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A practical access to acyl radicals from acyl hydrazides

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Various acyl radicals can be generated from the corresponding acyl triphenylmethyldiazo derivatives, produced by *in situ* oxidation of hydrazide precursors with phenylseleninic acid.

A few years before his landmark work on the triphenylmethyl radical, Gomberg, working under the supervision of Victor Meyer,[1] prepared tetraphenylmethane by thermally decomposing phenylazotriphenylmethane (PAT). Unbeknown to him at the time, this reaction also involved triphenylmethyl radicals. Since the pioneering studies of Victor Meyer and his school, azo derivatives have found extensive application as initiators for many of the classical radical processes.[2] Surprisingly, however, the use of azo derivatives as stoichiometric precursors of radicals has not been often exploited for preparative purposes. Some scattered examples can be found in the literature, the most synthetically interesting arising from the group of Baldwin.[3] In the present communication, we describe a practical approach to acyl radicals,[4] hinging on the thermal decomposition of acyl azotriphenylmethane derivatives.[5]

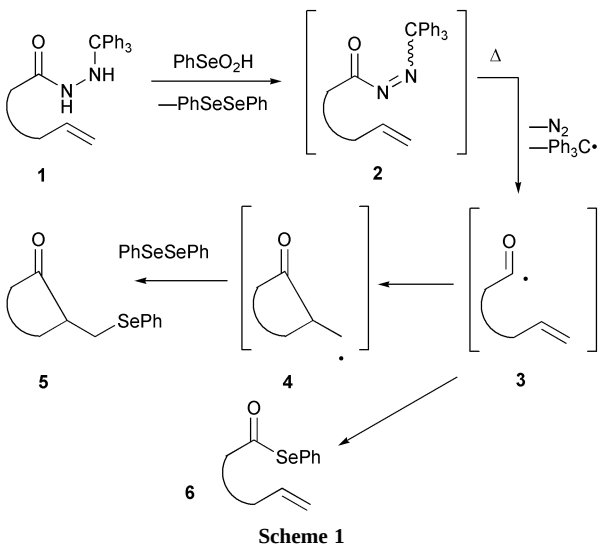
The reasoning underlying our work is outlined in Scheme 1. Oxidation of the hydrazide precursor **1** using phenylseleninic acid leads to the desired azo derivative **2** and to the corresponding amount of diphenyl diselenide.[6] If this oxidation is carried out at or above the decomposition temperature of the azo compound, an acyl radical **3** is generated that can undergo ring closure to a suitably located internal olefin. The resulting carbon centred radical **4** is then rapidly captured by the highly radicophilic diphenyl diselenide giving finally derivative **5**. Only a small amount of diphenyl diselenide needs to be added at the beginning of the reaction to ensure a sufficient initial concentration of the trap. One obvious pitfall is the premature capture of the acyl radical by the diselenide leading to the undesired acyl selenide **6**.

Triphenylmethylhydrazide **1a** was easily prepared from *O*-allyl salicylic acid chloride and triphenylmethylhydrazine. Portion-wise addition of phenylseleninic acid (0.5 mol equiv.) to a refluxing solution of **1a** and diphenyl diselenide (0.2 mol equiv.) in toluene (concentration in hydrazide: 0.027 M) provided the expected cyclic ketone **5a** in 66% yield (Table 1). The phenylseleninic acid oxidant must be added slowly, over 4–6 hours, to avoid a build up in the concentration of diphenyl diselenide and therefore increasing the chances of untoward capture of the acyl radical to give the corresponding acyl selenide.†

Under similar experimental conditions, a number of other cyclic ketones were prepared by this route, as shown by the examples compiled in Table 1. The internal olefinic trap may be varied and nitrogen or sulfur atoms may be included in the substrate. Furthermore, the process is successful starting from both aromatic and aliphatic carboxylic acids. The triphenyl radical generated upon thermolysis of the diazo intermediate is captured by the diphenyl diselenide to give non-polar, easily separated co-products.

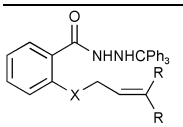
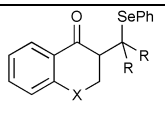
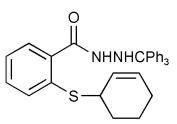
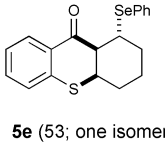
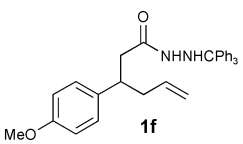
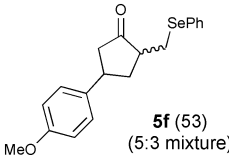
In the case where the loss of carbon monoxide from the intermediate acyl radical is especially favoured, then an overall decarboxylative phenylselenylation is observed. This is illustrated by the conversion of phenylacetyl derivative **1g** into benzyl phenyl selenide **7** in 78% yield (Scheme 2).

We also found that this approach could be used to make alkoxycarbonyl radicals from alcohols by starting with the corresponding chloroformate or oxalyl ester chloride (Scheme 2). In the latter case, the alkoxycarbonyl radical is formed upon extrusion of a molecule of carbon monoxide. Depending on the structure of the substrate, the alkoxycarbonyl radical may be captured to give a lactone, as shown by the transformation of hydrazide **1i** into lactone **8** in 45% yield. Alternatively, loss of carbon dioxide may be fast when it leads to a stabilised radical,[7]



Scheme 1

Table 1 Generation and capture of acyl radicals

Hydrazide **1**	Cyclic ketone **5** (yield %)
 **1a**, X = O, R = H **1b**, X = NSO_2Me, R = H **1c**, X = S, R = H **1d**, X = S, R = Me	 **5a** (66) **5b** (70) **5c** (74) **5d** (64)
 **1e**	 **5e** (53; one isomer)
 **1f**	 **5f** (53) (5:3 mixture)

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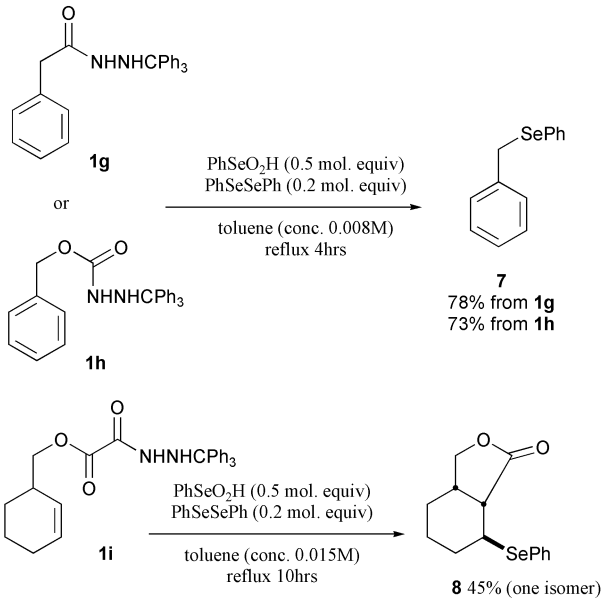

Scheme 2

and this is then captured by the diselenide. This variant is illustrated by the formation of benzyl phenyl selenide **7** in 73% yield from **1h**.

This approach to acyl radicals allies simplicity with the use of readily available substrates and reagents. None of the yields has been optimised and room for improvement certainly exists. One interesting feature of this approach to cyclic ketones and lactones is that the phenylselenide group ends up β- to the carbonyl group; it is therefore easily eliminated with base or *via* the selenoxide to provide the corresponding unsaturated derivatives. This is a distinct advantage in comparison to stannane based methods for generating acyl radicals (starting usually from acyl selenides), where the last propagation step is a hydrogen atom transfer.

Notes and references

† Typical experimental procedure: a solution of tritylhydrazide (**1c**, 135 mg, 0.3 mmol) and diphenyl diselenide (19 mg, 0.06 mmol) in 10 ml of dry toluene was refluxed for 10 minutes under an inert atmosphere. Solid phenylseleninic anhydride (54 mg, 0.15 mmol) was added in small portions every 15 min over a period of 4 h. The reaction mixture was allowed to cool and the solvent removed under reduced pressure. Chromatography of the residue on silica gel using a pentane–dichloromethane gradient afforded pure thiochromanone **5c** in 74%; δ_H (250 MHz; $CDCl_3$) 7.55 (m, 2H), 7.4–7.1 (m, 7H), 3.50 (dd, 1H, J = 12 Hz; J' = 3.6 Hz), 3.46–3.26 (m, 2H), 3.16–2.94 (m, 2H); δ_C (62.5 MHz; $CDCl_3$) 194.9, 141.9, 133.4, 133.1, 129.8, 129.4, 127.5, 125.1, 47.5, 30.9, 27.0; υ_{max} (film)/cm^{-1} 1672; MS(EI): 334 $[M]^+$, 256 $[M - Ph]^+$, 177 $[M - SePh]^+$; HRMS: found 333.9891 ($[M]^+$); $C_{16}H_{14}OSSe$ requires 333.9930.

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