

# Synthesis of 2-Indanones via [4 + 1] Annulation Reactions of (Trialkylsilyl)arylketenes

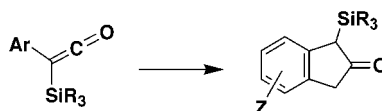
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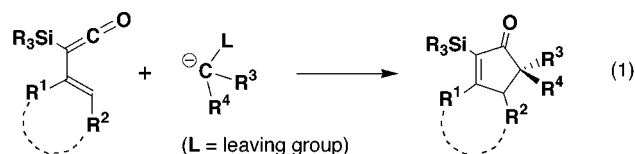
## ABSTRACT



(Trialkylsilyl)arylketenes combine with (trimethylsilyl)diazomethane in a new [4 + 1] annulation process leading to 2-indanone derivatives. The (trialkylsilyl)arylkene annulation substrates are available via the photochemical Wolff rearrangement of  $\alpha$ -silyl- $\alpha$ -diazo ketones, which are themselves prepared by silylation of the corresponding diazo ketones. The mechanism of the annulation reaction is proposed to involve the formation of a 2,3-bis(silyl)cyclopropanone, which is in equilibrium with an oxyallylic cation. Electrocyclic closure of this intermediate forms the new cyclopentenone ring.

In this Letter we describe a new [4 + 1] annulation strategy for the synthesis of 2-indanones based on the reaction of (trialkylsilyl)arylketenes (“TAS-arylketenes”) with (trimethylsilyl)diazomethane. The exceptional stability of silylketenes has been known for over 35 years,<sup>1</sup> and the utility of this remarkable class of ketenes in organic synthesis is now well established.<sup>2</sup> Prior research in our laboratory has focused on the synthesis and chemistry of TAS-*vinyl*ketenes. Silyl substituents suppress the tendency of vinylketenes to undergo dimerization and [2 + 2] cycloaddition, allowing them to express their underlying reactivity as electron-rich conjugated dienes in Diels–Alder and hetero Diels–Alder reactions leading to cyclohexenones, phenols, and oxygen and nitrogen heterocycles.<sup>3–5</sup> Recently, we have reported the application of TAS-*vinyl*ketenes as four-carbon components in a new,

stereoselective [4 + 1] annulation strategy for the synthesis of substituted cyclopentenones.<sup>6</sup> As outlined in eq 1, nucleophilic species bearing appropriate leaving groups (“carbenoid reagents”) add to TAS-*vinyl*ketenes to generate dienolate species that cyclize to form new five-membered rings.<sup>7</sup> The goal of the present study was to investigate the feasibility of extending this annulation strategy to TAS-*aryl*ketenes, i.e., systems in which the vinyl group is embedded within the framework of an aromatic ring.<sup>8</sup>



The TAS-arylketenes required for this study were prepared via the photochemical Wolff rearrangement of  $\alpha$ -silyl- $\alpha$ -diazo aryl ketones **2a–g** (Scheme 1),<sup>9,10</sup> which are themselves readily available by silylation of the corresponding diazo ketones.<sup>11</sup> Diazo derivatives of aryl ketones are easily prepared by addition of diazomethane to the appropriate acid chloride or, alternatively, via the application of our detri-fluoroacetylative diazo transfer process<sup>12</sup> to the corresponding

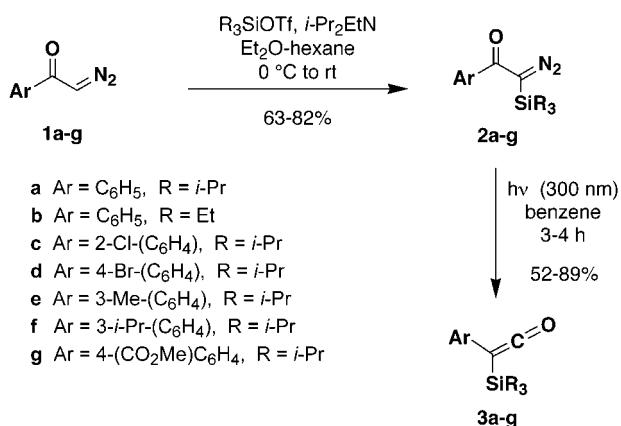
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(3) Danheiser, R. L.; Sard, H. *J. Org. Chem.* **1980**, *45*, 4810.

(4) Loebach, J. L.; Bennett, D. M.; Danheiser, R. L. *J. Org. Chem.* **1998**, *63*, 8380.

Scheme 1



methyl ketones.<sup>13</sup> As expected, TAS-arylketenes **3a–g** are remarkably robust ketenes, stable at 25 °C and at mildly elevated temperatures, and amenable to purification using conventional silica gel chromatography.

The feasibility of the 2-indanone [4 + 1] annulation strategy was initially examined using phenyl(triisopropylsilyl)ketene (**3a**). Treatment of **3a** with 1.1 equiv of TMS-diazomethane<sup>14</sup> in a mixture of dichloromethane and hexane at room temperature produced the desired 1,3-bis(silyl)-indanone in nearly quantitative yield. Purification of this compound could not be achieved without partial loss of the trimethylsilyl group, and consequently, the crude product was converted to the mono(silyl)indanone **4** by brief stirring at room temperature in the presence of silica gel. In this fashion, the desired indanone was obtained in 86% yield as a white solid, mp 81–82 °C. 2-Indanone itself can be accessed directly by employing phenyl(triethylsilyl)ketene for the reaction, in which case both the TMS and TES groups can

Table 1. [4 + 1] Indanone Annulation

entry	ketene	product(s)	% yield <sup>a</sup>
1	<b>3a</b>		86 <sup>b</sup>
2	<b>3b</b>		69 <sup>c</sup>
3	<b>3c</b>		54 <sup>d</sup>
4	<b>3d</b>		79 <sup>e</sup>
5	<b>3e</b>	+	65 <sup>b</sup> (66:34)
6	<b>3f</b>	+	91 <sup>f</sup> (46:54)
7	<b>3g</b>		36 <sup>g,h</sup>

<sup>a</sup> Isolated yields of products purified by column chromatography.

<sup>b</sup> Desilylation (of the Me<sub>3</sub>Si group) was achieved by stirring the crude product in CH<sub>2</sub>Cl<sub>2</sub> over silica gel at rt for 1 h. <sup>c</sup> Cleavage of both the Me<sub>3</sub>Si and Et<sub>3</sub>Si groups from the crude annulation product was accomplished by exposure to 1 N HCl in THF at rt for 4 h. <sup>d</sup> Treatment of the annulation product with 3 equiv of K<sub>2</sub>CO<sub>3</sub> in MeOH at room temperature for 3 min effected desilylation. <sup>e</sup> Cleavage of the Me<sub>3</sub>Si group from the annulation product occurred during the column chromatography on silica gel. <sup>f</sup> Exposure of the annulation product to 1 N HCl in THF (rt, 3.5 h) effected desilylation. <sup>g</sup> Overall yield for two steps from **2g** (photo-Wolff rearrangement and [4 + 1] annulation). <sup>h</sup> In this case, the annulation was carried out in the presence of 0.5 equiv of *i*-Pr<sub>2</sub>EtN.

(5) Bennett, D. M.; Okamoto, I.; Danheiser, R. L. *Org. Lett.* **1999**, *1*, 641.

(6) Loebach, J. L.; Bennett, D. M.; Danheiser, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 9690.

(7) For related transformations, see: (a) Colomvakos, J. D.; Egle, I.; Ma, J.; Pole, D. L.; Tidwell, T. T.; Warkentin, J. *J. Org. Chem.* **1996**, *61*, 9522. (b) Huang, W.; Tidwell, T. T. *Synthesis* **2000**, 457.

(8) Scattered reports have appeared previously in which indanone derivatives were observed in the reaction of diazo compounds with diarylketenes. See: (a) Kende, A. S. *Chem. Ind. (London)* **1956**, 1053. (b) Yates, P.; Abrams, G. D.; Betts, M. J.; Goldstein, S. *Can. J. Chem.* **1971**, *49*, 2850. (c) Frey, J.; Rappoport, Z. *J. Am. Chem. Soc.* **1995**, *117*, 1161. (d) Léost, F.; Doutheau, A. *Tetrahedron Lett.* **1999**, *40*, 847.

(9) For generation of silylketenes by photo-Wolff rearrangement, see refs 4–6 and: (a) Maas, G.; Brückmann, R. *J. Org. Chem.* **1985**, *50*, 2801. (b) Brückmann, R.; Schneider, K.; Maas, G. *Tetrahedron* **1989**, *45*, 5517.

(10) Wolff rearrangement of  $\alpha$ -silyl- $\alpha$ -diazo ketones can also be effected by heating in the presence of catalytic rhodium(II) octanoate; see: Marsden, S. P.; Pang, W.-K. *J. Chem. Soc., Chem. Commun.* **1999**, 1199.

(11) Silylation was achieved by using our modification<sup>4</sup> of the method of Maas.<sup>9a,b</sup>

(12) (a) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959. (b) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G. *Organic Syntheses*; Wiley: New York, 1998; Collect. Vol. IX, p 197.

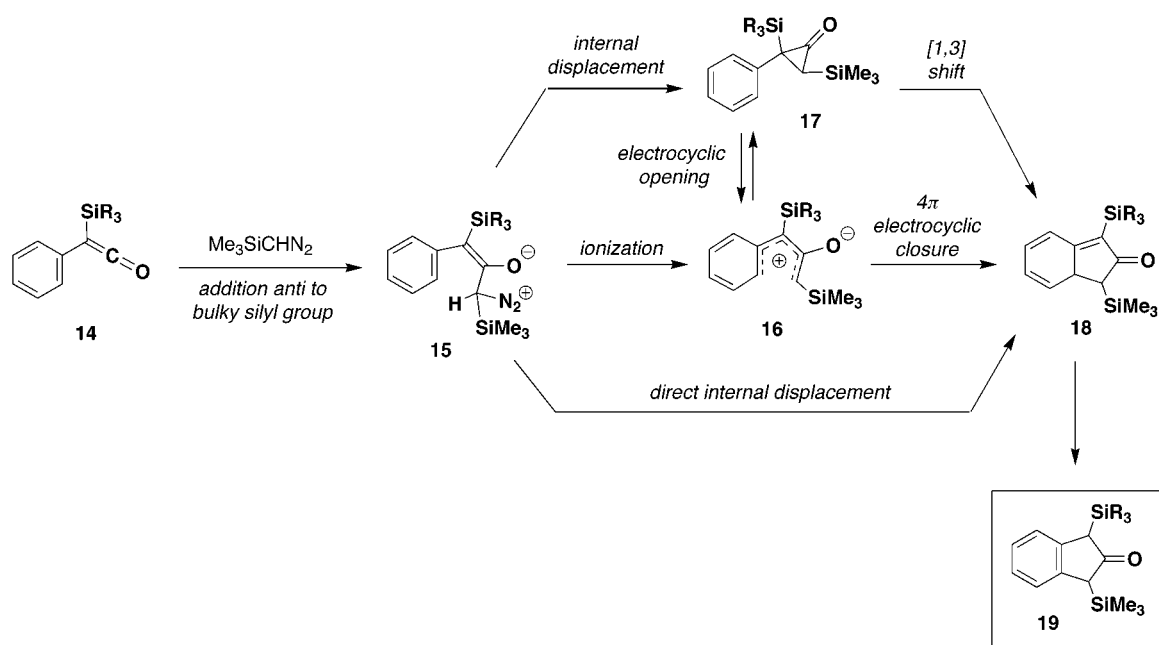
(13) The methyl ketone required for the synthesis of **1f** was prepared via Stille coupling of 3-(*i*-Pr)-C<sub>6</sub>H<sub>4</sub>OTf with H<sub>2</sub>C=C(OEt)SnBu<sub>3</sub>.

(14) (a) Seyferth, D.; Dow, A. W.; Menzel, H.; Flood, T. C. *J. Am. Chem. Soc.* **1968**, *90*, 1080. (b) Shioiri, T.; Aoyama, T.; Mori, S. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, pp 612–615.

be conveniently cleaved by exposure of the crude annulation product to dilute HCl in aqueous THF.

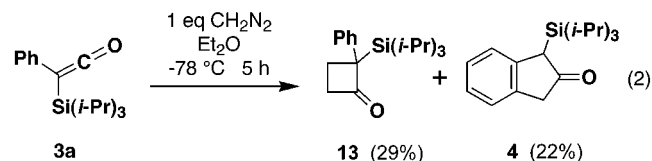
[4 + 1] Annulation with substituted arylketenes proceeds smoothly in a similar fashion (Table 1), except for the case of the 4-carbomethoxy derivative (entry 7), for which successful reaction requires the addition of 0.5 equiv of *i*-Pr<sub>2</sub>EtN (vide infra). As indicated in the Table, the optimal

Scheme 2



protocol for cleavage of the  $\text{Me}_3\text{Si}$  group varies from case to case and is achieved either by treatment with silica gel or under mild basic ( $\text{K}_2\text{CO}_3$ ,  $\text{MeOH}$ , rt, several min) or acidic (1 N  $\text{HCl}$ ,  $\text{THF}$ ) conditions. Surprisingly, application of the [4 + 1] strategy to arylketenes bearing *meta*-alkyl substituents leads to mixtures of isomeric indanones (entries 5 and 6). In these cases, the regiochemical outcome of the reaction appears to result from an intrinsic preference for cyclization adjacent to the alkyl substituent that is opposed by steric repulsion from this group.

As illustrated in eq 2, attempts to employ the more reactive reagent diazomethane in place of  $\text{Me}_3\text{SiCHN}_2$  for the [4 + 1] annulation were not fruitful. Addition of diazomethane to ketene **3a** proceeds rapidly at only  $-78^\circ\text{C}$  but affords the desired indanone accompanied by the cyclobutanone byproduct **13**, which is isolated in 29% yield.



Scheme 2 outlines several alternative pathways to account for the mechanistic course of the [4 + 1] annulation. As discussed previously,<sup>6</sup> addition of TMS-diazomethane to the silylketene should be highly stereoselective due to the shielding effect of the bulky trialkylsilyl group and should result in the formation of the  $(Z)$ -enolate **15**. Cyclization may then proceed via ionization to form the oxidopentadienylic-type cation **16**, which should undergo stereospecific conrotatory electrocyclic closure to **18**.<sup>15,16</sup> Alternatively, cyclization of **15** may occur to form the 2,3-bis(silyl)cyclopropanone

**17**, which would likely be in equilibrium with the oxyallyl cation **16**. Evidence in support of cyclopropanone intermediates of type **17** in the [4 + 1] annulation pathway includes the isolation of cyclobutanone **13** in the reaction of **3a** with  $\text{CH}_2\text{N}_2$  (eq 2). In this case, interception of the intermediate cyclopropanone by diazomethane may compete with ring opening and  $4\pi$  electrocyclic closure.

Also consistent with this mechanism are the findings of Zaitseva and co-workers, who have shown that simple silylketenes react with diazomethane and TMS-diazomethane to form mono- and bis(silyl)cyclopropanones.<sup>17</sup> Finally, it is noteworthy that 2-indanones and related hydrindenone derivatives are produced in the oxidation of phenyl-substituted allenes with peracid,<sup>18</sup> processes that may well involve the intermediacy of oxyallylic cations of type **16** generated via the ring opening of allene oxides.

As noted earlier, successful [4 + 1] annulation with the carbomethoxy-substituted ketene **3g** requires the presence

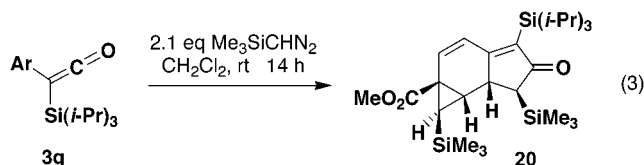
(15) Pentadienyl cation electrocyclic ring closures are involved in the mechanism of the Nazarov cyclization. For reviews, see: (a) Habermas, K. L.; Denmark, S. E. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1994; Vol. 45, pp 1–158. (b) Denmark, S. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 751.

(16) Alternatively, cyclization of intermediate **15** could produce the five-membered ring product **18** directly, although the planar structure of the dienolate system may not allow it to achieve an arrangement in which the  $\pi$  electrons are suitably situated for direct backside displacement of the leaving group.

(17) (a) Zaitseva, G. S.; Bogdanova, G. S.; Baukov, Yu. I.; Lutsenko, I. F. *J. Organomet. Chem.* **1976**, *121*, C21. (b) Zaitseva, G. S.; Bogdanova, G. S.; Baukov, Yu. I.; Lutsenko, I. F. *J. Gen. Chem. USSR (Engl. Transl.)* **1978**, *48*, 111. (c) Fedorenko, E. N.; Zaitseva, G. S.; Baukov, Yu. I.; Lutsenko, I. F. *J. Gen. Chem. USSR (Engl. Transl.)* **1986**, *56*, 2150. (d) Zaitseva, G. S.; Lutsenko, I. F.; Kisin, A. V.; Baukov, Yu. I.; Lorberth, J. *J. Organomet. Chem.* **1988**, *345*, 253.

(18) (a) Oku, A.; Shimada, K.; Mashio, F. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 275. (b) Greibrokk, T.; Skattebol, L. *Acta Chem. Scand.* **1973**, *27*, 1421.

of a basic additive such as *i*-Pr<sub>2</sub>EtN. In the absence of base, the major product of the reaction is the tricyclic enone **20**<sup>19</sup> (eq 3), which is obtained in 27% overall yield beginning with  $\alpha$ -silyl- $\alpha$ -diazo ketone **2g** when excess TMS-diazomethane is employed for the annulation. In this case, we believe that the intermediate of type **18** is intercepted by TMS-diazomethane in a 1,3-dipolar cycloaddition<sup>20</sup> that, due to the activating effect of the CO<sub>2</sub>Me group, is competitive with the isomerization of **18** to the indanone **19**. Addition of *i*-Pr<sub>2</sub>EtN serves to promote the isomerization step and delivers **12** in good yield without the formation of the tricyclic byproduct (Table 1, entry 7).



In summary, TAS-arylketenes combine with TMS-diazomethane in a new [4 + 1] annulation strategy leading to 2-indanones. Evidence has been obtained in support of a

mechanism involving the intermediacy of 2,3-bis(silyl)-cyclopropanones, which are in equilibrium with aryl-substituted oxyallylic cations of type **16**. Electrocyclic closure produces hydrindenone derivatives of type **18**, which upon isomerization furnish the 2-indanones. Further studies on the application of TAS-arylketenes and related silylketenes in organic synthesis are underway in our laboratory and will be reported in due course.

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**Supporting Information Available:** Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(19) Stereochemistry of **20** assigned as shown on the basis of NOE experiments and analysis of proton NMR coupling constant data; see Supporting Information for details.

(20) Regitz, M.; Heydt, H. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 1, p 394.