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Sequential One-Pot Addition of Excess Aryl-Grignard Reagents and Electrophiles to *O*-Alkyl Thioformates

Toshiaki Murai,*[a, b] Kenta Morikawa,[a] and Toshifumi Maruyama[a]

Abstract: The sequential addition of aromatic Grignard reagents to *O*-alkyl thioformates proceeded to completion within 30 s to give aryl benzylic sulfanes in good yields. This reaction may begin with the nucleophilic attack of the Grignard reagent onto the carbon atom of the *O*-alkyl thioformates, followed by the elimination of ROMgBr to generate aromatic thioaldehydes, which then react with a second molecule of the Grignard reagent at the sulfur atom to form arylsulfanyl benzylic Grignard reagents. To confirm the generation of aromatic thioaldehydes, the reaction between *O*-alkyl thioformates and phenyl Grignard reagent was carried out in the presence of cyclopentadiene. As a result, hetero-Diels–Alder adducts of the thioaldehyde and the diene were formed. The treatment of a mixture of the thioformate and phenyl Grignard reagent with iodine gave 1,2-bis(phenylsulfanyl)-1,2-diphenyl ethane as a product, which indicated the formation of arylsulfanyl benzylic Grignard reagents in the reaction mixture. When electrophiles were added to the Grignard reagents that were generated in situ, four-component coupling products, that is, *O*-alkyl thioformates, two molecules of Grignard reagents, and electrophiles, were obtained in moderate-to-good yields. The use of silyl chloride or allylic bromides gave the adducts within 5 min, whereas the reaction with benzylic halides required more than 30 min. The addition to carbonyl compounds was complete within 1 min and the use of lithium bromide as an additive enhanced the yields of the four-component coupling products. Finally, oxiranes and imines also participated in the coupling reaction.

Keywords: electrophilic addition · Grignard reaction · reaction mechanisms · sequential reactions · thioformates

Introduction

Since the first description of the addition of organomagnesium reagents to carbonyl compounds by Victor Grignard, the Grignard reaction has been the focus of tremendous amounts of research and industrial effort.[1] To expand the applicability of Grignard reactions, numerous studies have been devoted to improving the methods that are used to generate the reagents, to enhancing the efficiency of the addition step of Grignard reagents to electrophiles, and to expanding the number of available electrophiles. With regard to this latter issue, the possibility of using thiocarbonyl compounds as an electrophile has been studied for many years,[2] although there are much fewer results than with carbonyl compounds. As early as 1910, the addition of Grignard reagents to carbon disulfide was reported to give dithioic acid magnesium salts.[3] Dithioic acid esters have also been used as thiocarbonyl compounds.[4] One of the characteristic features of this reaction is that the addition of Grignard reagents to dithioic acid esters can take place on both the carbon and sulfur atoms of C=S groups, depending on the substituents that are attached to the C=S carbon atom and the substituents on the Grignard reagents. For example, an ethyl-Grignard reagent adds onto the sulfur atom of dithioacetic acid ethyl ester,[4b] whereas the addition of an allyl-Grignard reagent to aromatic dithioic acid esters takes place at the carbon atom.[4c] Recently, the reactivity and regioselectivity of perfluorinated dithioic acid esters toward Grignard reagents has been extensively studied.[5] The thiophilic attack of the reagent, followed by the elimination of a fluorine atom, gives dithioketene acetals as the major products. In the addition of Grignard reagents to cyclic dithiocarbamates, two equivalents of the reagents are introduced onto the carbon atom of the C=S group.[6] Two different Grignard reagents have been shown to add onto the carbon atom of the C=S group in thioformamides[7] in our series of studies[8] on thio-[9] and selenocarbonyl compounds.[10] Very recently, we also found that lithium silyl acetylides and Grignard reagents sequentially added to *O*-alkyl thioformates (**1**) to generate propargyl-Grignard reagents (**3**), which further added to a wide range of electrophiles to give propargyl phenyl sulfides (**4**, Scheme 1).[11] In this reaction, thiopropynal **2** may initially be generated and the phenyl Grignard reagent would add onto the sulfur atom of compound **2**. In this sequence, four components are coupled in a

[a] Prof. Dr. T. Murai, K. Morikawa, T. Maruyama
Department of Chemistry
Faculty of Engineering, Gifu University
Yanagido, Gifu 501-1193 (Japan)
Fax: (+81) 58-293-2614
E-mail: mtoshi@gifu-u.ac.jp

[b] Prof. Dr. T. Murai
JST, ACT-C
4-1-8 Honcho, Kawaguchi, Saitama 332-0012 (Japan)

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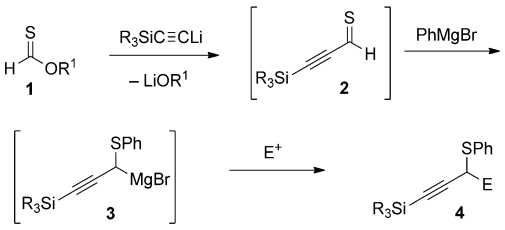
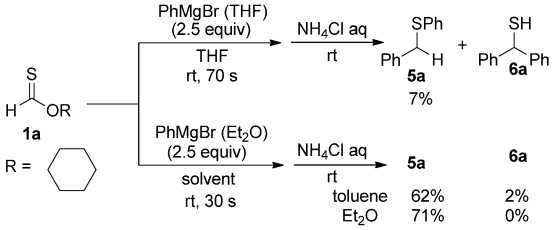


Scheme 1. Sequential addition of lithium acetylides, phenyl Grignard reagent, and electrophiles to *O*-alkyl thioformates.

single operation.[12] A survey of the literature on the reactivity of *O*-alkyl thioformates (**1**) did not reveal any systematic studies on the addition of Grignard reagents to compounds **1**.[13] Herein, we report the details of the reaction of aromatic Grignard reagents with *O*-alkyl thioformates (**1**) and electrophiles, which provides new four-component coupling products.

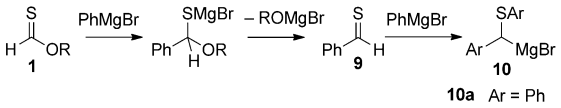
Results and Discussion

Initially, excess phenyl Grignard was added to thioformate **1a** in THF. The starting ester (**1a**) was consumed within 70 s, but the reaction mixture contained several types of unidentified products and, whilst benzyl phenyl sulfide **5a**[14a] was detected, the yield was only 7% (Scheme 2). This result



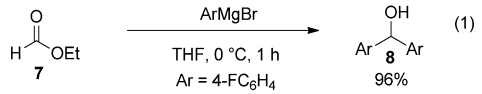
Scheme 2. Sequential addition of excess phenyl-Grignard reagent, followed by hydrolysis.

is in marked contrast to the reaction of formates with aryl-Grignard reagents [Eq. (1)]. Two equivalents of the Grignard reagent were efficiently incorporated onto the carbon atom of compound **7** to give the alcohol (**8**) in quantitative yield.[15] Then, several types of solvent were examined for the reaction shown in Scheme 2 and the combination of a solution of phenyl Grignard in Et_2O and the substrate in toluene gave compound **5a** in good yield, along with a small amount of thiol **6a**, which was formed from the addition of two equivalents of phenyl Grignard to the carbon atom of compound **1a**. As an initial step, phenyl Grignard may add onto the carbon atom of compound **1a**, followed by the elimination of magnesium alkoxide to generate thiobenzaldehyde **9** as an intermediate (Scheme 3). In the second step, phenyl Grignard adds, not onto the carbon atom of compound **9**, but rather onto the sulfur atom of

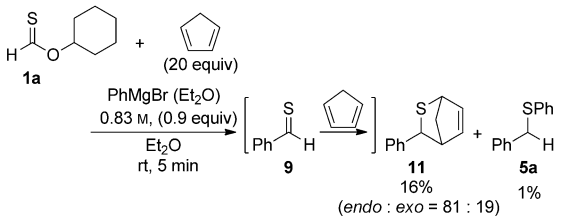


Scheme 3. Plausible reaction pathway for the sequential addition reactions.

compound **9** to form phenylsulfanyl benzyl Grignard (**10a**). The use of one equivalent of phenyl Grignard resulted in the formation of compound **5a** in a lower yield, along with recovery of the starting ester (**1a**).



To confirm the possibility of the generation of compound **9**, the hetero-Diels–Alder reaction of a putative intermediate, that is, thiobenzaldehyde **9**, with a diene[16] was carried out (Scheme 4). Thus, the reaction of compound **1a** with phenyl Grignard in the presence of cyclopentadiene gave



Scheme 4. Trapping experiment of thiobenzaldehyde that is generated in situ.

adducts **11**, albeit in low yields, but their diastereomeric ratio was consistent with the trapping of thiobenzaldehyde that was generated in situ by cyclopentadiene.[16a] The thiophilic attack of isolated thiobenzaldehyde by Grignard reagents, in which *tert*-butyl groups are introduced at the 2,4,6-position of the aromatic ring, has been described previously and the selectivity of the reaction depended on the solvent and Grignard reagent that were used.[17]

To further explore the reaction mode of thiobenzaldehyde **9**, DFT calculations were carried out at the B3LYP/6-31+G(d) level of theory, along with that of *O*-methyl thioformate (**1b**). The HOMOs of compounds **9** and **1b** correspond to the lone pairs of their sulfur atoms. The HOMO−1, LUMO, and NPA charges of compounds **1b** and **9** are shown in Figure 1 and Figure 2, respectively. The HOMO−1

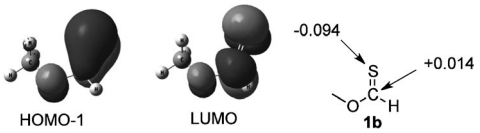


Figure 1. Natural population analysis (NPA) charge and molecular orbitals of compound **1b**.

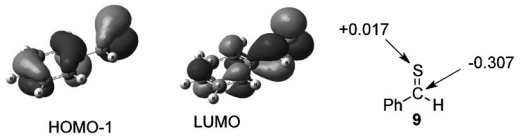
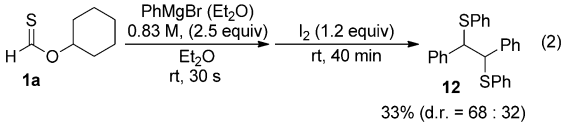


Figure 2. NPA charge and molecular orbitals of compound **9**.

of compound **1b** is localized on the sulfur atom, whereas that of compound **9** is spread over the sulfur and carbon atoms of the C=S bond and over the carbon atoms in the aromatic ring. In contrast, the LUMO of compound **9** is localized on the sulfur and carbon atoms. More importantly, unlike in compound **1b**, the atomic charge on the sulfur atom of compound **9** is rather positive, which implies that the sulfur atom in compound **9** can accept nucleophilic attack.

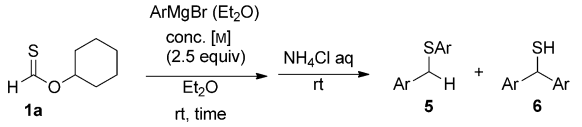
The addition of iodine to the reaction mixture of thioformate **1a** and phenyl Grignard gave compound **12** as the product, albeit in moderate yield [Eq. (2)]. Nevertheless, the formation of compound **12** can be understood by the homocoupling reaction[18] of Grignard **10a** (Ar = Ph) shown in Scheme 3.



Then, a range of aromatic Grignard reagents were tested in the reaction with ester **1a** (Table 1). The substituents on the aryl groups in the Grignard reagents, such as chlorine, methyl, and methoxy groups, had almost no effect on the reaction course and compounds **5c**,[14b] **5d**,[14c] and **5e** were obtained. However, aromatic-Grignard reagents with a methoxy group gave thiols **6** as by-products to some extent (Table 1, entries 2 and 3).

Grignard reagents **10** are not readily generated because the starting bromides and iodides are not readily available.[19] In contrast, in this reaction, phenylsulfanyl benzyl Grignard (**10a**) was generated very rapidly in the addition of phenyl Grignard to ester **1a** with high efficiency. Thus, we envisioned multi-component sequential addition reactions. First, silyl, allylic, and benzyl halides were used as electrophiles and the

Table 1. Reactions of thioformate **1a** with the aryl-Grignard reagents.[a]

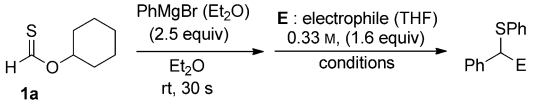


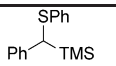
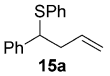
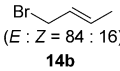
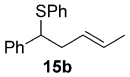
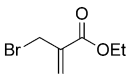
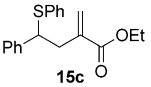
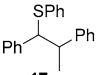
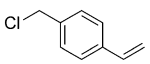
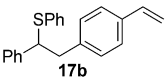
Entry	Ar	Concentration [M]	t	Yield [%]			
				5		**6**	
1	4-ClC_6H_4	0.83	30 s	**5b**	47	**6b**	0
2	4-$MeOC_6H_4$	0.93	2.5 min	**5c**	28	**6c**	13
3	2-$MeOC_6H_4$	0.98	2.5 min	**5d**	45	**6d**	21
4	o-Tol	0.86	30 s	**5e**	67	**6e**	0

[a] Thioformate **1a** was reacted with the aryl Grignard reagents (2.5 equiv) for an appropriate length of time. [b] Yield of isolated product.

results are shown in Table 2. Silylation of Grignard **10a** that was generated in situ proceeded smoothly within 5 min to give compound **13**[20] in 68% yield (Table 2, entry 1). Allylation of compound **10a** with allylic bromides **14a** and **14b** also took place at room temperature within 5 min to lead to homoallylic sulfides **15a** and **15b** (Table 2, entries 2 and 3), whereas the reaction with compound **14c** under identical conditions gave the corresponding product (**15c**), but in moderate yield (Table 2, entry 4). Whilst the reaction at higher temperatures did not improve the yield of compound **15c**, the use of lower temperatures for longer reaction times gave compound **15c** in higher yield (Table 2, entry 5). Like-

Table 2. Sequential addition of the phenyl Grignard reagent and electrophiles to thioformate **1a**.[a]



Entry	E	T [°C]	t	Product	Yield [%][b]
1	TMSCl (2.0 equiv)	RT	5 min	 **13**	68
2	 **14a**	RT	5 min	 **15a**	62[c]
3	 (*E* : *Z* = 84 : 16) **14b**	RT	5 min	 **15b**	69 (*E*/*Z* 78:22)
4	 **14c**	RT	5 min	 **15c**	38[d]
5		−78	6.5 h		89[d] (47)[e]
6	 **16a**	RT	5 min	 **17a**	13[f] (*syn*/*anti* 29:71)
7		RT	2 min		57[g] (*syn*/*anti* 38:62)
8	 **16b**	RT	30 min	 **17b**	63

[a] Thioformate **1a** was sequentially reacted with the phenyl Grignard reagent (2.5 equiv) and electrophiles (1.6 equiv). [b] Yield of isolated product after column chromatography on silica gel. [c] Sulfane **5a** was also formed in 5% yield. [d] Yield based on ^1H NMR spectroscopy by using $Cl_2CHCHCl_2$ as an internal standard. [e] Yield of isolated product after HPLC. [f] Sulfane **5a** was also formed in 57% yield. [g] Sulfane **5a** was also formed in 2% yield.

wise, the reaction with benzylic bromide **16a** and chloride **16b** required longer reaction times at room temperature, but gave the desired products (**17**) in good yields (Table 2, entries 7 and 8). In the reaction with compound **16a**, two diastereomers of compound **17a** were obtained in the ratio 38:62. These compounds were separated by flash column chromatography on silica gel and a major isomer was isolated in high purity. The structure of the major isomer of compound **17a** was unequivocally confirmed to be *anti*, as shown in Figure 3.

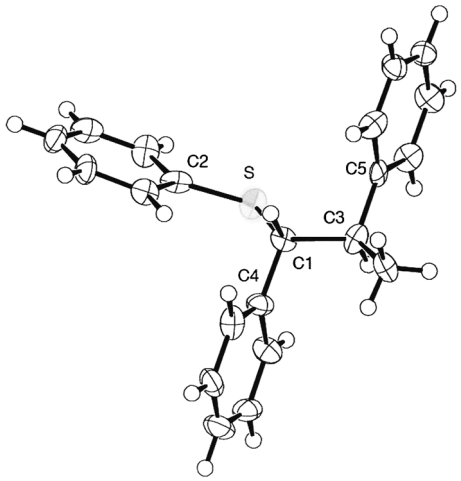
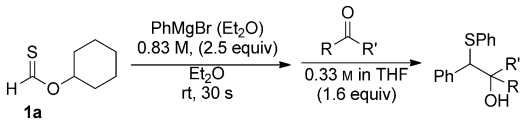


Figure 3. ORTEP of the major isomer of compound **17a**; thermal ellipsoids are set at 50% probability. Selected bond lengths [Å], bond angles [°], and dihedral angles [°]: C1–S 1.813, C2–S 1.757; C2-S-C1 106.63, S-C1=C3 107.94; C2-S-C1-C3 −161.10, C4-C1-C3-C5 177.99.

Then, aldehydes **18** and ketones **19** were used as the electrophile (Table 3). The addition of Grignard **10a** that was generated in situ to compounds **18** and **19** was complete within 10 min and no further improvement in the yields was achieved, even over longer reaction times. In all cases, despite the use of excess phenyl Grignard, the products that were derived from the addition of phenyl Grignard to carbonyl compounds were not observed. In the reactions of compounds **18a** and **18b**, two diastereomers were obtained in a ratio of about 22:78 (Table 3, entries 1 and 2). The use of benzophenone (**20a**) gave product **21a** in 61% yield (Table 3, entry 3), whereas the reaction with cyclohexanone (**20b**) gave product **21b** in a lower yield. In this case, phenyl benzyl sulfane (**5a**) was also formed in 18% yield.

The addition of Grignard reagents to acetophenone (**20c**) has been reported to not only give the corresponding adducts but also undesired products that were derived from the reduction of compound **20c** and the self-aldol condensation reaction of compound **20c**.[21] In fact, the use of compound **20c** as an electrophile in the sequential reaction of compound **1a** with phenyl Grignard also gave several products (Table 4, entry 1). Treatment with compound **20c** for 1 min gave the desired product (**21c**) in 39% yield, along with compounds **5a**, **22c**, and **23**. In this case, compound **22c** was formed by the addition of phenyl Grignard to compound **20c** and the self-aldol condensation of compound **20c** gave compound **23**. Performing the reaction for a longer reaction time did not decrease the formation of compounds **5a**, **22c**, and **23**. Recently, several types of additives have been elucidated to improve the selectivity of nucleophilic addition to compound **20c** and to decrease the Brønsted basicity of the Grignard reagents, which was ascribed to the unwanted aldol condensation reaction of enolizable ketones.[22] Early examples of these additives include lanthanide halides, such as $CeCl_3$ and $LaCl_3$.[23] Very recently, the combination of diglyme and a catalytic amount of Bu_4NCl has been reported to enhance the efficiency of the addition of several types of Grignard reagents to compound **20c** to give the desired adducts in high yields.[24] However, in our case, this combination did not work well, and the yield of compound **21c** was not improved. Next, a variety of readily available metal halides, such as LiX, $MgCl_2$, CuCl, $CuCl_2$, and ZnX_2, were added to the reaction mixture of phenyl Grignard and compound **1a**, followed by the addition of compound **20c**. The use of 0.25 equivalents of ZnX_2[25] slightly enhanced the efficiency of the addition reaction of Grignard reagent **10a** that was generated in situ (Table 4, entries 2–4), although the diastereoselectivity of product **21c** decreased. A longer reaction time after the addition of ketone **20c** did not improve the yield of compound **21c**. In contrast, the addition of LiBr (0.25 equiv) greatly enhanced the efficiency of the reaction that led to compound **21c** (Table 4, entry 5). In this case, product **22c** was also formed

Table 3. Sequential addition of the phenyl Grignard reagent and carbonyl compounds to thioformate **1a**.[a]

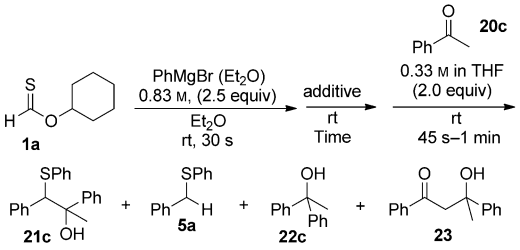


1a

Entry	Carbonyl compound	*t* [min]	Product	Yield [%][b]
1	**18a**	1	**19a**	58[c] (*syn*/*anti* 22:78)
2	**18b**	10	**19b**	52[d] (*syn*/*anti* 23:77)
3	**20a**	1	**21a**	61[d]
4[e]	**20b**	1	**21b**	45[f]

[a] Thioformate **1a** was sequentially reacted with the phenyl Grignard reagent (2.5 equiv) and carbonyl compounds (1.6 equiv). [b] Yield of isolated product after column chromatography on silica gel. [c] Yield of isolated product after GPC. [d] Less than 6% of compounds **5a** and **6b** were also obtained. [e] PhMgBr (2.2 equiv) and compound **20b** (1.3 equiv) were used. [f] Sulfane **5a** was also obtained in 18% yield.

Table 4. Sequential addition of the phenyl Grignard reagent and acetophenone (**20c**) to thioformate **1a**.[a]

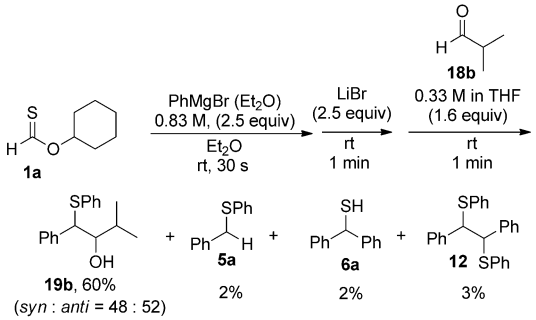


Entry	Additive (equiv)	t	Yield [%][b]			
			21c	**5a**	**22c**	**23**
1	none	–	39 (76:24)	21	38	8
2	$ZnCl_2(Et_2O)$ (0.25)	1 h	46 (62:38)	23	13	28
3	$ZnCl_2(Et_2O)$ (0.25)	1 h	46 (54:46)	27	33	22
4	$ZnCl_2(Et_2O)$ (0.25)	1 h	49 (54:46)	23	18	12
5	LiBr (0.25)	1 min	69[c] (45:55)	5	42	22
6	LiBr (1.0)	1 min	69 (48:52)	5	36	21
7	LiBr (2.5)	1 min	78 (56)[d,e] (35:65)	7	37	22
8	LiCl (2.5)	1 min	73 (38:62)	4	38	24
9	LiI (2.5)	1 min	79 (45:55)	8	39	23

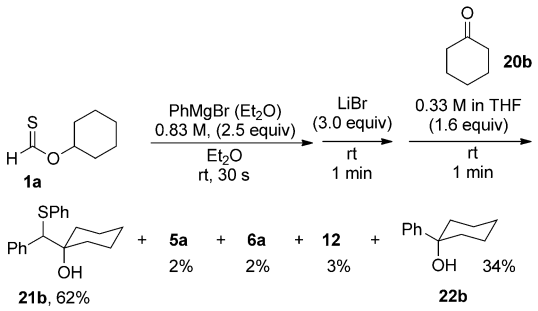
[a] Thioformate **1a** was sequentially reacted with the phenyl Grignard reagent (2.5 equiv) and acetophenone (**20c**, 2.0 equiv). [b] Yield based on ^{1}H NMR spectroscopy by using $Cl_2CHCHCl_2$ as an internal standard. [c] Thiol **6a** was also obtained in 12% yield. [d] Yield of isolated product after GPC. [e] The ratio of the diastereomers was 43:57.
In Figure 3, please add 50% probability.

in higher yield. This result shows that LiBr facilitates the addition of not only compound **10a**, but also of excess phenyl Grignard to compound **20c**, as reported by Knochel and coworkers.[26] Further studied of the additives and their amounts revealed that the use of excess LiCl, LiBr, or LiI as an additive gave compound **21c** in more than 73% yield (Table 4, entries 7–9).

With the results regarding additives in hand, LiBr was added to the reactions with aldehyde **18b** [Eq. (3)] and ketone **20b** [Eq. (4)]. In both cases, the products (**19b** and **21b**) were obtained in higher yields than in Table 3, entries 2 and 4.

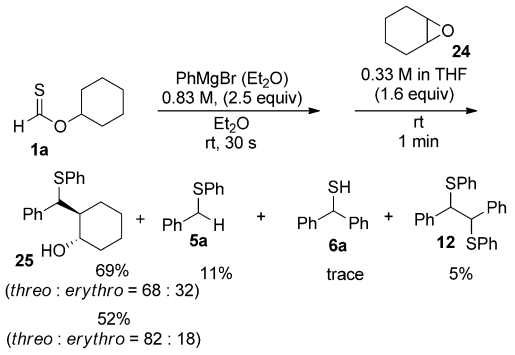


(3)

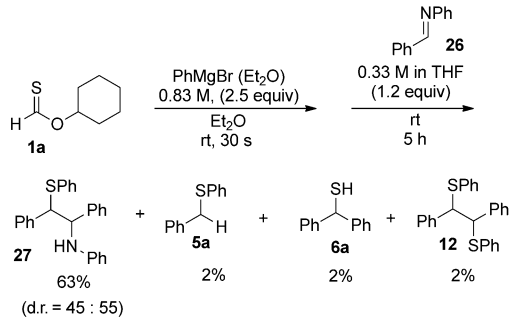


(4)

Finally, the availability of oxiranes and imines as electrophiles was examined. The reaction of cyclohexene oxide (**24**) with phenylsulfanyl benzyl Grignard (**10a**), which was derived from compound **1a** and phenyl Grignard, proceeded smoothly [Eq. (5)]. The ring-opening step of compound **24** proceeded to completion within 1 min in a *trans* fashion to give a diastereomeric mixture of two isomers of compound **25**[27] out of four possible isomers. For the addition to imine **26**, a much longer reaction time was necessary, but the reaction gave the desired product (**27**) in good yield [Eq. (6)].



(5)



(6)

Conclusion

In summary, we have described the first example of the sequential addition of aryl-Grignard reagents to *O*-alkyl thioformates. This reaction was complete within 30 s at room temperature to selectively give aryl benzylic sulfanes in good-to-high yields. In this reaction, two equivalents of the aryl-Grignard reagents add to the *O*-alkyl thioformates. One equivalent adds onto the carbon atom and the other formally adds onto the sulfur atom of the starting *O*-alkyl thioformate to generate arylsulfanyl benzylic Grignard reagents, which further participate in additions to a wide variety of

electrophiles, including allylic and carbonyl compounds, benzylic halides, oxiranes, and imines. The efficiency of the addition of Grignard reagents to carbonyl compounds was improved by the addition of lithium halides to the reaction mixture. As a further extension of this system, new types of organosulfur compounds that show unique physical or biological properties are being investigated.

Experimental Section

General remarks: IR spectra were obtained on a JASCO FTIR 410 spectrophotometer. ^{1}H NMR (399.7 MHz) and ^{13}C NMR spectra (100.4 MHz) were recorded on a JNM-α400 spectrometer. ^{1}H and ^{13}C chemical shifts are reported in δ with reference to tetramethylsilane and $CDCl_3$ as an internal standard, respectively. ^{13}C NMR spectra were acquired in proton-decoupled mode. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a JMS-700 mass spectrometer. Melting points were determined on a Yanaco Seisakusyo MP-S2 micro-melting-point apparatus and are uncorrected. Preparative recycling gel-permeation chromatography (GPC) was performed on Japan Analytical Industry LC-908 and LC9201R/U recycling preparative HPLC systems that were equipped with JAIGEL-1H and JAIGEL-2H columns (eluent: $CHCl_3$). HPLC was performed on a Japan Analytical Industry LC-908 recycling preparative HPLC system that was coupled to an RI indicator and a UV detector (256 nm) with a Mightysil Si60 column (250 mm × 20 mm).

Materials: Unless otherwise noted, the reagents were obtained commercially and used without further purification. Et_2O (dehydrated) and THF (dehydrated) were purchased from Kanto Chemical Co. and used without further purification. Thioformate **1a** was prepared by the thionation of *O*-cyclohexyl formate with Lawesson's reagent.[28] Column chromatography was performed on silica gel 60N (spherical, neutral, 40–50 μm) from Kanto Chemical Co., Ltd. All manipulations were carried out under an argon atmosphere.

General procedure for the sequential addition of Grignard reagents to thioformate 1a: To a solution of thioformate **1a** in Et_2O was quickly added a 0.83 M solution of arylmagnesium bromide in Et_2O (2.5 equiv) at RT and the mixture was stirred at RT for 30 s. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give aryl benzylic sulfanes **5**.

2-Methoxybenzyl(2-methoxyphenyl)sulfane (5d): Purified by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2, 3:1). Orange solid; yield: 45%; m.p. 33.2–34.2 °C; ^{1}H NMR ($CDCl_3$): δ = 3.81 (s, 3H; OMe), 3.86 (s, 3H; OMe), 4.12 (s, 2H; CH_2), 6.83–6.87, 7.14–7.23 ppm (m, 8H; Ar); ^{13}C NMR ($CDCl_3$): δ = 31.2 (SCH_2), 55.4 (OMe), 55.6 (OMe), 110.1, 110.3, 120.2, 120.8, 125.0, 125.6, 127.0, 128.3, 129.9, 130.2, 157.2 ppm (Ar, aromatic carbon atoms were partially overlapped); IR (KBr): $\tilde{\nu}$ = 3061, 3024, 3001, 2959, 2937, 2919, 2834, 1599, 1574, 1493, 1475, 1464, 1433, 1290, 1278, 1246, 1181, 1162, 1099, 1071, 1046, 1022, 778, 764, 754, 683 cm^{-1}; MS (EI): *m*/*z*: 260 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{15}H_{16}O_2S$: 260.0871 $[M]^+$; found: 260.0858.

2-Methylbenzyl(2-methylphenyl)sulfane (5e): Purified by flash column chromatography on silica gel (*n*-hexane). Colorless oil; yield: 67%; ^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3H; CH_3), 2.39 (s, 3H; CH_3), 4.04 (s, 2H; SCH_2), 7.06–7.18, 7.28–7.30 ppm (m, 8H; Ar); ^{13}C NMR ($CDCl_3$): δ = 19.0 (CH_3), 20.2 (CH_3), 36.5 (SCH_2), 125.9, 126.1, 126.3, 127.4, 129.2, 129.7, 129.9, 130.3, 134.8, 135.9, 136.7, 138.1 ppm (Ar); IR (neat) 3060, 3015, 2971, 2930, 1588, 1492, 1467, 1378, 1064, 1047, 742, 450 cm^{-1}; MS (EI): *m*/*z*: 228 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{15}H_{16}S$: 228.0973 $[M]^+$; found: 228.0975.

Sequential addition of phenyl Grignard to thioformate 1a in the presence of cyclopentadiene: To a solution of thioformate **1a** (0.1446 g, 1.0 mmol) in Et_2O (5.0 mL) was added cyclopentadiene (1.68 mL, 20 mmol) at RT. To this mixture was added a 0.83 M solution of phenylmagnesium bromide in Et_2O (1.08 mL, 0.9 mmol) at RT and the solution was stirred at RT for 5 min. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 1:0 to 50:1) to give compounds **11** (30.6 mg) as a yellow oil along with sulfide **5a** (3.4 mg, 1%). Yield: 16% (*endo*/*exo*, 81:19); ^{1}H NMR ($CDCl_3$): δ = 1.60 (*exo*, d, *J* = 9.2 Hz, 0.19H; CH_2), 1.75 (*endo*, d, *J* = 8.7 Hz, 0.81H; CH_2), 1.80 (*endo*, d, *J* = 9.2 Hz, 0.81H; CH_2), 1.87 (*exo*, d, *J* = 9.2 Hz, 0.19H; CH_2), 3.24 (*exo*, m, 0.19H; SCH(Ph)*CH*), 3.55 (*endo*, m, 0.81H; SCH(Ph)*CH*), 4.13 (*endo*, m, 0.81H; S*CH*(CH_2)CH), 4.21 (*exo*, m, 0.19H; S*CH*(CH_2)CH), 4.91 (*endo* and *exo*, d, *J* = 3.4 Hz, 1H; S*CH*Ph), 5.51 (*endo*, dd, *J* = 4.8, 3.4 Hz, 0.81H; *CH*=CHCHS), 6.12 (*exo*, dd, *J* = 4.8, 3.4 Hz, 0.19H; *CH*=CHCHS), 6.40 (*exo*, dd, *J* = 5.3, 2.4 Hz, 0.19H; CH=*CH*CHS), 6.50 (*endo*, dd, *J* = 4.8, 2.9 Hz, 0.81H; CH=*CH*CHS), 7.17–7.52 ppm (m, 5H; Ar); MS (EI): *m*/*z*: 188 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{12}H_{12}S$: 188.0660 $[M]^+$; found: 188.0648.

Synthetic procedure for the homocoupling reaction of Grignard reagent 10a that was generated in situ: To a solution of thioformate **1a** (0.1443 g, 1.0 mmol) in Et_2O (5.0 mL) was quickly added a 0.83 M solution of phenylmagnesium bromide in Et_2O (3.01 mL, 2.5 mmol) at RT and the mixture was stirred at RT for 30 s. Then, iodine (0.305 g, 1.2 mmol) was added at RT and the mixture was stirred at RT for 40 min. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 50:1) and GPC to give compound **12** as a yellow solid (67 mg). Yield: 33% (d.r. 68:32); ^{1}H NMR ($CDCl_3$): δ = 4.54 (minor, s, 0.64H; SCH), 4.59 (major, s, 1.36H; SCH), 6.92–7.26 ppm (major and minor, m, 20H; Ar); ^{13}C NMR ($CDCl_3$): δ = 58.1, 59.7 (SCH), 127.1, 127.2, 127.2, 127.4, 127.5, 127.9, 128.5, 128.7, 128.7, 129.2, 132.4, 132.7, 134.5, 134.6, 138.3, 139.5 ppm (Ar, aromatic carbon atoms were partially overlapped); IR (KBr): $\tilde{\nu}$ = 3060, 3023, 1451, 1437, 747, 703, 691 cm^{-1}; MS (EI): *m*/*z*: 398 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{26}H_{22}S_2$: 398.1163 $[M]^+$; found: 398.1164.

General procedure for the sequential addition of Grignard reagents and electrophiles to thioformate 1a: To a solution of thioformate **1a** in Et_2O was added quickly a 0.83 M solution of phenylmagnesium bromide in Et_2O (2.5 equiv) at RT and this mixture was stirred at RT for 30 s. Then, a 0.33 M solution of an electrophile in THF (2.0 equiv) was added at RT and the mixture was stirred at RT for 5 min. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, GPC, and/or HPLC.

Trimethyl(phenyl(phenylsulfanyl)methyl)silane (13):[20] Purified by flash column chromatography on silica gel (*n*-hexane). Yield: 68%; ^{1}H NMR ($CDCl_3$): δ = 0.02 (s, 9H; TMS), 3.65 (s, 1H; SCH), 6.90–7.20 ppm (m, 10H; Ar).

Phenyl(1-phenylbut-3-en-1-yl)sulfane (15a):[29] Purified by flash column chromatography on silica gel (*n*-hexane). Yield: 62%; ^{1}H NMR ($CDCl_3$): δ = 2.62 (m, 2H; CH_2), 4.20 (t, *J* = 7.3 Hz, 1H; SCH), 4.89–4.96 (m, 2H; CH=CH_2), 5.63 (ddt, *J* = 17, 9.7, 6.8 Hz, 1H; C*H*=CH_2), 7.08–7.32 ppm (m, 10H; Ar).

(*E*)-Phenyl(1-phenylpent-3-en-1-yl)sulfane (15b): Purified by flash column chromatography on silica gel (*n*-hexane). Yield: 69% (*E*/*Z* = 78:22); ^{1}H NMR ($CDCl_3$): δ = 1.51 (*Z*, d, *J* = 6.3 Hz, 0.66H; CH_3), 1.59 (*E*, d, *J* = 5.8 Hz, 2.34H; CH_3), 2.62–2.67 (*E*, m, 1.56H; CH_2), 2.69–2.74 (*Z*, m, 0.44H; CH_2), 4.18 (*E* and *Z*, m, 1H; SCH), 5.35 (*E* and *Z*, m, 1H; CH=*CH*CH_3), 5.45 (*E* and *Z*, m, 1H; *CH*=CHCH_3), 7.14–7.41 ppm (*E* and *Z*, m, 10H; Ar); ^{13}C NMR ($CDCl_3$): δ = 12.8, *17.8* (CH_3), 33.6, *39.3* (CH_2), 53.3, *53.5* (SCH), 126.0, 126.7, 126.8, 126.9, 126.9, 127.0, 127.0, 127.5, 127.7, 127.8, 128.1, 128.4, 128.5, 128.5, 128.7, 132.1, 132.1, 134.9, 141.5, 141.6 ppm (Ar and *CH*=*CH*CH_3); IR (neat) 3059, 3025, 2963, 2915, 1583, 1491, 1479, 1452, 1437, 1025, 966, 746, 695 cm^{-1}; MS (EI): *m*/*z*: 254 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}S$: 254.1129 $[M]^+$; found: 254.1105.

Ethyl-2-methylene-4-phenyl-4-(phenylsulfanyl)butanoate (15c): Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 40:1) and HPLC. Yield: 47%; ^{1}H NMR ($CDCl_3$): $\delta=1.25$ (t, $J=7.1$ Hz, 3H; CH_3), 2.86 (dd, $J=14.0$, 8.7 Hz, 1H; SCHCH_2), 3.00 (dd, $J=14.1$, 6.5 Hz, 1H; SCHCH_2), 4.15 (q, $J=7.1$ Hz, 2H; OCH_2), 4.49 (dd, $J=8.7$, 6.5 Hz, 1H; SCH), 5.39 (d, $J=1.3$ Hz, 1H; C=CH_2), 6.09 (d, $J=1.3$ Hz, 1H; C=CH_2), 7.13–7.31 ppm (m, 10H; Ar); ^{13}C NMR ($CDCl_3$): $\delta=14.1$ (CH_3), 39.2 (SHCH_2), 51.6 (SCH), 60.6 (OCH_2), 126.8, 127.2, 127.8, 127.9, 128.3, 128.6, 131.8, 134.8, 137.1, 140.9 (Ar, C=C), 166.6 ppm (C=O); IR (neat) 3059, 3027, 2981, 2935, 1713, 1629, 1583, 1491, 1480, 1452, 1438, 1368, 1327, 1301, 1189, 1134, 1025, 951, 745, 697 cm^{-1}; MS (EI): *m*/*z*: 312 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}O_2S$: 312.1184 $[M]^+$; found: 312.1183.

Phenyl(1,2-diphenylpropyl)sulfane (17a): Purified by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2, 30:1). Yield: 57% (*syn*/*anti*=38:62); ^{1}H NMR ($CDCl_3$): $\delta=1.18$ (major, d, $J=7.3$ Hz, 2.4H; CH_3), 1.54 (minor, d, $J=6.8$ Hz, 0.6H; CH_3), 3.23–3.33 (m, 1H; CH), 4.31 (d, $J=9.2$ Hz, 1H; SCH), 7.03–7.32 ppm (m, 15H; Ar); ^{13}C NMR ($CDCl_3$): $\delta=19.8$ (major and minor, CH_3), 45.5, 45.8 (CH), 60.9, 61.1 (SCH), 126.2, 126.5, 126.6, 126.6, 126.9, 127.4, 127.6, 127.7, 127.8, 127.9, 127.9, 128.1, 128.2, 128.4, 128.5, 128.6, 131.7, 132.2, 135.4, 135.4 140.7, 141.1, 143.7, 144.2 ppm (Ar); IR (KBr): $\tilde{\nu}=3059$, 3023, 3001, 2967, 2914, 2868, 1598, 1583, 1490, 1478, 1449, 1437, 1091, 1069, 1024, 1007, 732, 693 cm^{-1}; MS (EI): *m*/*z*: 304 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{21}H_{20}S$: 304.1286 $[M]^+$; found: 304.1297.

Phenyl(1-phenyl-2-(4-vinyl)phenyl)sulfane (17b): Purified by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2, 1:0 to 10:1). Yield: 65%; ^{1}H NMR ($CDCl_3$): $\delta=3.16$ (dd, $J=13.6$, 8.7 Hz, 1H; SHCH_2), 3.24 (dd, $J=13.8$, 6.1 Hz, 1H; SHCH_2), 4.36 (dd, $J=8.2$, 6.3 Hz, 1H; SCH), 5.17 (d, $J=10.7$ Hz, 1H; CH=CH_2), 5.66 (d, $J=17.5$ Hz, 1H; CH=CH_2), 6.63 (dd, $J=17.8$, 10.9 Hz, 1H; CH=CH_2), 6.94–7.26 ppm (m, 14H; Ar); ^{13}C NMR ($CDCl_3$): $\delta=42.4$ (SHCH_2), 54.9 (SCH), 113.1, 125.9, 126.9, 127.1, 127.9, 128.1, 128.6, 129.2, 132.1, 134.9, 135.6, 136.4, 138.3, 141.0 ppm (Ar and CH=CH_2); IR (neat) 3082, 3058, 3026, 3003, 1627, 1583, 1510, 1492, 1479, 1452, 1438, 1406, 1025, 989, 907, 827, 747, 696 cm^{-1}; MS (EI): *m*/*z*: 316 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{22}H_{20}S$: 316.1286 $[M]^+$; found: 316.1275.

1,2-Diphenyl-2-(phenylsulfanyl)ethanol (19a):[20] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 40:1 to 30:1). Yield: 58% (*syn*/*anti*, 22:78); ^{1}H NMR ($CDCl_3$): $\delta=2.50$ (s, 1H; OH), 4.37 (*syn*, d, $J=8.7$ Hz, 0.22H; SCH), 4.46 (*anti*, d, $J=5.3$ Hz, 0.78H; SCH), 4.94 (*syn*, d, $J=8.2$ Hz, 0.22H; *CH*OH), 5.04 (*anti*, d, $J=5.3$ Hz, 0.78H; *CH*OH), 7.02–7.30 ppm (*syn* and *anti*, m, 15H; Ar).

3-Methy-1-phenyl-1-(phenylsulfanyl)butan-2-ol (19b):[20] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 1:0 to 30:1). Yield: 60% (*syn*/*anti*, 48:52); ^{1}H NMR ($CDCl_3$): $\delta=0.86$ (*syn*, d, $J=6.8$ Hz, 1.44H; CH_3), 0.91 (*anti*, d, $J=6.8$ Hz, 1.56H; CH_3), 0.95 (*anti*, d, $J=6.3$ Hz, 1.56H; CH_3), 0.98 (*syn*, d, $J=6.8$ Hz, 1.44H; CH_3), 1.55–1.66 (*syn*, m, 0.48H; $CH(CH_3)_2$), 1.74–1.86 (*anti*, m, 0.52H; $CH(CH_3)_2$), 2.44 (*syn* and *anti*, s, 1H; OH), 3.61 (*anti*, dd, $J=6.3$, 5.8 Hz, 0.52H; CHO), 3.74 (*syn*, dd, $J=8.7$, 3.4 Hz, 0.48H; CHO), 4.15 (*syn*, d, $J=8.7$ Hz, 0.48H; SCH), 4.31 (*anti*, d, $J=5.3$ Hz, 0.52H; SCH), 7.10–7.39 ppm (*syn* and *anti*, m, 10H; Ar); MS (EI): *m*/*z*: 272 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{17}H_{20}OS$: 272.1235 $[M]^+$; found: 272.1231.

Phenyl(1,2,2-triphenyl-2-hydroxy)ethylsulfane (21a):[30] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 40:1). Yield: 61%; ^{1}H NMR ($CDCl_3$): $\delta=3.30$ (s, 1H; OH), 5.25 (s, 1H; SCH), 6.87–7.74 ppm (m, 20H; Ar).

1-(Phenyl(phenylsulfanyl)methyl)cyclohexanol (21b):[30] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc/CH_2Cl_2, 1:0:0 to 15:0:1 to 20:1:0) and GPC. Yield: 55%; ^{1}H NMR ($CDCl_3$): $\delta=1.03$–1.88 (m, 10H), 2.09 (s, 1H; OH), 4.16 (s, 1H; SCH), 7.08–7.40 ppm (m, 10H; Ar).

1,2-Diphenyl-1-(phenylsulfanyl)propan-2-ol (21c):[30] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc, 10:1) and GPC. Yield: 56% (d.r. 43:57); ^{1}H NMR ($CDCl_3$): $\delta=1.51$ (major, s, 1.71H; CH_3), 1.75 (minor, s, 1.29H; CH_3), 2.86 (minor, s, 0.43H; OH), 3.01 (major, s, 0.57H; OH), 4.45 (major, s, 0.57H; SCH), 4.46 (minor, s, 0.43H; SCH), 7.05–7.33 ppm (major and minor, m, 15H; Ar).

2-(Phenyl(phenylsulfanyl)methyl)cyclohexanol (25):[27] Purified by flash column chromatography on silica gel (*n*-hexane/EtOAc/CH_2Cl_2, 15:0:1 to 1:0:0 to 5:1:0) and GPC. Yield: 52% (*trans-threo*/*trans-erythro*, 82:18); ^{1}H NMR ($CDCl_3$): $\delta=0.82$–2.04 (*trans-threo* and *trans-erythro*, m, 10H; CH_2, OH, *CH*CHOH), 3.08 (*trans-threo*, td, $J=10.2$, 4.3 Hz, 0.68H; *CH*OH), 3.80 (*trans-erythro*, td, $J=9.7$, 4.3 Hz, 0.32H; *CH*OH), 4.87 (*trans-erythro*, d, $J=3.4$ Hz, 0.32H; SCH), 4.90 (*trans-threo*, d, $J=4.3$ Hz, 0.68H; SCH), 7.02–7.49 ppm (*trans-threo* and *trans-erythro*, m, 10H; Ar).

***N*-(1,2-diphenyl-2-(phenylsulfanyl)ethyl)aniline (27)**: Purified by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2, 10:1 to 2:1) and GPC. Yield: 63% (d.r. 45:55); ^{1}H NMR ($CDCl_3$): $\delta=4.46$ (major, d, $J=8.0$ Hz, 0.55H; NH*CH* or SCH), 4.60 (minor, d, $J=4.9$ Hz, 0.45H; NH*CH* or SCH), 4.70 (major, d, $J=7.6$ Hz, 0.55H; NH*CH* or SCH), 4.66 (minor, s, 0.45H; NH), 4.74 (minor, d, $J=4.5$ Hz, 0.45H; NH*CH* or SCH), 4.94 (major, s, 0.55H; NH), 6.47–6.53, 6.54–6.68, 6.95–7.24 ppm (major and minor, m, 20H; Ar); ^{13}C NMR ($CDCl_3$): $\delta=60.4$, 60.7, 61.5, 62.5 (SCH, NHCH), 113.8, 113.8, 117.7, 117.8, 126.9, 127.1, 127.2, 127.3, 127.4, 127.4, 127.5, 127.6, 127.9, 127.9, 128.1, 128.7, 128.8, 128.8, 129.0, 129.0, 131.4, 132.0, 134.2, 134.8, 137.5, 138.9, 139.6, 140.3, 146.6, 146.7 ppm (Ar, aromatic carbon atoms were partially overlapped); IR (KBr): $\tilde{\nu}=3420$, 3374, 3072, 3055, 3015, 3000, 2906, 2832, 1599, 1583, 1497, 1478, 1449, 1436, 1424, 1310, 1078, 1025, 748, 729, 698, 682 cm^{-1}; MS (EI): *m*/*z*: 381 $[M]^+$; HRMS (EI): *m*/*z* calcd for $C_{26}H_{23}NS$: 381.1551 $[M]^+$; found: 381.1547.

X-ray structure analysis: The analysis of compound **17a** was carried out on a Rigaku/MSC Mercury CCD diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda=0.71069$ Å). Reflection data were collected at 123–203 K by using a Rigaku XR-TCS-2–050 temperature controller. The structure was solved and refined by using direct methods with SHELXL-97[31] and the Yadokari-XG crystallographic software package from the Molecular Structure Corporation.[32] A crystal suitable for X-ray diffraction was obtained by the slow diffusion of distilled water into a solution of compound **17a** in acetone. A crystal was cut from the grown crystals and attached onto the tip of a MiTeGen MicroMount. Crystal data and the measurement procedure are summarized in the Supporting Information, Table S1.

CCDC-934116 (**17a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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