Kinoshita, Jun; Baralle, Alexandre; Yoshida, Akira; Yanagi, Tomoyuki; Nogi, Keisuke; Yorimitsu, Hideki

京都大学
KYOTO UNIVERSITY

WILEY-VCH

FULL PAPER

A Route to Indoles via Modified Fischer Indole Intermediates from Sulfonanilides and Ketene Dithioacetal Monoxides

Jun Kinoshita, Alexandre Baralle, Akira Yoshida, Tomoyuki Yanagi, Keisuke Nogi, Hideki Yorimitsu*[a]

Dedication ((optional))

[a]   J. Kinoshita, Dr. A. Baralle, A. Yoshida, T. Yanagi, Dr. K. Nogi, Prof. Dr. H. Yorimitsu
        Department of Chemistry, Graduate School of Science
        Kyoto University
        Sakyo-ku, Kyoto 606-8502, Japan
        E-mail: yori@kuchem.kyoto-u.ac.jp

        Supporting information for this article is given via a link at the end of the document.
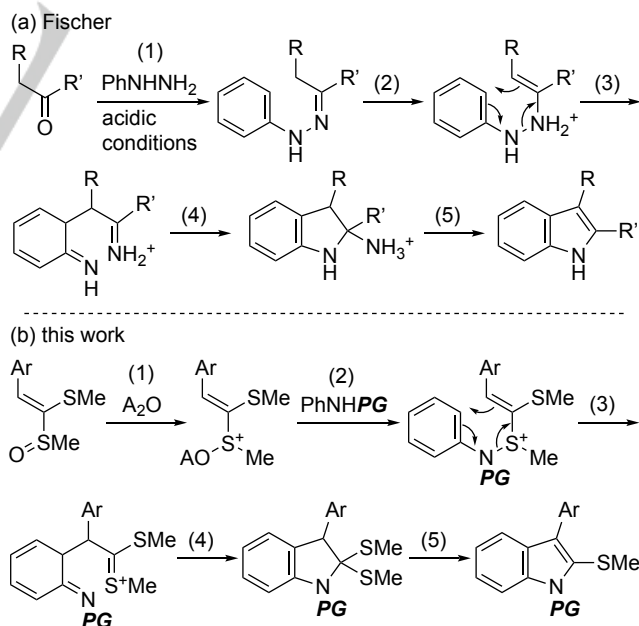
Abstract: An S–N variant of the N–N-based Fischer indole synthesis has been developed. Treatment of sulfonanilides and ketene dithioacetal monoxides with a powerful acid anhydride provides *N*-sulfonyl-2-methylsulfanylindoles. The initial interrupted Pummerer reaction would yield the key S–N-tethered precursor in situ that then undergoes [3,3] sigmatropic rearrangement, after which the endgame to the indole ring follows the Fischer manner.

Introduction

The indole ring system constitutes an extremely important class of heterocycles that are found in a broad range of natural sciences and industries. Unsurprisingly, development of new methods for the synthesis of indoles has been a pivotal topic in organic synthesis.[1] Since its discovery in 1883,[2] the Fischer indole synthesis has been the preeminent method.[1a-i,3] This reliable reaction is composed of (1) condensation of arylhydrazine with ketone under acidic conditions, (2) tautomerization of the hydrazone to the corresponding N–N-tethered protonated alkenyl aryl hydrazine as the key intermediate, (3) charge-accelerated [3,3] sigmatropic rearrangement, (4) rearomatization via proton shift and cyclization to construct a dihydroindole skeleton, and (5) elimination of ammonia to aromatize into indole (Scheme 1a). The key unstable intermediate is characterized by the weak N–N bond that links the two π-systems, the phenyl and 1-alkenyl groups. We envisioned that a new alternative method to generate a similar key intermediate would lead to taking a new twist in the Fischer indole technology.

Having been interested in the modern Pummerer chemistry,[4] we designed a modified Fischer indole synthesis by means of the reaction of protected aniline with alkenyl sulfoxide in the presence of acid anhydride. A presumed mechanism is shown in Scheme 1b. Instead of arylhydrazine and ketone, protected aniline and ketene dithioacetal monoxide (KDM) are used as starting materials. The reaction would consist of the following steps: (1) Treatment of a mixture of these two components with acid anhydride (A$_2$O) results in the formation of an unstable alkenylsulfonium intermediate. (2) The subsequent interrupted Pummerer reaction with the protected aniline affords an S–N-tethered intermediate. (3) Charge-accelerated rearrangement,[5-7] (4) rearomatization and cyclization, and (5) elimination of

methanethiol should similarly yield an indole framework. This mechanistic picture would be supported by our previous success in the synthesis of benzofurans from phenols and KDM.[8] However, differences between phenols and protected anilines would complicate this putative indole synthesis. One can easily imagine that the protective group in the aniline substrates would have a significant impact on the outcome of the reaction. This was indeed the case in the synthesis of biaryls from *N*-protected anilines and aryl sulfoxides by means of trifluoroacetic anhydride, wherein sulfonyl protections are crucial.[9,10] Given these circumstances, here we report our endeavors to achieve a modified Fischer indole synthesis from protected anilines and KDM.[11]

Scheme 1. The Fischer Indole Synthesis and the New Variant. *PG* = protective group.

京都大学
KYOTO UNIVERSITY

京都大学学術情報リポジトリ
KURENAI 紅
Kyoto University Research Information Repository

WILEY-VCH

FULL PAPER

Results and Discussion

According to the previous successes,[8,9a] the reaction of *p*-anisylsulfonyl-protected *p*-toluidine **1a** with aryl KDM **2a** by means of trifluoroacetic anhydride was chosen as a model reaction. Treatment of **1a** and **2a** (1.5 equiv) with $(CF_3CO)_2O$ (1.8 equiv) in toluene at –40 ˚C for 15 h provided the expected indole **3aa** in 77% yield (Table 1, entry 1). To our delight, the yield of **3aa** was improved up to 87% by using a stronger activator, pentafluoropropanoic anhydride (entry 2). A higher temperature did not improve the yield of **3aa** (entry 3). Methanesulfonic and toluenesulfonic anhydrides did not promote the reaction while the starting materials were recovered (entries 4 and 5). Triflic anhydride is likely to be too reactive, providing a complex mixture albeit with a full conversion of **2a** (entry 6). Toluene was the best solvent although halogenated solvents, dichloromethane and benzotrifluoride, also worked (entries 7 and 8). Polar solvents such as acetonitrile and nitromethane were inferior to nonpolar solvents, decomposition of **2a** taking place. (entries 9 and 10). Sulfonyl protective groups are suitable in this reaction; Tosyl and mesyl groups were compatible in the indole synthesis albeit with lower yields (entries 11 and 12). A more electron-withdrawing trifluoromethanesulfonyl group is not suitable (entry 13). Acetanilide **1e** did not react under the conditions and only decomposition of **2a** was observed (entry 14).

Table 1. Optimization of Reaction Conditions.

entry	1	PG[a]	A_2O	solvent	3	yield /%[b]
1	**1a**	Ans	$(CF_3CO)_2O$	toluene	**3aa**	77
2	**1a**	Ans	$(C_2F_5CO)_2O$	toluene	**3aa**	87 (77[c])
3	**1a**	Ans	$(C_2F_5CO)_2O$	toluene	**3aa**	73[d]
4	**1a**	Ans	Ms_2O	toluene	**3aa**	0
5	**1a**	Ans	Ts_2O	toluene	**3aa**	0
6	**1a**	Ans	Tf_2O	toluene	**3aa**	7
7	**1a**	Ans	$(C_2F_5CO)_2O$	CH_2Cl_2	**3aa**	81
8	**1a**	Ans	$(C_2F_5CO)_2O$	$PhCF_3$	**3aa**	75
9	**1a**	Ans	$(C_2F_5CO)_2O$	CH_3CN	**3aa**	14
10	**1a**	Ans	$(C_2F_5CO)_2O$	CH_3NO_2	**3aa**	13
11	**1b**	Ts	$(C_2F_5CO)_2O$	toluene	**3ba**	58
12	**1c**	Ms	$(C_2F_5CO)_2O$	toluene	**3ca**	71
13	**1d**	Tf	$(C_2F_5CO)_2O$	toluene	**3da**	0
14	**1e**	Ac	$(C_2F_5CO)_2O$	toluene	**3ea**	0

[a] Ans = *p*-methoxybenzenesulfonyl. [b] NMR yield. [c] Isolated yield. [d] Performed at –20 ˚C for 2 h. KDM **2a** was fully consumed.

The reaction scope with respect to KDM **2** was surveyed and the results are summarized in Table 2. A range of *para*-substituted aryl substituents in **2** including an ester group and a cyano group were found to be compatible (entries 1–7), except for a *p*-methoxyphenyl group (entry 8). The strongly electron-donating *p*-methoxy group would significantly influence the stability and reactivity of the sulfonium species that the activation of **2h** by the acid anhydride generates, leading to the formation of a complex mixture. The *m*-methoxy group in **2i** should not affect the nature of the corresponding sulfonium species, and the expected product **3ai** was obtained in 80% yield (entry 9). A substituent at the *ortho* position showed a detrimental effect, leading to the formation of a complex mixture containing a trace amount of product **3aj** and the recovered sulfonanilide (entry 10), probably because the *ortho* substituent would hamper effective conjugation over the entire KDM. Alkyl-substituted KDM **2k** was also converted to a complex mixture with the sulfonanilide mostly untouched (entry 11).
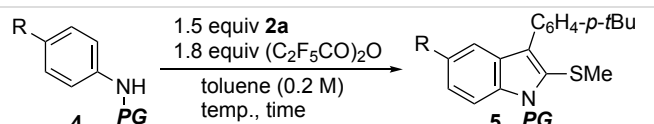
Table 2. Reaction Scope with Respect to KDM.

entry	2	R	3	isolated yield /%
1	**2a**	*p*-tBu-C_6H_4	**3aa**	77
2	**2b**	C_6H_5	**3ab**	76
3	**2c**	*p*-Br-C_6H_4	**3ac**	73
4	**2d**	*p*-CF_3-C_6H_4	**3ad**	68
5	**2e**	*p*-MeOCO-C_6H_4	**3ae**	72
6	**2f**	*p*-CN-C_6H_4	**3af**	60
7	**2g**	*p*-NO_2-C_6H_4	**3ag**	46
8	**2h**	*p*-MeO-C_6H_4	**3ah**	0
9	**2i**	*m*-MeO-C_6H_4	**3ai**	80
10	**2j**	*o*-CF_3-C_6H_4	**3aj**	<5
11	**2k**	$n$$C_{11}H_{23}$	**3ak**	0

Examination about the scope with respect to sulfonanilides **4** revealed that the reaction is very sensitive to the substituents in **4**. Sulfonanilide **4a**, the methoxy analogue of **1a**, was converted to the corresponding indole **5a** in only 9% NMR yield together with a complex mixture under the optimized conditions (Table 3, entry 1). To improve the yield of **5a**, a temperature as low as –78˚C was effective to afford **5a** in 58% isolated yield (entry 2). In contrast, simple sulfonanilide **4b** can be expected to be only a little more electron-deficient than **1a**, and a higher temperature of –20 ˚C was necessary to obtain a reasonable yield of product **5b** (entries 3 and 4). The reaction of *p*-chloro sulfonanilide **4c** was sluggish even at –20 ˚C (entries 5 and 6). Alternatively, the Ans group was replaced with a less electron-withdrawing sulfamoyl group to make the nitrogen atom in **4d** more nucleophilic (entries 7 and 8), and the reaction of **4d** at –40 ˚C for 40 h afforded the expected indole **5d** in 70% isolated yield. A strongly electron-

WILEY-VCH

FULL PAPER

withdrawing cyano group in **4e** had a totally detrimental effect (entry 9). After extensive re-screening of protective groups and reaction conditions, we found that the trifluoromethanesulfonyl protection in **4f** is helpful (entry 10) and that the reaction of **4f** in the presence of (CF$_3$CO)$_2$O in nitromethane at room temperature gave a satisfactory result (entry 11).   These results in Table 3 indicate that an optimization of reaction conditions including a protective group, a temperature, and a reaction time, is necessary for each sulfonanilide of interest.

Table 3. Reaction Scope with Respect to Sulfonanilides.

entry	4	R	PG[a]	Temp /°C	time /h	5	yield /%[b]
1	**4a**	MeO	Ans	–40	15	**5a**	9
2	**4a**	MeO	Ans	–78	15	**5a**	58[c]
3	**4b**	H	Ans	–40	15	**5b**	7
4	**4b**	H	Ans	–20	15	**5b**	58[c]
5	**4c**	Cl	Ans	–40	15	**5c**	17
6	**4c**	Cl	Ans	–20	15	**5c**	37
7	**4d**	Cl	Pip	–40	15	**5d**	56
8	**4d**	Cl	Pip	–40	40	**5d**	76 (70[c])
9	**4e**	CN	Ans	–40	15	**5e**	0
10	**4f**	CN	Tf	–40	15	**5f**	29 (25[c])
11[d]	**4f**	CN	Tf	20	3	**5f'**	(58[c])

[a] Ans = *p*-methoxybenzenesulfonyl. Pip = piperidinosulfamoyl. [b] NMR yield. [c] Isolated yield. [d] With 2.5 equivalents of (CF$_3$CO)$_2$O and **2b** in nitromethane at room temperature.

Finally, several transformations of one of the indole products were investigated (Scheme 2). Removal of the Ans group in indole **3af** proceeded smoothly according to Bajwa's protocol[12] using cesium carbonate in hot methanol/THF to provide **6** in 88% yield. Attempts to remove the 2-methylsulfanyl group in **3af** resulted in incomplete reduction even under harsh conditions to yield the expected product **7** along with the 46% recovery of **3af**. Alternatively, the 2-methylsulfanyl group in deprotected **6** could be reduced to yield **8** under the Nakada conditions.[13]
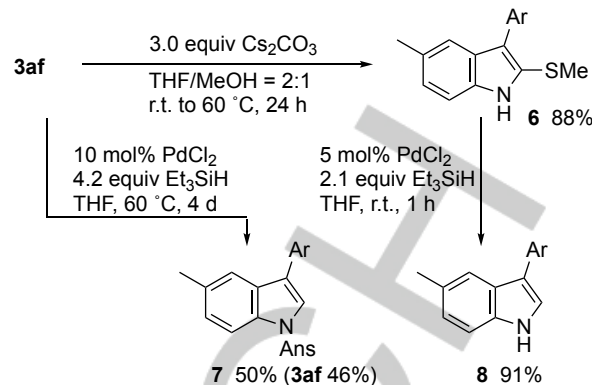
Scheme 2. Transformations of Indole **3af**. Ar = C$_6$H$_4$-*p*-CN

Conclusion

The modern Pummerer chemistry has allowed the development of a new route to indoles from sulfonanilides and ketene dithioacetal monoxides.   Upon activation of the sulfoxide with pentafluoropropanoic anhydride, an interrupted Pummerer reaction with sulfonanilide yielded an S–N variant of the N–N-based Fischer indole intermediate.   The S–N-tethered intermediate follows a pathway that resembles the Fischer indole mechanism to the corresponding *N*-sufonyl-2-methylsulfanylindole.   The scope with respect to the aryl-substituted KDMs is reasonably broad, while the use of different sulfonanilides requires re-optimization of reaction conditions. The products are expected to undergo a series of transformations. The development of strategies to overcome the sensitivity with regard to sulfonanilides in order to increase the synthetic utility of this new repertoire of indole synthesis remains to be accomplished.

Experimental Section

General procedure for the synthesis of indoles from KDMs and *N*-protected anilines

Synthesis of **3aa** is representative. A Schlenk tube was charged with sulfonanilide **1a** (139 mg, 0.50 mmol), KDM **2a** (201 mg, 0.75 mmol), and toluene (2.5 mL). The solution was cooled to –40 ºC, and pentafluoropropionic anhydride (171 µL, 0.90 mmol) was added slowly. The resulting solution was stirred at the same temperature for 15 h. The reaction was then terminated with saturated aqueous NaHCO$_3$ (2 mL), and the resulting biphasic solution was extracted with EtOAc (15 mL × 3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (eluent: Hexane/EtOAc = 5/1) to provide **3aa** (184 mg, 0.38 mmol, 77%) as a white solid.

Acknowledgements

3

WILEY-VCH

FULL PAPER

Keywords: indole • alkenyl sulfoxide • aniline • sigmatropic rearrangement • interrupted Pummerer reaction

[1]   a) R. J. Sundberg, *The Chemistry of Indoles*, Academic Press, New York, **1970**; b) R. J. Sundberg, *Indoles*, Academic Press, London, **1996**; c) J. A. Joule, in *Science of Synthesis, Vol. 10* (Ed.: E. J. Thomas), Thieme, Stuttgart, **2000**, Chapter 10.13; d) D. L. Hughes, *Org. Prep. Proced. Int.* **1993**, *25*, 607-632; e) G. W. Gribble, *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045-1075; f) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875-2911; g) D. F. Taber, P. K. Tirunahari, *Tetrahedron* **2011**, *67*, 7195-7210; h) M. Inman, C. J. Moody, *Chem. Sci.* **2013**, *4*, 29-41; i) M. M. Heravi, S. Rohani, V. Zadsirjan. N. Zahedi, *RSC Adv.* **2017**, *7*, 52852-52887; j) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873-2920; k) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2011**, *111*, PR215-PR283; l) J. Campo, M. Garcia-Valverde, S. Marcaccini, M. J. Rojo, T. Torroba, *Org. Biomol. Chem.* **2006**, *4*, 757-765; m) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. Biomol. Chem.* **2011**, *9*, 641-652; n) R. Vicente, *Org. Biomol. Chem.* **2011**, *9*, 6469-6480; o) N. Yoshikai, Y. Wei, *Asian J. Org. Chem.* **2013**, *2*, 466-478; p) G. Bartoli, R. Dalpozzo, M. Nardi, *Chem. Soc. Rev.* **2014**, *43*, 4728-4750; q) R. Mancuso, R. Dalpozzo, *Catalyst* **2018**, *8*, 458; r) A. K. Clarke, H. E. Ho, J. A. Rossi-Ashton, R. J. K. Taylor, W. P. Unsworth, *Chem. Asian J.* **2019**, *14*, 1900-1911; s) H. Lim, S. Seong, S. Han, *Synthesis* **2019**, *51*, 2737-2758; t) P. Sun, J. Yang, Z. Song, Y. Cai, Y. Liu, C. Chen, X. Chen, J. Peng, *Synthesis* **2020**, *52*, 75-84 and references cited therein; u) A. Baralle, T. Inukai, T. Yanagi, K. Nogi, A. Osuka, A. Nagaki, J. Yoshida, H. Yorimitsu, *Chem. Lett.* **2020**, *49*, 160-163 and references cited therein.

[2]   E. Fischer, F. Jourdan, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241-2245.

[3]   a) B. Robinson, *The Fischer Indole Synthesis*, John Wiley & Sons Inc., New York, **1982**; b) B. Robinson, *Chem. Rev.* **1963**, *63*, 373-401; c) B. Robinson, *Chem. Rev.* **1969**, *69*, 227-250; d) G. M. Robinson, R. Robinson, *J. Chem. Soc.* **1924**, *125*, 827-840; e) A. Kaga, T. Fukushima, J. Shimokawa, M. Kitamura, *Synthesis* **2019**, *51*, 3214-3220 and references cited therein.

[4]   Reviews: a) S. K. Bur, A. Padwa, *Chem. Rev.* **2004**, *104*, 2401-2432; b) K. S. Feldman, *Tetrahedron* **2006**, *62*, 5003-5034; c) S. Akai, Y. Kita, *Top. Curr. Chem.* **2007**, *274*, 35-76; d) L. H. S. Smith, S. C. Coote, H. F. Sneddon, D. J. Procter, *Angew. Chem. Int. Ed.* **2010**, *49*, 5832-5844; *Angew. Chem.* **2010**, *49*, 5968-5980; e) H. Yorimitsu, *J. Synth. Org. Chem., Jpn.* **2013**, *71*, 341-354; f) A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.* **2016**, *55*, 9842-9860; *Angew. Chem.* **2016**, *128*, 9996-10014; g) A. Shafir, *Tetrahedron Lett.* **2016**, *57*, 2673-2682; h) H. Yorimitsu, *Chem. Rec.* **2017**, *17*, 1156-1167; i) Z.-Y. Tian, Y.-H. Hu, H.-B. Teng, C.-P. Zhang, *Tetrahedron Lett.* **2018**, *59*, 299-309; j) T. Yanagi, K. Nogi, H. Yorimitsu, *Tetrahedron Lett.* **2018**, *59*, 2951-2959; k) D. Kaiser, I. Klose, R. Oost, J. Neuhaus, N. Maulide, *Chem. Rev.* **2019**, *119*, 8701-8780; l) Z. He, A. P. Pulis, G. J. P. Perry, D. J. Procter, *Phosphorus Sulfur Relat. Elem.* **2019**, *194*, 669-677.

[5]   X. Huang, S. Klimczyk, N. Maulide, *Synthesis* **2012**, *44*, 175-183.

[6]   Selected recent reports on organic synthesis based on charge-accelerated sigmatropic rearrangement of sulfur-tethered intermediates: a) M. Šiaučiulis, S. Sapmaz, A. P. Pulis, D. J. Procter, *Chem. Sci.* **2018**, *9*, 754-759; b) D. Kaldre, I. Klose, N. Maulide, *Science* **2018**, *361*, 664-667; c) B. Maryasin, D. Kaldre, R. Galaverna, I. Klose, S. Ruider, M. Drescher, H. Kählig, L. González, M. N. Eberlin, I. D. Jurberg, N. Maulide, *Chem. Sci.* **2018**, *9*, 4124-4131; d) A. Pons, J. Michalland, W. Zawodny, Y. Chen, V. Tona, N. Maulide, *Angew. Chem. Int. Ed.* **2019**, *58*, 17303-17306; *Angew. Chem.* **2019**, *131*, 17463-17467; e) J. Yan, A. P. Pulis, G. J. P. Perry, D. J. Procter, *Angew. Chem. Int. Ed.* **2019**, *58*, 15675-15679; *Angew. Chem.* **2019**, *131*, 15822-15826.

[7]   Peng reported α-arylation of nitriles with aryl sulfoxides through [3,3] or [5,5] sigmatropic rearrangement from S–N-tethered intermediates. a) L. Shang, Y. Chang, F. Luo, J.-N. He, X. Huang, L. Zhang, L. Kong, K. Li, B. Peng, *J. Am. Chem. Soc.* **2017**, *139*, 4211-4217; b) F. Luo, Y. Lu, M. Hu, J. Tian, L. Zhang, W. Bao, C. Yan, X. Huang, Z.-X. Wang, B. Peng, *Org. Chem. Front.* **2018**, *5*, 1756-1762; c) L. Zhang, J.-N. He, Y. Liang, M. Hu, L. Shang, X. Huang, L. Kong, Z.-X. Wang, B. Peng, *Angew. Chem. Int. Ed.* **2019**, *58*, 5316-5320; *Angew. Chem.* **2019**, *131*, 5370-5374; d)

L. Zhang, M. Hu, B. Peng, *Synlett* **2019**, *30*, 2203-2208; e) Hu, J.-N. He, T. Dong, M. Chen, C. Yan, Y. Ye, B. Peng, *Eur. J. Org. Chem.* **2020**, *2*, 193-197.

[8]   a) T. Kobatake, D. Fujino, S. Yoshida, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2010**, *132*, 11838-11840; b) Y. Ookubo, A. Wakamiya, H. Yorimitsu, A. Osuka, *Chem. Eur. J.* **2012**, *18*, 12690-12697; c) K. Murakami, H. Yorimitsu, A. Osuka, *Angew. Chem. Int. Ed.* **2014**, *53*, 7510-7513; *Angew. Chem.* **2014**, *126*, 7640-7643; d) K. Murakami, H. Yorimitsu, A. Osuka, *Bull. Chem. Soc. Jpn.* **2014**, *87*, 1349-1366; e) K. Okamoto, M. Hori, T. Yanagi, K. Murakami, K. Nogi, H. Yorimitsu, *Angew. Chem. Int. Ed.* **2018**, *57*, 14230-14234; *Angew. Chem.* **2018**, *130*, 14426-14430; f) M. Hori, T. Yanagi, K. Murakami, H. Yorimitsu, *Bull. Chem. Soc. Jpn.* **2019**, *92*, 302-311; g) T. Yanagi, K. Nogi, H. Yorimitsu, *Synlett* **2020**, *31*, 153-157.

[9]   a) A. Yoshida, K. Okamoto, T. Yanagi, K. Nogi, H. Yorimitsu, *Tetrahedron* **2020**, *76*, 131232; b) T. Yanagi, K. Nogi, H. Yorimitsu, *Chem. Eur. J.* **2020**, *26*, 783-787.

[10]   Similar synthesis of biaryls from phenols and aryl sulfoxides by means of acid anhydride: a) T. Yanagi, S. Otsuka, Y. Kasuga, K. Fujimoto, K. Murakami, K. Nogi, H. Yorimitsu, A. Osuka, *J. Am. Chem. Soc.* **2016**, *138*, 14582-14585; b) H. J. Shrives, J. A. Fernández-Salas, C. Hedtke, A. P. Pulis, D. J. Procter, *Nat. Commun.* **2017**, *8*, 14801; c) Z. He, H. J. Shrives, J. A. Fernández-Salas, A. Abengózar, J. Neufeld, K. Yang, A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.* **2018**, *57*, 5759-5764; *Angew. Chem.* **2018**, *130*, 5861-5866; d) K. Yang, A. P. Pulis, G. J. P. Perry, D. J. Procter, *Org. Lett.* **2018**, *20*, 7498-7503; e) K. Okamoto, K. Nogi, J. Shimokawa, H. Yorimitsu, *Chem. Eur. J.* **2020**, *26*, 5615-5618; f) K. Okamoto, K. Nogi, H. Yorimitsu, *Org. Lett.* **2020**, *22*, 5540-5544; g) ref 8g.

[11]   The Gassman indole synthesis provides a route from aniline and alpha-methylsulfanyl carbonyl compounds. Although the Gassman route and ours are similar in that S–N-tethered sulfonium intermediates are involved, the reaction scopes, the substitution patterns of the products, and the reaction mechanisms are fairly different. a) P. G. Gassman, T. J. van Bergen, D. P. Gilbert, B. W. Cue, Jr., *J. Am. Chem. Soc.* **1973**, *95*, 6508-6509; b) P. G. Gassman, T. J. van Bergen, D. P. Gilbert, B. W. Cue, Jr., *J. Am. Chem. Soc.* **1974**, *96*, 5495-5508.

[12]   J. S. Bajwa, G.-P. Chen, K. Prasad, O. Repič, T. J. Blacklock, *Tetrahedron Lett.* **2006**, *47*, 6425-6427.

[13]   T. Matsumura, T. Niwa, M. Nakada, *Tetrahedron Lett.* **2012**, *53*, 4313-4316.

WILEY-VCH

FULL PAPER

Entry for the Table of Contents
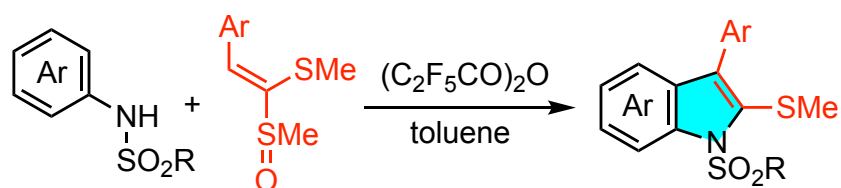
The modern Pummerer chemistry has allowed the development of a new route to indoles from sulfonanilides and ketene dithioacetal monoxides. Upon activation of the sulfoxide with acid anhydride, an interrupted Pummerer reaction with sulfonanilide yielded an S–N variant of the N–N-based intermediate in the Fischer indole synthesis. The S–N-tethered intermediate follows a Fischer-like pathway to the corresponding *N*-sufonyl-2-methylsulfanylindole of synthetic use.

Institute and/or researcher Twitter usernames: @yorimitsu_lab