Reaction of sterically congested thiones with benzyne. The first isolation of a thioaldehyde–benzyne adduct

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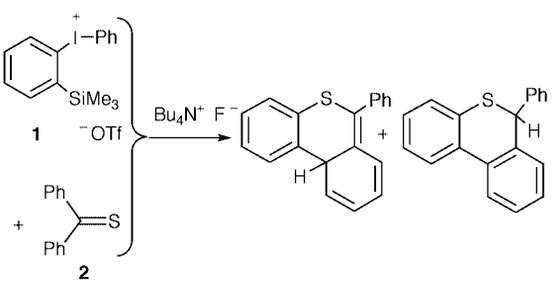
Reaction of 2,4,6-tri-*tert*-butylthiobenzaldehyde (**3**) with benzyne prepared from phenyl[2-(trimethylsilyl)-phenyl]iodonium trifluoromethanesulfonate (**1**) and tetrabutylammonium fluoride afforded 5,7-di-*tert*-butyl-3,3-dimethylindan-1-yl phenyl sulfide (**5**) in 92% yield, whereas a [2 + 2] cycloadduct and an ene-reaction product were obtained by the reaction of sterically congested aliphatic thiones with benzyne.

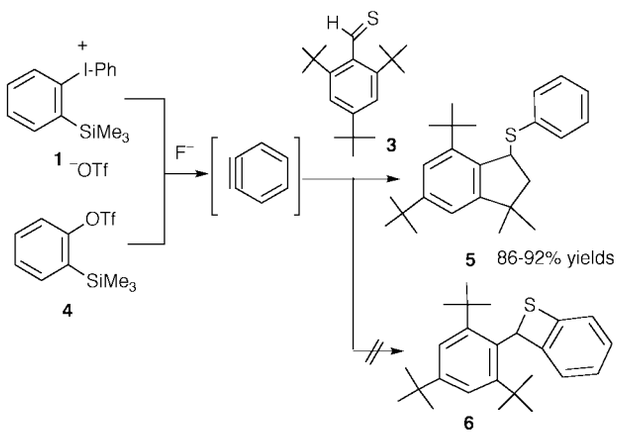
The chemistry of thioketone and thioaldehyde moieties has been studied extensively in recent years because of their unique and interesting properties.[1] Benzyne is a reactive intermediate and reacts with many dienes to afford the corresponding cycloadducts.[2] Recently, we have reported that the reaction of benzyne produced from phenyl[2-(trimethylsilyl)phenyl]-iodonium trifluoromethanesulfonate (**1**) (Kitamura's reagent) with thiobenzophenone (**2**) afforded the corresponding [4 + 2] cycloadducts (Scheme 1).[3,4]



Scheme 1

We have also reported that the reaction of thiopivalophenones with **1** in the presence of tetrabutylammonium fluoride gave the corresponding [2 + 2] cycloadducts in moderate yields.[5] However, there is no report on the reaction of thioaldehyde with benzyne. Thioaldehydes generally oligomerize to give the corresponding trimers or polymers.[1] In 1982, Okazaki and co-workers isolated the first stable sterically congested monomeric thioaldehyde, 2,4,6-tri-*tert*-butylthiobenzaldehyde (**3**), by the reaction of tri-*tert*-butylphenyllithium with ethyl thioformate.[6] Other sterically congested thiones, such as thiofenchone and thiocamphor are easily prepared by the reaction with P_4S_{10} in pyridine.[7] Their reactions with olefins were relatively few because of their reduced reactivity toward olefins.[1] These results prompted us to investigate the reaction of these sterically congested thiones with benzyne. We herein report the first example of the reaction of **3** with benzyne.

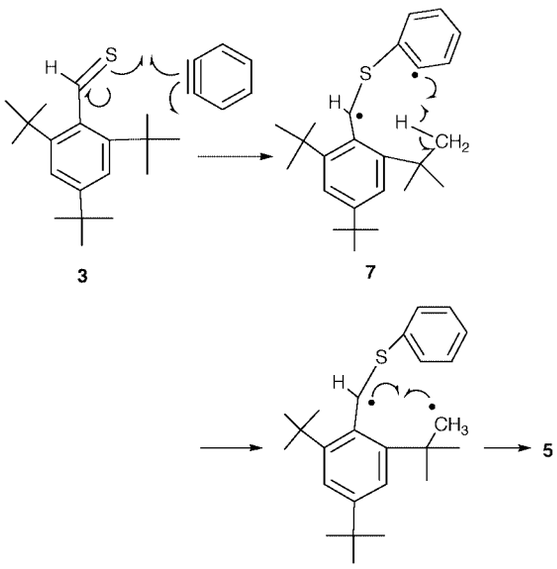
Treatment of thiobenzaldehyde **3** with **1** followed by the addition of tetrabutylammonium fluoride resulted in the formation of colorless crystals (**5**). Mass spectroscopy of **5** has shown that we are dealing with 1:1 adduct. If the present reaction proceeded through a [2 + 2] cycloaddition pathway analogous to that of thiopivalophenones with benzyne,[5] the corresponding benzothiete (**6**) would be formed. The spectroscopic data of the adduct (^{1}H NMR, ^{13}C NMR, IR) was however incompatible with the structure of **6**. Its ^{1}H NMR spectrum suggests two *tert*-butyl (1:1 integral ratio), two methyl, one methylene and one methine proton along with two aromatic, mono-substituted phenyl protons. Careful investigation of the above result suggests that the structure of **5** is 5,7-di-*tert*-butyl-3,3-dimethylindan-1-yl phenyl sulfide (92% yield). Similarly, the reaction of **3** with *o*-trimethylsilylphenyl trifluoromethanesulfonate (**4**)[8] in the presence of tetrabutylammonium fluoride afforded the same product **5** in 86% yield (Scheme 2).



Scheme 2

This result is quite different from that of **2** or thiopivalophenone, which gave [4 + 2] or [2 + 2] cycloaddition products.[3,5] The reaction most likely proceeded as follows: thioaldehyde **3** reacted with benzyne to give the corresponding biradical **7**. Proton abstraction followed by internal combination of **7** afforded the final product **5**. Benzyne is generally thought to react *via* a concerted mechanism. In the present reaction, thioaldehyde **3** is too sterically congested, thus, the reaction would proceed *via* a radical intermediate (Scheme 3).

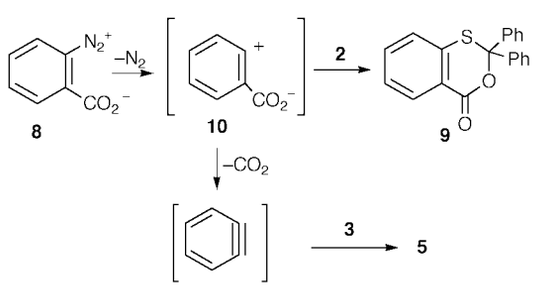
Ishii *et al*. reported that thermolysis of thioaldehyde **3** at 200 °C led to dihydrobenzothiopyran *via* a radical mechanism.[9] The reaction of **3** with substituted benzylmagnesium bromide afforded the same thiopyran in 65% yield. Intramolecular reaction may proceed due to its steric hindrance. Intermolecular cycloaddition required a more elevated temperature because of steric hindrance; thioaldehyde **3** undergoes [4 + 2] cycloaddition with 2,3-dimethylbuta-1,3-diene at 160 °C in a sealed tube in only 26% yield whereas thiobenzophenone and thioacetophenone reportedly react with 2,3-dimethylbuta-1,3-diene at room temperature.[10] Thioaldehyde **3** is able to react with more



Scheme 3

reactive 1,3-dipolar reagents such as diphenylnitrilimine and mesitonitrile oxide at room temperature.[9] Photolytic [2 + 2] cycloaddition of **3** with allenes was observed at room temperature.[11] The present reaction is the first example of intermolecular addition of **3** with olefin at room temperature.

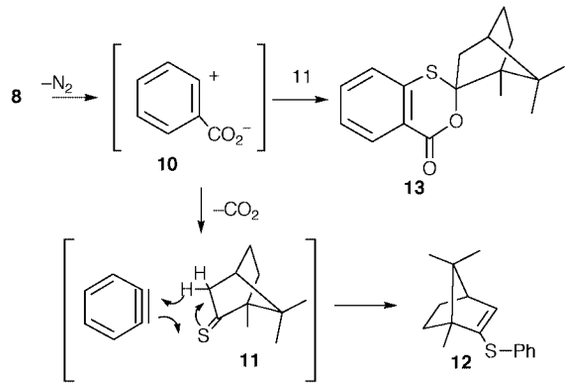
It is known that the reaction of thiobenzophenone (**2**) with benzenediazonium *o*-carboxylate (**8**), which is a well-known benzyne precursor, affords only the corresponding 3,1-benzoxathiin-4-one (**9**).[12] Interestingly, the reaction of **8** with thioaldehyde **3** in refluxing dichloromethane afforded the same benzyne–thioaldehyde adduct **5** in 72% yield, suggesting that compound **8** acts as a benzyne precursor. The difference in the reactivity between **2** and **3** may be attributed to the difference between their steric hindrance. Presumably, *tert*-butyl groups at the *ortho* position of **3** prevent the addition of the phenyl cation **10** onto the thioaldehyde sulfur, which enables decarboxylation of **10** to give the corresponding benzyne intermediate (Scheme 4).



Scheme 4

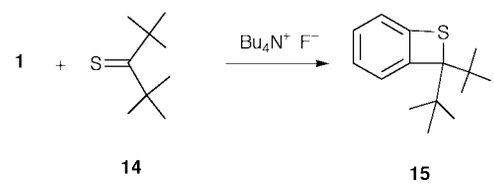
Actually, the reaction of thiocamphor (**11**), a less hindered and isolable thioketone containing an α-hydrogen, with **8** in refluxing dichloromethane led to the two products, 1,7,7-trimethyl-2-(phenylthio)bicyclo[2.2.1]hept-2-ene (**12**) and 1′,7′,7′-trimethyl(3,1-benzooxathiine-2-spiro-2′-bicyclo[2.2.1]heptan)-4-one (**13**), in 72 and 11% yields, respectively. The structures of **12** and **13** were confirmed by their spectroscopic analysis. This result suggested that both intermediates, **10** and benzyne, existed in the present reaction. Thus, less hindered thioketone **11** can react with both intermediates to give the corresponding ene-reaction and ionic reaction products (Scheme 5). When **4** was used as a benzyne precursor, compound **12** was isolated in 82% yield at room temperature.

Another sterically crowded stable thione, di-*tert*-butyl thioketone (**14**) was then carried out to investigate whether a similar radical or an ionic reaction pathway would occur. Treatment



Scheme 5

of **14** with **1** followed by the addition of tetrabutylammonium fluoride resulted in the formation of the corresponding cycloadduct 2,2-di-*tert*-butyl-2*H*-benzo[*b*]thiete (**15**) in 85% yield (Scheme 6). The structure of **15** was confirmed by its spectroscopic analysis (see Experimental section). The reaction of **14** with **8** in refluxing dichloromethane also afforded **15** in 71% yield. Presumably, normal cycloaddition of **14** with benzyne prepared from **8** and **1** led to the corresponding [2 + 2] cycloadduct (**15**). Although compound **14** is sterically congested, the reactivity toward benzyne is similar to **2** and thiopivalophenone.



Scheme 6

In summary, we have succeeded in the first isolation of a thioaldehyde–benzyne adduct, which has a novel indane phenyl sulfide structure. The reaction most likely proceeded through a radical mechanism. Other sterically congested thiones reacted with benzyne to afford a [2 + 2] cycloadduct or an ene-reaction product.

Experimental

General

All chemicals were obtained from commercial suppliers and used without further purification. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and flash column chromatography was performed with silica (Merck, 70–230 mesh). NMR spectra (^{1}H at 400 MHz; ^{13}C at 100 MHz) were recorded in $CDCl_3$ solvent, and chemical shifts are expressed in ppm relative to internal TMS.

Reaction of 3 with 1 followed by the addition of tetrabutylammonium fluoride

To a solution of **3** (0.145 g, 0.5 mmol) and **1** (0.518 g, 1.0 mmol) in dichloromethane (15 mL), was added dropwise a solution of tetrabutylammonium fluoride (1.0 M in THF, 1.1 mL, 1.1 mmol). After being stirred for 1 h, the reaction mixture was washed with water to remove tetrabutylammonium triflate. The dried dichloromethane solution was evaporated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to give **5** (0.166 g, 0.46 mmol). 5,7-Di-*tert*-butyl-3,3-dimethylindan-1-yl phenyl sulfide (**5**); colorless crystals; mp 119–120 °C; ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H, Me), 1.35 (s, 9 H, *t*-Bu), 1.50 (s, 3 H, Me), 1.56 (s, 9 H, *t*-Bu), 2.23 (m, 2 H, CH_2), 5.14 (br d, 1 H, J = 5 Hz, CH), 7.04

(br s, 1 H, Ar), 7.20 (br t, 1 H, $J = 8$ Hz, Ar), 7.31 (br t, 2 H, $J = 8$ Hz, Ar), 7.37 (s, 1 H, Ar), 7.38 (d, 2 H, $J = 8$ Hz, Ar). ^{13}C NMR ($CDCl_3$) δ 30.9 (Me), 31.5 (Me), 31.6 (*t*-Bu), 32.5 (*t*-Bu), 35.0 (C), 37.5 (C), 42.4 (C), 47.3 (CH_2), 51.2 (CH), 117.5, 123.7, 125.7, 128.8, 129.3, 133.9, 137.7, 146.7, 151.2, 153.9 (Ar). HRMS. Found: *m*/*z* 366.2393. Calcd. for $C_{25}H_{34}S$ (M^+): *m*/*z* 366.2381. Anal. Calcd. for $C_{25}H_{34}S$: C, 81.91; H, 9.35. Found: C, 82.26; H, 9.34%.

Reaction of 3 with 4 in the presence of tetrabutylammonium fluoride

To a solution of **3** (0.145 g, 0.5 mmol) and **4** (0.399 g, 1.5 mmol) in dichloromethane (15 mL), was added dropwise a solution of tetrabutylammonium fluoride (1.0 M in THF, 1.6 mL, 1.6 mmol). After being stirred for 1 h, the reaction mixture was washed with water to remove tetrabutylammonium triflate. The dried dichloromethane solution was evaporated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to give **5** (0.157 g, 0.43 mmol).

Reaction of 3 with 8

To a solution of **3** (0.145 g, 0.5 mmol) in dichloromethane (15 mL), was added **8** (0.444 g, 3.0 mmol) portionwise. After being refluxed for 2 h, the reaction mixture was concentrated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to give **5** (0.132 g, 0.36 mmol).

Reaction of thiocamphor 11 with 8

To a refluxing solution of **11** (0.156 g, 1.0 mmol) in dichloromethane (20 mL) was added **8** (0.444 g, 3.0 mmol) portionwise. After refluxing for 2 h, the reaction mixture was evaporated to afford a pale brown oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to afford **12** (0.176 g, 0.72 mmol) and **13** (0.031 g, 0.11 mmol). 1,7,7-Trimethyl-2-(phenylthio)bicyclo[2.2.1]hept-2-ene (**12**); colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 3 H, Me), 0.87 (s, 3 H, Me), 0.94 (s, 3 H, Me), 0.98 (m, 1 H, C*H*H), 1.16 (m, 1 H, CH*H*), 1.53 (m, 1 H, C*H*H), 1.87 (m, 1 H, CH*H*), 2.33 (br t, 1 H, $J = 4$ Hz, CH), 5.68 (d, 1 H, $J = 4$ Hz, =CH), 7.20–7.45 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$) δ 11.7 (Me), 19.6 (Me), 19.6 (Me), 25.9 (CH_2), 31.7 (CH_2), 52.3 (CH_2), 55.9 (C), 57.2 (C), 127.1 (Ar), 128.8 (Ar), 132.3 (Ar), 132.8 (Ar), 134.4 (olefinic), 142.9 (Ar). HRMS: Found: *m*/*z* 244.1313. Calcd. for $C_{16}H_{20}S$ (M^+): *m*/*z* 244.1285. 1′,7′,7′-Trimethyl-3,1-benzooxathiin-2-spiro-2′-bicyclo[2.2.1]-heptan-4-one (**13**); colorless crystals; mp 132–134 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 3 H, Me), 1.15 (s, 3 H, Me), 1.18 (s, 3 H, Me), 1.24 (m, 1 H, C*H*H), 1.65 (m, 1 H, CH*H*), 1.76–1.98 (m, 3 H, CH_2), 1.96 (d, 1 H, $J = 14$ Hz, C*H*H), 2.62 (m, 1 H, $J = 14$ Hz, C*H*H), 7.24 (t, 1 H, $J = 8$ Hz), 7.33 (d, 1 H, $J = 8$ Hz), 7.45 (t, $J = 8$ Hz), 8.11 (d, 1 H, $J = 8$ Hz). ^{13}C NMR ($CDCl_3$) δ 11.5 (Me), 20.7 (Me), 21.2 (Me), 26.1 (CH_2), 31.5 (CH_2), 45.2 (CH_2), 49.4 (C), 49.5 (C), 54.4 (CH), 99.3 (O–C–S), 124.3 (Ar), 125.9 (Ar), 128.3 (Ar), 131.3 (Ar), 133.3 (Ar), 137.5 (Ar), 163.9 (COO). HRMS: Found: *m*/*z* 288.1153. Calcd. for $C_{17}H_{20}O_2S$ (M^+): *m*/*z* 288.1184. Anal. Calcd. for $C_{17}H_{20}O_2S$: C, 70.81; H, 6.99. Found: C, 70.61; H, 7.05%.

Reaction of 11 with 3 in the presence of tetrabutylammonium fluoride

To a solution of **11** (0.078 g, 0.5 mmol) and **3** (0.518 g, 1.0 mmol) in dichloromethane (20 mL) was added tetrabutylammonium fluoride (1.0 M in THF, 1.1 mL, 1.1 mmol) dropwise at room temperature. After being stirred for 1 h, the reaction mixture was washed with water to remove tetrabutylammonium triflate. The reaction mixture was dried over magnesium sulfate and filtered. The filtrate was concentrated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to give a pale yellow oil of the adduct **12** (0.100 g, 0.41 mmol).

Reaction of 11 with 4 in the presence of tetrabutylammonium fluoride

To a solution of **11** (0.078 g, 0.5 mmol) and **4** (0.266 g, 1.0 mmol) in dichloromethane (15 mL) was added tetrabutylammonium fluoride (1.0 M in THF, 1.1 mL, 1.1 mmol) dropwise at room temperature. After being stirred for 1 h, the reaction mixture was washed with water to remove tetrabutylammonium triflate. The reaction mixture was dried over magnesium sulfate and filtered. The filtrate was concentrated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to give a pale yellow oil of the adduct **12** (0.100 g, 0.41 mmol).

Reaction of di-*tert*-butylthioketone 14 with 1 in the presence of tetrabutylammonium fluoride

To a solution of **14** (0.079 g, 0.5 mmol) and tetrabutylammonium fluoride (1.1 mL, 1.0 M in THF, 1.1 mmol) in dichloromethane (15 mL) was added a solution of **1** (0.777 g, 1.5 mmol) in dichloromethane (25 mL) at room temperature. After being stirred for 1 h, the reaction mixture was washed with water to remove tetrabutylammonium triflate. The dichloromethane layer was dried over magnesium sulfate, filtered, and concentrated to give a pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane. The adduct **15** (0.099 g, 0.43 mmol) was obtained. 2,2-Di-*tert*-butyl-2*H*-benzo[*b*]thiete (**15**); colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 18 H, *t*-Bu), 6.80 (d, 1 H, $J = 8$ Hz, Ar), 6.94 (d, 1 H, $J = 8$ Hz, Ar), 7.00 (t, 1 H, $J = 8$ Hz, Ar), 7.13 (t, 1 H, $J = 8$ Hz, Ar). ^{13}C NMR ($CDCl_3$) δ 30.9 (*t*-Bu), 40.2 (*t*-Bu), 88.5 (S–C), 121.0 (Ar), 122.5 (Ar), 122.9 (Ar), 127.8 (Ar), 141.4 (Ar), 145.9 (Ar). HRMS. Found: *m*/*z* 234.1441. Calcd. for $C_{15}H_{22}S$ (M^+): *m*/*z* 234.1442.

Reaction of 14 with 8

To a refluxing solution of **14** (0.79 g, 0.5 mmol) in dichloromethane (15 mL) was added diazonium carboxylate (0.444 g, 3.0 mmol) portionwise. After refluxing for 2 h, the reaction mixture was evaporated to afford a pale brown oil, which was chromatographed over silica gel by elution with hexane–dichloromethane to afford **15** (0.083 g, 0.36 mmol).

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