

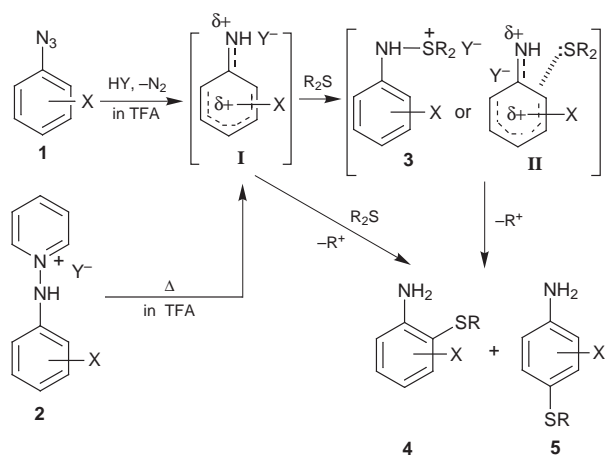
Novel generation of phenylnitrenium ions from *S,S*-dialkylanilinosulfonium salts in trifluoroacetic acid and formation of anilines by a new intramolecular hydride-shift to the phenylnitrenium ions

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Reactions of *S,S*-dialkylanilinosulfonium salts in trifluoroacetic acid give anilines, trifluoroacetanilides and dialkyl sulfoxides *via* novel intramolecular hydride-shift from the *α*-C–H of sulfide to phenylnitrenium ions (not completely free from the sulfide) interacting with both the unshared electron pair of the sulfide and the counter ion.

We have inferred that reactions of dialkyl sulfide with phenylnitrenium ions **I** generated by acid decomposition of phenyl azides **1**^{1,2} or 1-anilino-pyridinium salts **2**³ in trifluoroacetic acid (TFA) give alkyl 2- and 4-aminophenyl sulfides **4** and **5** *via* *S,S*-dimethylanilinosulfonium salts **3** or intermediates **II** in which the nitrenium ions interact with the unshared electron pair of sulfide and the counter ion (Scheme 1). However, under basic or



Scheme 1

neutral conditions, the anilinosulfonium salts **3** were converted into 2-aminoarylmethyl methyl sulfides **8** by Sommelet-Hauser-type rearrangement² without giving **4** and **5** (Scheme 2). In this paper, the reaction of the tilted anilinosulfonium salts **3** is performed in order to investigate the possibility that **4** and **5** are formed *via* **3** in an acidic solvent such as TFA. We here rule out this possibility, and find instead the formation of anilines by a novel hydride-shift to phenylnitrenium ions as seen in Scheme 2.

Results and discussion

Reactions of *S,S*-dimethylanilinosulfonium salt **3a** in TFA

S,S-Dimethylanilinosulfonium picrate was used as a precursor of anilinosulfonium trifluoroacetate **3a**. The dissolution of this picrate in TFA at 20 °C resulted in complete conversion to **3a**, as was seen from the immediate colour change of the solution from the yellow of the picrate to colourless on dissolution. Reaction of the picrate in TFA (*i.e.* reaction of **3a** in TFA) did not give **4a** and **5a**, but instead gave aniline **6a**, trifluoroacetanilide **7a** and 2-aminophenylmethyl methyl sulfide **8a** (Table 1). This result rules out the possibility of the intermediacy of **3** in the formation of **4** and **5** in Scheme 1.

Table 1 Effect of counter ion on the reaction of *S,S*-dimethylanilinosulfonium salt **3a** (0.5 mmol) in TFA (30 cm³) containing acid (1.2 molar equivalent to **3a**) at 20 °C for 5 h

Acid HY	Counter ion Y ⁻	Yield ^a (%)			Ratio (6a + 7a): 8a
		6a	7a	8a	
HCl	Cl ⁻	35	Trace	2.5	14
None	OCOCF ₃ ⁻	21	Trace	10	2.1
AcOH	OCOCF ₃ ⁻	27	Trace	14	1.9
TFSA	OSO ₂ CF ₃ ⁻	27	Trace	21	1.3
H ₂ SO ₄	OSO ₃ H ⁻	22	Trace	18	1.2
HClO ₄	ClO ₄ ⁻	18	Trace	33	0.55

^a The yields are based on the amount of **3a** used.

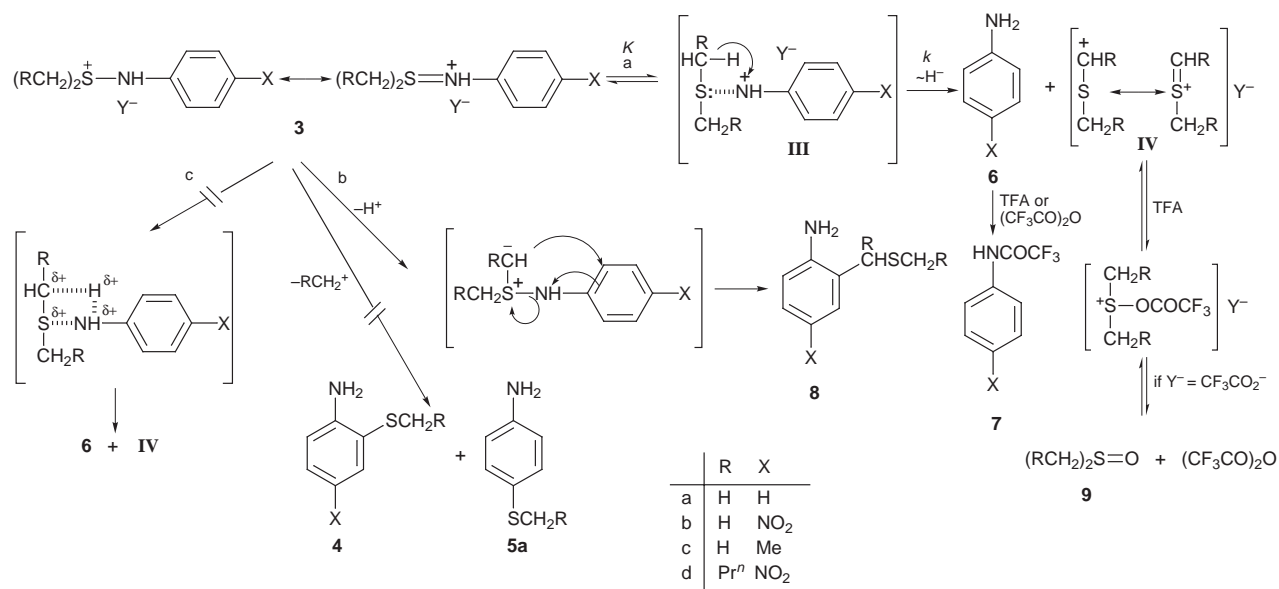
Table 2 Effect of solvent-nucleophilicity on reaction of *S,S*-dimethylanilinosulfonium salt **3a** (0.50 mmol) in solvent (25 cm³) containing TFA (1.2 molar equivalent to **3a**) at 20 °C for 20 h

Solvent	Yield ^a (%)			Ratio (6a + 7a): 8a
	6a	7a	8a	
TFA	45	Trace	9.0	5.0
CF ₃ CH ₂ OH	31	Trace	36	0.86
CH ₂ Cl ₂	11	Trace	46	0.24
MeOH	11	Trace	60	0.18

^a The yields are based on the amount of **3a** used.

Effects of counter ion and solvent nucleophilicity. The ratio (**6a** + **7a**):**8a** decreased with the increased softness of the counter ion (Table 1). The counter ion corresponds to the anion formed from acid added to the reaction system; the counter ion is OCOCF₃⁻ using TFA only as the acid. The ratio also decreased with an increase in the solvent-nucleophilicity⁴ (TFA < CF₃CH₂OH < CH₂Cl₂ < MeOH) (Table 2); although the solvent nucleophilicity of CH₂Cl₂ has not been calculated, its order seems to be between the orders of MeOH and CF₃CH₂OH.

These results can be explained by considering competing paths a and b (see Scheme 2). The hard counter ion of **3a** increases the resonance contribution of the sulfonium ion structure with an *S*-*N* single bond to give a high ratio of products from the favoured path a involving an *S*-*N* scission. However, a soft counter ion for **3a** increases the delocalisation of the positive charge over the *N*-atom as well as the *S*-atom to enhance the double-bond nature of the bond between the *S*- and *N*-atoms, giving an unfavourable path a. On the contrary, path b as a rate-determining step (a cyclisation after the path b might be very fast) for the formation of **8** would be insensitive to the counter ion. A more nucleophilic solvent



Scheme 2

Table 3 Reactions of *S,S*-dialkylanilinosulfonium salts **3b–d** (0.50 mmol) in TFA (5.0 cm³)

Salt	<i>T</i> /°C	<i>t</i> /h	Yield ^a (%)			
			6	7	8	9
3b	50	5	93	6.0	0	—
3c	50	5	95	3.0	0	67
3d	72	72	2.0	98	0	79

^a The yields are based on the amount of **3** used.

may disfavour path a by solvation with the phenylnitrenium ion and/or by reaction of the nitrenium ion with solvent. Thus, the path b suppresses path a, leading to a lower ratio of (**6a** + **7a**):**8**.

Formation of 6 and 7 via an intramolecular reaction. The reaction of **3a** in benzene (70% v/v)–TFA (30% v/v) for 2 h at 25 °C or under reflux did not produce diphenylamine and 2- and 4-aminobiphenyls which are formed by the intermolecular reaction⁵ of the phenylnitrenium ion with benzene, but instead gave **6a** and **7a** (see Experimental section). This result indicates that an intermediate **III** formed by path a is subject to an intramolecular reaction which is much faster than the intermolecular reaction with benzene, leading to the formation of **6** and **7**. Thus, the intramolecular reaction would be an intramolecular hydride-shift to the nitrenium ion interacting with sulfide as seen in Scheme 2. The hydride-shift from *a*-C–H of the sulfide should give a carbocation **IV** as well as **6**. In fact, the reaction of **3c** or **3d** in TFA produced sulfoxide **9c** (*i.e.* **9a**) or **9d**, respectively (Table 3); the formation of **9** can be interpreted by a retro-Pummerer reaction of **IV** (Scheme 2).

The nitrenium ion in **III** interacts with both the unshared electron pair on sulfur and the counter ion (Scheme 2). We have proposed a similar interaction of the parent nitrenium ion (NH₂⁺)⁶ or the arylsulfonium ion (ArS⁺)⁷. The following findings also support the formation of the phenylnitrenium ions interacting in such a way.

Reactions of *S,S*-dialkylanilinosulfonium salts **3b–d** in TFA

We dissolved *S,S*-(dimethyl- or di-*n*-butyl)-*N*-(4-nitrophenyl)imino-λ⁴-sulfanes and *S,S*-dimethyl-4-methylanilinosulfonium picrate as precursors of **3b** or **3d** and **3c**, respectively, in TFA at 20 °C. The colour of the solution immediately converted from orange (of the λ⁴-sulfanes) or yellow (of the

Table 4 Rate constants and activation parameters for decomposition of *S,S*-dialkylanilinosulfonium salts **3b–d** in TFA^a

Salt	<i>T</i> /°C	<i>k</i> _{obs} /10 ⁻⁵ s ⁻¹	Δ <i>H</i> [‡] /Kcal mol ⁻¹	Δ <i>S</i> [‡] /cal mol ⁻¹ K ⁻¹	Δ <i>G</i> [‡] /Kcal mol ⁻¹
3b	20	1.2			
	30	3.7	19	-17	24
	50	26			
3c	20	5.2			
	30	11	12	-39	24
	50	34			
3d	20	0.27			
	50	0.81	8.0	-57	25
	72	2.6			

^a Δ*H*[‡], Δ*S*[‡] and Δ*G*[‡] are the values at 25 °C.

picrate) to colourless, showing the conversion of the precursors to anilinosulfonium trifluoroacetates **3b–d** in TFA. The solution was allowed to stand under the conditions described in Table 3, affording **6** and **7** without giving **8** (Table 3).

This preferential formation of **6** and **7**, not **8**, results from path a being favoured over path b by a high positive charge on the *S*-atom of **3** rather than the *N*-atom in the cases of **3b** and **3d** which have an electron-withdrawing NO₂, and by the stability of the 4-tolylnitrenium ion compared to the phenylnitrenium ion in the case of **3c** (Scheme 2). The observation that the total yield of **6** and **7** is nearly 100% (see Table 3) means that the rate of decomposition of **3** should be equal to the rate of total production of **6** and **7**.

Rate constants and activation parameters for the decomposition of *S,S*-dialkylanilinosulfonium salts **3b–d** in TFA

We obtained the first-order rate constants *k*_{obs} for the decomposition of **3b–d** (*i.e.* the rate constants for the total production of the corresponding **6** and **7**) at three different temperatures, determining the activation parameters (Table 4).

The formation of **6** and **IV** by an intramolecular concerted mechanism (path c in Scheme 2) can be clearly ruled out by the fact that the rate of decomposition of **3d** is lower than that of **3b** as seen in Table 4. If the concerted mechanism were correct, its rate, giving a secondary carbocation **IVd**, should be higher than path a, forming a primary carbocation **IVb** (*i.e.* **IVa**). Thus, **3** equilibrates with **III** (*i.e.* *K* in Scheme 2), followed by an intramolecular hydride-shift (*i.e.* *k* in Scheme 2) giving **6** and

IV. In this case, **7** was obtained from **6** under the reaction conditions. The intermediate **III**d is more unstable than **III**b because of the substitution of two butyl groups on the *S*-atom rather than two methyl groups, so that the formation of **III**b would be favoured over formation of **III**d. Thus, the rate of decomposition of **3**d may be lower than that of **3**b.

The low ΔH^\ddagger of **3**d compared to that of **3**b (Table 4) may arise from the greater stability of **IV**d compared to **IV**b. The lower ΔH^\ddagger value of **3**c compared to that of **3**b (Table 4) can be explained by the facile formation of a more stable 4-tolyl-nitrenium ion rather than the 4-nitrophenylnitrenium ion.

From the above results, showing that the rate of decomposition depends upon the ease of formation of both **III** and **IV**, k_{obs} might be represented as kK . The variation in which the softer sulfonium ion **3** changes to the harder nitrenium ion of **III** would mostly affect ΔS^\ddagger , leading to the large negative ΔS^\ddagger due to an increase in the ion pair-association with the counter-anion. The magnitudes of ΔH^\ddagger and ΔS^\ddagger and those of the free energy are given in Table 4.

The thermal reaction of **1**^{1,2} or **2**³ with sulfides in TFA has been proposed to produce **4** and **5** without giving **6** and **7** via nitrenium species such as **I** and **II**, not by a bimolecular aromatic substitution of **1** or **2** (Scheme 1). However, the reaction of **3** in TFA yields **6** and **7** without giving **4** and **5** via **III** (Scheme 2). These facts imply that the nitrenium ion in **III** must be different from the nitrenium ion in **II**. Thus, the nitrenium ion in **III** may be in a lower energy state than **II**, and is interacting strongly with sulfide as compared with the interaction of **II** with sulfide. Because of such a strong interaction, **III** could give **6** and **IV** by the intramolecular hydride-shift from the α -C-H of the sulfide. The details of the interaction between the nitrenium ion and sulfide as shown in **II** will be reported in the future.

Experimental

IR spectra were obtained on a Hitachi EPI-G3 spectrometer. ¹H NMR spectra were taken with a Nippondenshi PMX-60SI instrument (*J* values are given in Hz). GLC-MS were recorded with a Shimadzu QP-5000 spectrometer linked to a Shimadzu GC-17A column (15 m × 0.25 mm) coated with DC-1 (0.25 μm film thickness), made by J & W Scientific. GLC was performed with a Shimadzu GC-8A instrument using a glass column (1 m × 3 mm) packed with 10% SE-30 on 60–80 mesh Chromosorb W (AW-DMCS). Two runs agreed to within 3% error for the yields of the products which are determined by replicated GLC analyses.

TFA, CF₃CH₂OH, dimethyl sulfoxide **9a** and aniline **6a** were purified by distillation of reagent grade materials (Nacalai Tesque). The following compounds were reagent grade (Nacalai Tesque) and were used without further purification; trifluoromethanesulfonic acid (TFSA), H₂SO₄, diphenylamine, 2-amino-biphenyl, 4-nitroaniline **6b**, 4-methylaniline **6c**. Benzene, AcOH, CH₂Cl₂ and MeOH were purified by standard methods before use. HClO₄ used in TFA was dehydrated by addition of trifluoroacetic anhydride (TFAA); HClO₄ and TFAA were reagent grade (Nacalai Tesque). 4-Aminobiphenyl⁸ and di-*n*-butyl sulfoxide **9d**⁹ were prepared by the methods described in the literature.

S,S-Dimethylanilinosulfonium picrate, *S,S*-dimethyl-*N*-(4-nitrophenyl)imino- λ^4 -sulfane and *S,S*-dimethyl-4-methylanilinosulfonium picrate were prepared by the literature method,¹⁰ and had mp 129.6 °C (lit.,¹⁰ 130–130.6 °C), 167 °C (lit.,¹⁰ 166–167 °C) and 167–169 °C (lit.,¹⁰ 165–166 °C), respectively. The following λ^4 -sulfane was synthesized by a similar method to that described in the above literature, and confirmed as indicated below.

S,S-Di-*n*-butyl-*N*-(4-nitrophenyl)imino- λ^4 -sulfane

This yellow crystalline compound had mp 68–69 °C; ν_{max} (KBr)/cm⁻¹ 3960, 3930, 2860, 1580 (N=S), 1570 (N=O), 1485,

1465, 1320, 1290, 1260 (C–N), 1190, 1120, 1097, 1082, 1000, 900, 850 (C–NO₂), 800 (*para*-substituted phenyl), 762, 707, 655, 626, 540, 502 and 480; δ_{H} (CDCl₃) 0.98 (6H, t, *J* 6.0, Me), 1.0–2.0 (8H, m, MeCH₂CH₂), 2.9 (4H, t, *J* 5.0, SCH₂) and 7.38 (4H, ABq, *J* 9.6, phenyl H); *m/z* 226 (M⁺ – Bu + 1), 170 (M⁺ – 2Bu + 2), 138 (M⁺ – 2BuS + 2), 57, 45 and 41 (Found: C, 59.85; H, 7.85; N, 9.65. C₁₄H₂₂N₂O₂S requires C, 59.55; H, 7.8; N, 9.95%).

2,2,2-Trifluoroacetanilide derivatives **7a**, **7b** and **7c** were synthesized by reactions of trifluoroacetic anhydride with **6a**, **6b** and **6c**, respectively, and identified by the following data.

2,2,2-Trifluoroacetanilide 7a. The white crystalline compound had mp 87–88 °C (lit.,¹¹ 87.6 °C); δ_{H} (CDCl₃) 6.9–7.7 (5H, m, phenyl H) and 7.9–8.6 (1H, br, NH); *m/z* 189 (M⁺), 120 (M⁺ – CF₃), 92 (M⁺ – CF₃C=O), 77 (Ph⁺), 65 and 51 (Found: C, 50.55; H, 3.2; N, 7.5. Calc. for C₈H₆F₃NO: C, 50.8; H, 3.2; N, 7.4%).

2,2,2-Trifluoro-4'-nitroacetanilide 7b. The white crystalline compound had mp 139–140 °C; ν_{max} (nujol)/cm⁻¹ 3285 (NH), 1740 (C=O), 1695, 1618, 1565 (N=O), 1500, 1338 (N=O), 1288, 1253, 1203, 1148 (C–F), 1118, 903, 862 (C–NO₂), 828 (*para*-substituted phenyl), 755, 739, 693, 670, 655 and 502; δ_{H} (CDCl₃–[²H₆]dimethyl sulfoxide) 5.6 (4H, ABq, *J* 9.0, phenyl H) and 8.3–8.8 (1H, br, NH); *m/z* 234 (M⁺), 218, 204, 188, 168, 165 (M⁺ – CF₃), 140, 134, 119, 109, 91, 69, 64 and 40 (Found: C, 41.3; H, 2.25; N, 11.95. Calc. for C₈H₅F₃N₂O₃: C, 41.05; H, 2.15; N, 11.95%).

2,2,2-Trifluoro-4'-methylacetanilide 7c. The white crystalline product had mp 102–102.5 °C; ν_{max} (nujol)/cm⁻¹ 3280 (NH), 1700 (C=O), 1613, 1553, 1512, 1415, 1357, 1308, 1273, 1243, 1202, 1160 (C–F), 1132, 945, 820 (*para*-substituted phenyl), 728, 710 and 505; δ_{H} (CDCl₃) 2.3 (3H, s, Me), 7.26 (4H, ABq, *J* 9.0, phenyl H) and 7.6–8.4 (1H, br, NH); *m/z* 203 (M⁺), 184 (M⁺ – CF₃), 156 (M⁺ – CF₃C=O), 134, 106, 91, 65 and 40 (Found: C, 53.4; H, 3.8; N, 6.85. Calc. for C₉H₈F₃NO: C, 53.2; H, 3.95; N, 6.9%).

Reactions of *S,S*-dimethylanilinosulfonium salt **3a** in TFA

The reaction of **3a** in TFA was carried out with a variety of acids as shown in Table 1. After the reaction, aq. Na₂CO₃ was added until the solution reached pH > 7. The organic layer was extracted with CH₂Cl₂ and the yields were determined by GLC analysis. The products were isolated by thin layer chromatography using silica gel (Merk 60F254) after column chromatography (Fujisiriaru Chem. BW-127ZH). The structures of the products **6a**, **7a** and **8a** were characterised by comparison of their mass spectra and retention times of GLC-MS with those of authentic samples; we have already described the characterisation of the structure of **8a**.² The effect of the counter ion is summarised in Table 1.

The effect of solvent-nucleophilicity was investigated by variation of solvent as shown in Table 2. The procedures used for isolation and characterisation of the products and the determination of their yields are indicated above.

The reaction of **3a** (5.0 mmol) was carried out in a mixture of TFA (7.5 cm³) and benzene (17.5 cm³) for 2 h at 25 °C or under reflux. The reaction mixture was treated as described above. According to the GLC analysis, diphenylamine and 2- and 4-aminobiphenyl were not detected, but **6a** and **7a** were formed in 12% and trace or 25 and 46% yields for the reaction at 25 °C or under reflux, respectively.

Reactions of *S,S*-dialkylanilinosulfonium salts **3b–d** in TFA

The detailed reaction conditions and the results are indicated in Table 3. Isolation of the products **6b**, **6c**, **7b** and **7c** was carried out as shown above. The products **9a** and **9d** were identified by comparison of GC-MS and IR spectra with authentic specimens. The reaction mixtures showed no peaks except those of **6**, **7** and **9** for the GLC analysis, and thus we thought that **8b** and **8c** were not formed in the reactions.

Rate constants and activation parameters for decomposition of *S,S*-dialkylanilinosulfonium salts **3b–d** in TFA

S,S-Dimethyl-*N*-(4-nitrophenyl)imino- λ^4 -sulfane (precursor of **3b**), or *S,S*-di-*n*-butyl-*N*-(4-nitrophenyl)imino- λ^4 -sulfane (precursor of **3d**), 0.5 mmol, was dissolved in TFA (5.0 cm³). The solution was allowed to stand for various times (1, 3 and 5 h) at a given temperature. *S,S*-Dimethyl-*N*-(4-methylanilino)-sulfonium picrate (precursor of **3c**), 0.5 mmol, was dissolved in 27, 22 and 6.0 cm³ of TFA at 20, 30 and 50 °C, respectively, and allowed to stand for various times; 1, 2 and 4 h at 20 °C, 0.5, 1 and 2 h at 30 °C and 0.5, 0.75 and 1 h at 50 °C. After the reaction mixture was treated as shown above, the first-order rate constants k_{obs} of decomposition of **3b–d** at a given temperature were obtained by determination of the amount of **3b–d** as a function of time, and are shown in Table 4. In this case, the molar amount of **3** was obtained by deducting the total molar amount of the products **6** and **7** from the molar quantity of the precursor of **3**. The total molar amount of the products was measured by GLC analysis.

Activation parameters ΔH^\ddagger , ΔS^\ddagger and ΔG^\ddagger were calculated from the equation derived from transition state theory, and are shown in Table 4.

References

- 1 H. Takeuchi, S. Hirayama, M. Mitani and K. Koyama, *J. Chem. Soc., Perkin Trans. 1*, 1988, 521.
- 2 H. Takeuchi, K. Itou, H. Murai and K. Koyama, *J. Chem. Res. (S)*, 1991, 347; H. Takeuchi, K. Itou, H. Murai and K. Koyama, *J. Chem. Res. (M)*, 1991, 3156.
- 3 H. Takeuchi and K. Koyama, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2277.
- 4 N. S. Isaacs, *Reactive Intermediates in Organic Chemistry*, Wiley, London, New York, Sydney and Toronto, ch. 2, p. 106.
- 5 H. Takeuchi, K. Takano and K. Koyama, *J. Chem. Soc., Chem. Commun.*, 1982, 1254; H. Takeuchi and K. Takano, *J. Chem. Soc., Perkin Trans. 1*, 1986, 611.
- 6 H. Takeuchi, S. Hayakawa and H. Murai, *J. Chem. Soc., Chem. Commun.*, 1988, 1287; H. Takeuchi, S. Hayakawa, T. Tanahashi, A. Kobayashi, T. Adachi and D. Higuchi, *J. Chem. Soc., Perkin Trans. 2*, 1991, 847; H. Takeuchi, D. Higuchi and T. Adachi, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1525.
- 7 H. Takeuchi, T. Yanase, K. Itou, H. Oya and T. Adachi, *J. Chem. Soc., Chem. Commun.*, 1992, 916; H. Takeuchi, H. Oya, T. Yanase, K. Itou, T. Adachi, H. Sugiura and N. Hayashi, *J. Chem. Soc., Perkin Trans. 2*, 1994, 827.
- 8 G. T. Morgan and L. P. Walls, *J. Soc. Chem. Ind. London Trans. Commun.*, 1930, **49**, 15.
- 9 K. Orito, T. Hatakeyama, M. Takeo and H. Sugimoto, *Synthesis*, 1995, 1357.
- 10 A. K. Sharama, T. Ku, A. D. Dawson and D. Swern, *J. Org. Chem.*, 1975, **40**, 2758.
- 11 F. Swarts, *Bull. Sci. Acad. R. Belg.*, 1922, **8**, 343.

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