

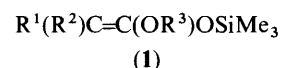
## Addition of *O*-Alkyl *O'*-Trimethylsilyl Ketene Acetals to Arynes Generated from Several Aryl Halides with $\text{NaNH}_2$

Syed Masarrat Ali and Shigeo Tanimoto\*

*Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan*

A number of alkyl-substituted aromatic carboxylic acids, in which an alkyl substituent and the carboxy group are situated *ortho* to each other, could be synthesized by treatment of *O*-alkyl *O'*-trimethylsilyl ketene acetals with several aryl halides in the presence of an excess of  $\text{NaNH}_2$  at room temperature followed by hydrolysis with aqueous hydrochloric acid.

It is well known<sup>1,2</sup> that as soon as a charged particle approaches benzyne, a partial ionic structure is induced which otherwise contributes only little to the ground state of benzyne. The dipolar structure of benzyne will facilitate polar addition with a properly selected nucleophilic reagent. Thus, the reaction of benzyne or other arynes with *O*-alkyl *O'*-trimethylsilyl ketene acetals (1)<sup>3</sup> should be possible.



In this report we describe a new addition reaction of *O*-alkyl *O'*-trimethylsilyl ketene acetals (1) to arynes generated from some aryl halides with  $\text{NaNH}_2$  at room temperature. In a

**Table 1.** Reaction of *O*-alkyl *O'*-trimethylsilyl ketene acetals (1) with arynes generated from several aryl halides with  $\text{NaNH}_2$

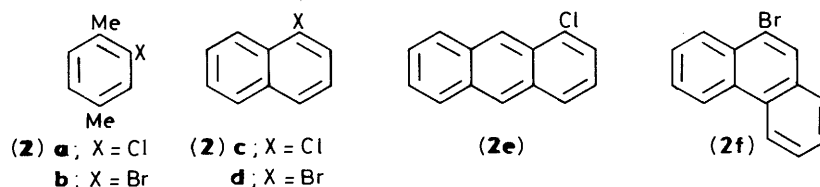
Entry	$\text{R}^1(\text{R}^2)\text{C}=\text{C}(\text{OR}^3)\text{OSiMe}_3$ (1)			Aryne source	Procedure	Product	Yield (%) <sup>a</sup>
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>				
1	Et	Me	Et	(2a)	A	(7)	48
2	Et	Me	Et	(2b)	A	(7)	44
3	Pr <sup>i</sup>	H	Et	(2a)	A	(6)	50
4	Pr <sup>i</sup>	H	Et	(2b)	A	(6)	48
5	Et	Et	Et	(2a)	A	(5)	55
6	Et	Et	Et	(2b)	A	(5)	56
7	Et	H	Et	(2c)	A	(8) (9)	40
8	Et	H	Et	(2d)	A	(8) (9)	40
9	Et	Me	Et	(2c)	A	(10) (11)	54
10	Et	Me	Et	(2d)	A	(10) (11)	51
11	Pr <sup>i</sup>	H	Et	(2c)	A	(12) (13)	48
12	Pr <sup>i</sup>	H	Et	(2e)	A	(12) (13)	45
13	Et	Et	Et	(2c)	A	(14) (15)	50
14	Et	Et	Et	(2d)	A	(14) (15)	50
15	Et	Me	Et	(2e)	B	(16) (17)	47
16	Pr <sup>i</sup>	H	Et	(2e)	B	(18) (19)	48
17	Et	Et	Et	(2e)	B	(20) (21)	50
18	Et	H	Et	(2f)	B	(22)	56
19	Et	Me	Et	(2f)	B	(23)	52
20	Pr <sup>i</sup>	H	Et	(2f)	B	(24)	58
21	Et	Et	Et	(2f)	B	(25)	48

<sup>a</sup> Isolated by column chromatography.

**Table 2.** Characterization of the obtained compounds

Compd.	M.p. (°C)	$\delta_{\text{H}}$ (CDCl <sub>3</sub> ) <sup>a</sup>	$\nu_{\text{max}}$ (Nujol) (cm <sup>-1</sup> )	$m/z$ ( $M^+$ )	Found (%) (Required)	
					C	H
(5)	153—154	0.98 (t, 6 H), 1.52 (m, 4 H), 2.21 (s, 3 H), 2.31 (s, 3 H), 2.39 (m, 1 H), 6.91 (d, 1 H), 7.04 (d, 1 H), 12.40 (s, 1 H)	3 280, 3 050, 1 655, 1 580, 1 435, 1 460, 1 380, 730, 705	220	76.5 (76.32)	9.1 (9.15)
(6)	108—110	1.69 (d, 6 H), 1.94 (m, 1 H), 2.27 (s, 3 H), 2.31 (s, 3 H), 2.58 (d, 2 H), 6.91 (d, 1 H), 7.02 (d, 1 H), 11.49 (s, 1 H)	3 250, 3 050, 1 660, 1 590, 1 420, 1 350, 740, 680	206	75.4 (75.69)	8.7 (8.80)
(7)	128	0.98 (t, 3 H), 1.24 (d, 3 H), 1.67 (m, 2 H), 2.21 (s, 3 H), 2.32 (s, 3 H), 2.42 (m, 1 H), 6.87 (d, 1 H), 7.51 (d, 1 H), 11.10 (br s, 1 H)	3 270, 3 020, 1 660, 1 600, 1 435, 1 360, 760, 690	206	75.4 (75.69)	8.8 (8.80)
(8) + (9)	Oil	0.89 (t, 3 H), 1.50 (m, 2 H), 2.40 (t, 2 H), 7.4—7.8 (m, 6 H)	3 260, 3 020, 1 660, 1 600, 1 430, 1 350, 760, 690	214	78.5 (78.48)	6.55 (6.59)
(10) + (11)	Oil	0.83 (t, 3 H), 0.89 (d, 3 H), 1.61 (m, 2 H), 2.39 (m, 1 H), 7.4—7.8 (m, 6 H), 11.73 (br s, 1 H)	3 235, 3 070, 1 670, 1 600, 1 510, 1 410, 1 350, 750, 695	228	78.9 (78.92)	6.9 (7.06)
(12) + (13)	130—136	0.98 (d, 6 H), 1.80 (m, 1 H), 2.31 (d, 2 H), 7.5—7.8 (m, 6 H), 13.20 (s, 1 H)	3 250, 3 050, 1 665, 1 590, 1 430, 1 340, 760, 690	228	78.8 (78.92)	7.1 (7.06)
(14) + (15)	Oil	0.82 (t, 6 H), 1.52 (m, 4 H), 2.43 (m, 1 H), 7.4—7.8 (m, 6 H)	3 250, 3 050, 1 665, 1 610, 1 450, 1 345, 700	242	79.5 (79.31)	7.5 (7.49)
(16) + (17)	Oil	0.84 (t, 3 H), 1.09 (d, 3 H), 1.54 (m, 2 H), 2.32 (m, 1 H), 7.3—8.4 (m, 8 H), 11.91 (br s, 1 H)	3 280, 3 040, 1 665, 1 600, 1 430, 1 340, 760, 690	278	81.95 (81.98)	6.5 (6.52)
(18) + (19)	Oil	1.10 (d, 6 H), 1.52 (m, 1 H), 2.34 (d, 2 H), 7.3—8.5 (m, 8 H)	3 325, 3 050, 1 670, 1 600, 1 460, 1 380, 740, 670	278	81.85 (81.98)	6.65 (6.52)
(20) + (21)	185—192	0.88 (t, 6 H), 1.66 (m, 4 H), 2.41 (m, 1 H), 7.3—8.4 (m, 8 H), 11.90 (s, 1 H)	3 250, 3 050, 1 670, 1 600, 1 420, 1 340, 740, 690	292	82.0 (82.16)	6.7 (6.89)
(22) <sup>b</sup>	165—166	0.96 (t, 3 H), 1.50 (m, 2 H), 2.46 (t, 2 H), 7.6—8.7 (m, 8 H)	3 300, 3 050, 1 670, 1 600, 1 440, 1 320, 780, 700	264	81.5 (81.79)	5.9 (6.10)
(23)	191	1.04 (t, 3 H), 1.30 (d, 3 H), 1.51 (m, 2 H), 2.47 (m, 1 H), 7.6—8.7 (m, 8 H), 12.01 (s, 1 H)	3 285, 3 050, 1 665, 1 610, 1 450, 1 325, 760, 680	278	81.7 (81.98)	6.5 (6.52)
(24) <sup>b</sup>	182	1.10 (d, 6 H), 1.55 (m, 1 H), 2.44 (d, 2 H), 7.6—8.7 (m, 8 H), 12.13 (s, 1 H)	3 250, 3 040, 1 670, 1 600, 1 430, 1 350, 750, 700	278	81.9 (81.98)	6.3 (6.52)
(25)	194	0.99 (t, 6 H), 1.58 (m, 4 H), 2.32 (m, 1 H), 7.6—8.7 (m, 8 H), 12.40 (br s, 1 H)	3 260, 3 040, 1 650, 1 580, 760, 690	292	81.9 (82.16)	6.8 (6.89)

<sup>a</sup> Carboxylic proton could not be detected in some cases up to  $\delta$  14. <sup>b</sup> Compounds (22) and (24) are known, see A. I. Negaideli, N. I. Tabashidze, and I. I. Abkhazava, *Zh. Org. Khim.*, 1968, 4, 104, and N. I. Tabashidze, L. D. Melikadze, Sh. Sh. Barabadze, L. D. Tsalalashvili, and M. M. Machabeli, *Izv. Akad. Nauk Gruz. SSR. Ser. Khim.*, 1978, 4, 35 (*Chem. Abstr.*, 1978, 89, 108797s). However, the m.p.s of these compounds were not apparent from the literature cited.

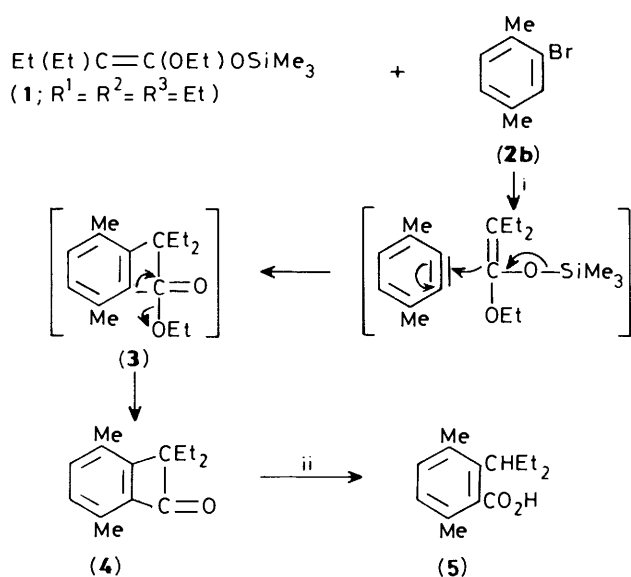


preliminary communication<sup>4</sup> of this work, we reported that the reaction of benzyne, generated from chlorobenzene with excess of NaNH<sub>2</sub>, and a few *O*-alkyl *O'*-trimethylsilyl ketene acetals (1) proceeded smoothly at room temperature to yield *ortho*-alkylbenzoic acids in moderate yields. However, several other aryl halides such as 2-chloro- (2a) and 2-bromo-*p*-xylene (2b), 1-chloro- (2c) and 1-bromo-naphthalene (2d), 1-chloroanthracene (2e), and 9-bromophenanthrene (2f) can also be used as aryne precursors in this reaction. In the present investigation, it was found that a number of alkyl-substituted aromatic carboxylic acids (5)—(25), in which the newly introduced alkyl and carboxy groups are *ortho* to each other, can be synthesized by treatment of acetals (1) with these aryl halides (2a—f) in the presence of excess of NaNH<sub>2</sub> at room temperature (Table 1).

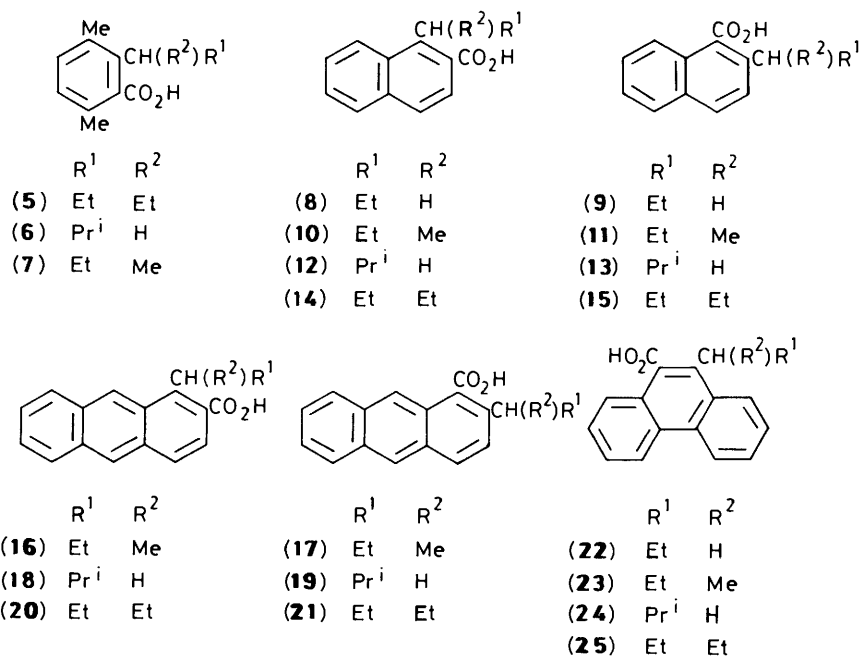
We isolated an intermediate in the experiment when 2-bromo-*p*-xylene (2b), NaNH<sub>2</sub>, and the *O*-alkyl *O'*-trimethylsilyl ketene acetal (1; R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = Et), derived from ethyl 2-ethylbutyrate, were allowed to react for 36 h (see entry 6, Table 1). The reaction mixture was carefully extracted with ether without

pretreatment with water, and the ethereal extract was then dried over MgSO<sub>4</sub> and concentrated under reduced pressure to afford a residue. None of the final product (5) was observed in the residue by t.l.c. examination. Instead the spectral properties of the residue indicated that it was the benzocyclobutenone derivative (4): the <sup>1</sup>H n.m.r. spectrum showed signals at  $\delta$  0.97 (t, 6 H), 1.58 (q, 4 H), 2.23 (s, 3 H), 2.31 (s, 3 H), and 7.1—7.9 (m, 2 H) and the mass spectrum showed  $m/z$  ( $M^+$ ) 220. On the other hand, when an ethereal solution of the residue with 10% aqueous hydrochloric acid was shaken, compound (5) was the sole product. Thus, this reaction as well as the others probably proceeds *via* a process involving an initial attack of (1) to the aryne intermediate to provide an ionic species (3), followed by its intramolecular substitution with the release of an ethoxy group to afford a benzocyclobutenone derivative (4), which is hydrolysed to the product (5) during aqueous work-up (Scheme).

As can be seen from Table 1, the reactions using aryl halides (2a), (2b), or (2f) as the aryne sources provided single products, because the nucleophilic attack of (1) on either carbon of the



Scheme. Reagents: i,  $\text{NaNH}_2$ ; ii, water



dehydro bond of 2,3-didehydro-*p*-xylene or 9,10-didehydrophenanthrene leads to the same product. On the other hand, the reactions using aryl halides (2c), (2d), or (2e) provided two isomeric products, because 1,2-didehydronaphthalene and 1,2-didehydroanthracene derived from (2c), (2d), or (2e) are not symmetrical with regard to the dehydro bond. The ratio of the isomers formed was determined by g.l.c. analysis. Although the structural assignment to each peak in g.l.c. was impossible, the ratio varied widely, but the content of the main isomer never exceeded 85% in all cases depicted in Table 1.

### Experimental

M.p.s were determined with a Yamato M-21 capillary melting point apparatus and are uncorrected. The mass spectral data were obtained on a JEOL JMX-DX-300 spectrometer.  $^1\text{H}$

N.m.r. spectra were obtained on a Varian VXR-200 spectrometer in  $\text{CDCl}_3$  with  $\text{SiMe}_4$  as an internal standard. The i.r. spectra were recorded on a JASCO IR-810 spectrophotometer. The starting substrates (1) were prepared by the method of Ainsworth *et al.*<sup>5</sup>

*Reaction of O-Alkyl O'-Trimethylsilyl Ketene Acetals (1) with Liquid Aryl Halides [(2a), (2b), (2c), or (2d)] in the Presence of  $\text{NaNH}_2$ . Procedure A.*—To a stirred mixture of a liquid aryl halide [any of (2a), (2b), (2c), and (2d)] (10 mmol) and  $\text{NaNH}_2$  (1.17 g, 30 mmol) under nitrogen was added an *O*-alkyl *O'*-trimethylsilyl ketene acetal (1) (10 mmol) through a syringe. After being stirred for 36 h at room temperature the stirred mixture was treated with water (50 ml) and extracted with dichloromethane ( $3 \times 30$  ml). The combined extracts were washed successively with water, 10% aqueous hydrochloric acid, and again with water, dried over  $\text{MgSO}_4$ , and distilled under reduced pressure to afford a residue, which was subjected to column chromatography on silica gel with ethyl acetate-hexane (2:3) as eluant.

*Reaction of O-Alkyl O'-Trimethylsilyl Ketene Acetals (1) with Solid Aryl Halides [(2e) or (2f)] in the Presence of  $\text{NaNH}_2$ . Procedure B.*—To a stirred solution of a solid aryl halide [either

(2e) or (2f)] (10 mmol) in dry toluene (5 ml) under nitrogen were added successively  $\text{NaNH}_2$  (1.17 g, 30 mmol) and an *O*-alkyl *O'*-trimethylsilyl ketene acetal (1) (10 mmol) through a syringe. After the mixture had been stirred at room temperature for 24 h, the volatile components were removed from the mixture under reduced pressure to afford a residue, which was treated with water (50 ml) (stirring) and extracted with dichloromethane ( $3 \times 30$  ml). The combined organic layers were worked up according to procedure A.

M.p.s and spectral and analytical data of the products obtained are given in Table 2.

### Acknowledgements

Financial support from Monbusho (Ministry of Education,

Japan) in the form of a postdoctoral fellowship to S. M. Ali is gratefully acknowledged.

### References

- 1 H. E. Simmons, *J. Am. Chem. Soc.*, 1961, **83**, 1657.
- 2 C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, 1958, **80**, 6360.

- 3 P. Brownbridge, *Synthesis*, 1983, 85, and references cited therein.
- 4 S. M. Ali and S. Tanimoto, *J. Chem. Soc., Chem. Commun.*, 1988, 1465.
- 5 C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organomet. Chem.*, 1972, **46**, 59.

*Received 22nd September 1988; Paper 8/03707H*