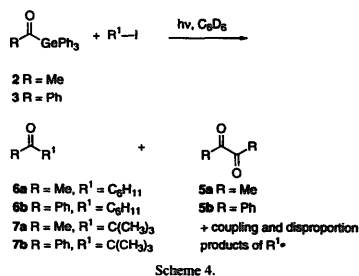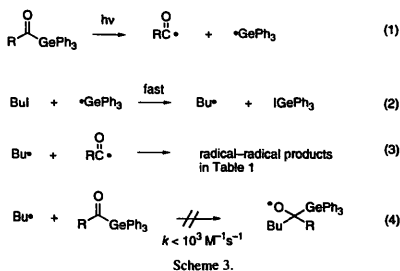
The yields of ketones **4a,b** (about 20%) are very low compared with the yields of ketones in the related 5-*exo* cyclizations (typically 90–95% yield). Furthermore, ketones **4a,b**, diketones **5a,b** and octane were all formed in about the same amount, and the combined yield of these three products (50–60%) was not quantitative. All this, coupled with the difficulties in initiating chains, implies that the products are formed in non-chain reactions. We suggest that the non-chain mechanism shown in Scheme 3 accounts for these observations. An acyl radical and a germyl radical are generated by homolytic carbonyl–germanium bond cleavage (step 1). The germyl radical then rapidly abstracts iodine from the iodobutane (step 2) [9]. This forms equal amounts of acyl and butyl radicals. Reactions of these two radicals with themselves and each other provide the observed products (step 3). The fact that the radical chain process analogous to the intramolecular cyclization mechanism was not observed in the bimolecular reaction must be because the addition of the alkyl radical to the acylgermane (step 4) is slow. The lack of a chain process suggests that this addition step must have a rate constant less than 10^3 M^{-1} s^{-1}.

The increased nucleophilicity of 2°- and 3°-radicals could conceivably accelerate addition to an acylgermane, though the higher steric hindrance might have the opposite effect. We examined the reactions of the cyclohexyl iodide and the *tert*-butyl iodide with acylgermanes. Experiments were conducted as described above,

and the results are summarized in Scheme 4 and Table 2. The reaction of cyclohexyl iodide with acylgermane **2** or **3** provides the ketone **6a,b** in less than 15% yield along with the diketone **5a,b** and bis(cyclohexane). Furthermore, we observed cyclohexane and cyclohexene in equal amounts. These presumably arise from disproportionation of the cyclohexyl radical. In the reaction with the *tert*-butyl iodide, the ketone **7a,b** was only found in trace amounts. As expected for 3°-radicals, the major reaction was the disproportionation to isobutane and isobutylene. The higher yields of alkane and alkene in these experiments compared with ketone and diketone suggest that direct photolysis of the *tert*-butyl iodide may also be occurring.

Hypothesizing that the size of the germyl ligands in **2** and **3** could prevent the attack of the radicals, we synthesized the acylgermane **8** with methyl ligands [10] (acylgermane **8** was here prepared by addition of lithium trimethylgermane to benzaldehyde followed by oxidation with DIAD). But the reaction of **8** with butyl iodide gave only 7% of the ketone **4b** (Scheme 5). The tris(pentafluorophenyl) acylgermane **9** was synthesized in an attempt to create a more electrophilic carbonyl carbon by adding electron-withdrawing ligands to the germanium [11]. The reaction of iodobutane with the acylgermane **9** provided no significant change in the product ratio compared with the results in Scheme 1, but the reaction time with **9** was more than three times longer. This probably reflects a less efficient photo-

Table 2
Bimolecular addition of cyclohexyl and *tert*-butyl iodide to acylgermanes **2** and **3**

Entry	[RCOGePh₃]	Iodide	Ketone **6a,b**	Diketone **5a,b**	Alkane	Alkene
1 [a]	0.1 M **2**	*c*-HexI	< 15%	16%	16%	12%
2 [b]	0.1 M **2**	*c*-HexI	< 15%	17%	16%	10%
3 [a]	0.2 M **3**	*c*-HexI	12%	n.d.	8%	12%
4 [a]	0.1 M **2**	¹BuI	< 2%	21%	35%	38%
5 [b]	0.1 M **2**	¹BuI	< 2%	13%	29%	33%
6 [a]	0.2 M **3**	¹BuI	< 2%	n.d.	20%	26%

[a] Conditions: 1 h Hg [400 W], 1.1 equiv. alkyl iodide.
[b] Conditions: 2 h sunlamp, 1.1 equiv. alkyl iodide.

Scheme 5.
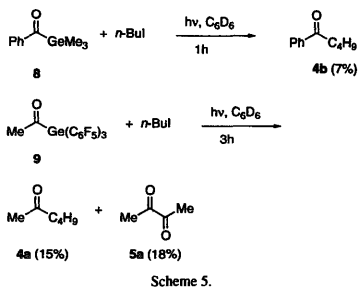
cleavage of the acylgermane. Given the preliminary observations, the reactions of **8** and **9** were not investigated in any detail.

In summary, the photolytic addition of alkyl iodides to acylgermanes does produce ketones in some cases, but the yields are low and a number of products are formed by radical–radical reactions. The formation of radical–radical products, the lack of reaction when using thermal initiation conditions, and other observations suggest that simple alkyl radicals will not add bimolecularly to acylgermanes with rates sufficiently high to propagate radical chains.

3. Experimental part

3.1. General procedure for bimolecular radical reactions with acylgermanes 2 and 3

A solution of the acylgermane **2** or **3** (0.1 or 0.2 M) in benzene-d_6 (400 μl) was degassed in an NMR tube. The respective alkyl iodide (0.8–2.3 equiv., Tables 1 and 2) was added and the reaction mixture was irradiated at room temperature with a 400 W Hg lamp (1 h) or a sunlamp (2 h). The product mixture was analyzed directly by ^{1}H NMR, TLC and GC-MS. Significant proton signals for determining the product ratios were (benzene-d_6, 300 MHz): 3.97 (hept, H(Cα) in cyclohexyl iodide), 3.03 (m, H(Cα) in cyclohexyl phenyl ketone), 2.74 (t, H(Cδ) in butyl iodide), 2.61 (t, H(Cα) in butyl phenyl ketone), 2.47 (m) and 1.77 (s, H(Cα) in

cyclohexyl methyl ketone), 2.22 (s, in $CH_3COGePh_3$), 1.96 (t) and 1.70 (s, H(Cα) in butyl methyl ketone), 1.83 (s) and 0.96 (s, in *tert*-butyl methyl ketone), 1.68 (s, *tert*-butyl iodide), 1.66 (s, isobutene), 1.45 (s, cyclohexane) ppm.

3.2. Acetyl tris(pentafluorophenyl)germane (9)

This was prepared in 63% yield by addition of lithium tris(pentafluorophenyl)germane to acetyl bromide in THF at −60 °C. ^{1}H NMR (300 MHz, CDCl$_3$) $\delta = 2.67$ (s, 3H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) $\delta = 219.1$, 148.3 ($J_{CF} = 243$ Hz), 146.0 ($J_{CF} = 257$ Hz), 137.7 ($J_{CF} = 255$ Hz), 104.4, 35.5 ppm; MS (EI) m/z (rel. intensity) 575 (M$^+$–Ac, 35), 555 (5), 525 (5), 425 (15), 375 (12), 296 (100). HRMS $C_{18}F_{15}$Ge (M–Ac) m/z Calc. 570.9003; m/z Found 570.8972.

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