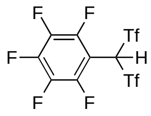
Polystyrene-Bound Tetrafluorophenylbis(triflyl)methane as an Organic-Solvent-Swellable and Strong Brønsted Acid Catalyst**

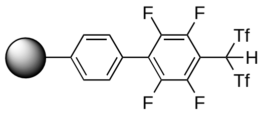
Kazuaki Ishihara, Aiko Hasegawa, and Hisashi Yamamoto*

Perfluororesinsulfonic acids such as Nafion are highly acidic solid catalysts, and they are superior to conventional resinsulfonic acids such as Dowex-50, Amberlite IR-112, and Permutit-Q with regard to catalytic activity, thermal stability, and chemical resistance.[1, 2] However, like inorganic solid acids such as zeolites, they are not effectively swollen by most aprotic organic solvents.[3] A resin-bound superacidic Brønsted acid that is effectively swollen by such solvents may offer several advantages over Nafion, including a broader range of applications, improved yields, improved selectivity, and milder reaction conditions.

The trifluoromethanesulfonyl (triflyl, Tf) group is one of the strongest neutral electron-withdrawing groups.[4] In particular, it greatly increases the acidity of α-hydrogen atoms.[5–7] For example, phenylbis(triflyl)methane (**1**, $pK_a = 7.83$ in MeCN)[6] is a strong nonoxidizing acid. The steric and electronic effects of the aromatic ring in arylbis(triflyl)-methanes are expected to greatly influence their Brønsted acidity and their catalytic activity and selectivity for organic reactions. We report here on concise syntheses of the new strong organic Brønsted acids pentafluorophenylbis(triflyl)-methane (**2**) and polystyrene-bound tetrafluorophenylbis(triflyl)methane (**3**) and their catalytic applications in organic synthesis.

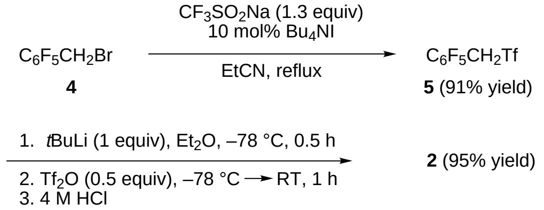


2



3

The synthetic strategy for **2** involves the preparation of 2,3,4,5,6-pentafluorobenzyltriflone (**5**) by nucleophilic substitution of 2,3,4,5,6-pentafluorobenzyl bromide (**4**) with sodium trifluoromethanesulfinate and subsequent reaction of **5** with triflic anhydride [Eq. (1)].[8, 9] The first step was accomplished in 91 % yield by a slight modification of the method described by Hendrickson et al.[4] The second step was achieved by successive addition of *t*BuLi (1 equiv) and triflic anhydride (0.5 equiv) to a solution of **5**. Thus, **2** was obtained in 95 % yield based on triflic anhydride, and **5** was recovered in ca. 50 % yield. When *t*BuLi (2 equiv) and triflic anhydride (1 equiv) were used with **5**, 4-*tert*-butyl-2,3,5,6-tetrafluorophenylbis(triflyl)methane (**6a**) was obtained instead of **2** as a major product.



$$\underset{\mathbf{4}}{C_6F_5CH_2Br} \xrightarrow[\text{EtCN, reflux}]{\substack{CF_3SO_2Na\text{ (1.3 equiv)}\\ \text{10 mol\% }Bu_4NI}} \underset{\mathbf{5}\text{ (91\% yield)}}{C_6F_5CH_2Tf} \xrightarrow[\substack{\text{2. }Tf_2O\text{ (0.5 equiv), }-78\,^\circ C \rightarrow RT\text{, 1 h}\\ \text{3. 4 M HCl}}]{\text{1. }t\text{BuLi (1 equiv), }Et_2O\text{, }-78\,^\circ C\text{, 0.5 h}} \mathbf{2}\text{ (95\% yield)} \qquad (1)$$

To explore the generality and scope of the nucleophilic *para* substitution of **2**, the reaction was examined with several alkyllithium reagents (Table 1). We confirmed that compound **6** was always produced as a single isomer by *para* substitution by ^1H, ^{13}C, ^{19}F, F-F COSY, and NOE difference NMR spectroscopy, and by single-crystal X-ray analysis on **6c**[10] (Figure 1). The C13–H13 bond in **6c** is almost coplanar with the tetrafluorobenzene ring, and the torsion angle C9-C10-C13-H13 is 6.2°. Furthermore, **6** may prefer an asymmetrical conformation in $CDCl_3$ at room temperature, according to NMR spectroscopic data. These experimental results can be explained by conformational relaxation to avoid steric repulsion between the triflyl groups and the *ortho*-fluoro substituents of the tetrafluorobenzene moiety in **6**.

Table 1. Regiospecific nucleophilic *para* substitution of **2**.

RLi[a]	Conditions	6	Yield [%]
*t*BuLi	– 78 °C, 1 h	**6a**	87
BuLi	– 78 °C, 1 h	**6b**	> 95
PhLi	– 78 °C → RT, 1 d	**6c**	> 95

[a] RLi (3 equiv) was added.

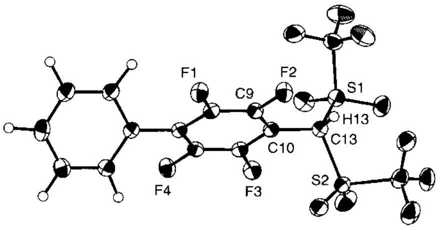


Figure 1. ORTEP plot of **6c**. Ellipsoids are drawn at 26 % probability. Selected distances [Å] and torsion angles [°]: C13-H13 0.993(4), H13 ··· F2 2.2516; C9-C10-C13-H13 6.2(3), C9-C10-C13-S1 – 116.7(4).

To understand the *para* selectivity of the nucleophilic substitution of **2**, we recorded the ^{13}C NMR spectra of **2** and its lithium salt in CD_3OD, and compared the chemical shifts of the reaction sites. The ^{13}C NMR signals of C4 were observed at $\delta = 143.0$.[11] This means that conjugation between the anionic carbon center and the pentafluorobenzene ring is lost. In addition, the next lowest unoccupied molecular orbital (NLUMO) coefficients[12] and charges on the pentafluorophenyl carbon atoms of the lithium salt were estimated by theoretical calculations (RHF/STO-3G) (Figure 2).[13] The

---

[*] Prof. Dr. H. Yamamoto, Assoc. Prof. Dr. K. Ishihara, A. Hasegawa
Graduate School of Engineering, Nagoya University
CREST, Japan Science and Technology Corporation (JST)
Furo-cho, Chikusa, Nagoya 464-8603 (Japan)
Fax: (+81) 52-789-3222
E-mail: yamamoto@cc.nagoya-u.ac.jp

[**] The authors thank Mr. Shoichi Kondo for the single-crystal X-ray analysis. Sodium triflate was generously donated by Central Glass Co., Ltd., Japan. The authors also acknowledge Dr. Yuko Wasada and Dr. Manabu Kubota for their helpful discussions on the theoretical calculations.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

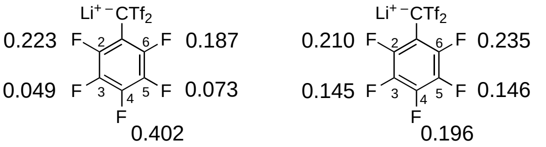


Figure 2. Frontier electron densities (left) and atomic charges (right) of the NLUMO at C2–C5 in the lithium salt of **2**.

frontier electron density of NLUMO and the positive charge at the C4 position are much greater than those at the C3 and C5 positions. Therefore, interception of the electron donation from the anionic carbon atom to the aromatic ring and the steric hindrance of triflyl groups on the *ortho* position cause higher reactivity at the *para* position.[14]

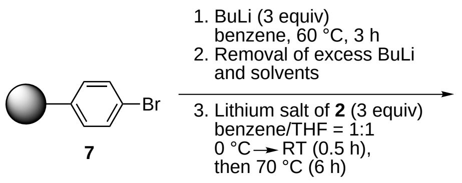
To determine the acid strengths of **2** and **6c**, the ^{1}H NMR signals of their acidic protons were compared, and their pK_a values in glacial acetic acid were measured by the ^{1}H NMR method of Schantl et al. (Table 2).[15] Their ^{1}H NMR signals were observed at a lower field in the order **1**, **2** ≈ **6c**, CHTf$_3$. If the pK_a values shown in Table 2 are valid, **2** is a remarkably strong acid (superacid). In addition, **6c** is still of equal acidity to concentrated sulfuric acid, although the *para* substitution of **2** by phenyllithium lowered the Brønsted acidity.

Table 2. ^{1}H NMR signals and pK_a for R_nCHTf_{3-n} ($n = 0, 1$; R = H, aryl).

	CH_2Tf_2	**1**	H_2SO_4	**6c**	**2**	$CHTf_3$
δ^1H[a]	4.98	5.97	–	6.31	6.21	7.21
pK_a in AcOH[b]	13	12.5	7.5 (7.0)[c]	7.5	1.5	–

[a] ^{1}H NMR chemical shift for the acidic proton of R_nCHTf_{3-n} in CDCl$_3$. [b] See ref. [15]. [c] Literature data.[15]

Our goal was to develop a highly acidic heterogeneous catalyst that can be effectively swollen by organic solvents. Polystyrene, 1 or 2% cross-linked with divinylbenzene (DVB), is fully swollen by aprotic solvents such as aromatic solvents, chlorinated hydrocarbons, dioxane, and THF.[16] We envisioned that the nucleophilic *para* substitution of **2** with an alkyllithium could be adapted to prepare polystyrene-bound tetrafluorophenylbis(triflyl)methane **3** [Eq. (2)]. Three equivalents of the lithium salt of **2** were added to lithiated polystyrene beads,[16a] prepared from commercially available poly(4-bromostyrene) (**7**; 2.71 mmol Br g^{-1} resin, 2% DVB cross-linker, 200–400 mesh[17]) in situ, and the reaction mixture was heated at 70 °C. After treatment with 4 M HCl, **3** was obtained as a brownish resin. The loading of **2** on the resin was estimated to be 1.01 mmol of Tf$_2$CHC$_6$F$_4$ units per gram of resin, based on fluorine content (elemental analysis).



(2)

The catalytic activities of Brønsted acids **2** and **3** were first tested in the acylation of alcohols with carboxylic anhydrides, which is known to be catalyzed by Lewis acids (Table 3).[18] As expected, **3** exhibited an extremely high catalytic activity for the acetylation of (−)-menthol with acetic anhydride: the reaction was complete within 1 h in the presence of **3** (0.1 mol% Tf$_2$CH units, entry 1). Benzoic anhydride is much less reactive than acetic anhydride.[18] Nevertheless, the benzoylation reaction proceeded quantitatively in the presence of **3** (6 mol% Tf$_2$CH units, entry 5). Moreover, **2** and **6c** were more active than **3** for the benzoylation (entries 2 and 3 vs entry 4). Surprisingly, Nafion-H/silica nanocomposite (Nafion SAC-13[19]), which has a 10^4-fold higher surface area than Nafion-H beads (Nafion NR50),[19] was inert in the benzoylation (entry 6).

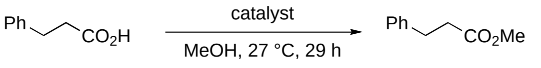
Table 3. Acetylation of (−)-menthol with carboxylic anhydrides (1.5 equiv).

Entry	Catalyst [mol% Tf$_2$CH units]	(RCO)$_2$O[a]	t [h]	Yield [%]
1	**3** (0.1)	Ac$_2$O	< 1	> 99
2	**2** (3)	Bz$_2$O	< 1	> 99
3	**6c** (3)	Bz$_2$O	< 1	> 99
4	**3** (3)	Bz$_2$O	4	71
5	**3** (6)	Bz$_2$O	17	> 99
6	Nafion SAC-13[b]	Bz$_2$O	17	0

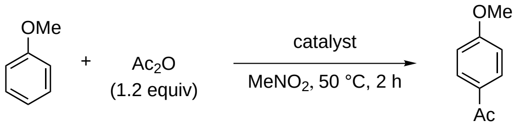
[a] Ac = acetyl, Bz = benzoyl. [b] Nafion SAC-13 (60 g mol^{-1}) was used.

To demonstrate the usefulness and effectiveness of **3**, its catalytic activities in several important synthetic reactions were compared with those of Nafion SAC-13 (Equations (3)–(7) and Table 4). Catalyst **3** was highly active and reusable for all of the reactions examined: direct esterification [Eq. (3)],[1] Friedel–Crafts acylation [Eq. (4)],[1] acetalization [Eq. (5)],[1] the Mukaiyama aldol reaction [Eq. (6)], and Sakurai–Hosomi allylation [Eq. (7)]. The catalytic activity of **3** in the reactions examined was superior to that of Nafion, which may be the strongest Brønsted acid among the known solid acids.

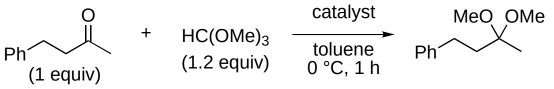
The polymer catalyst **3** was quantitatively recovered by simple filtration and could be reused.[20] For example, **3**



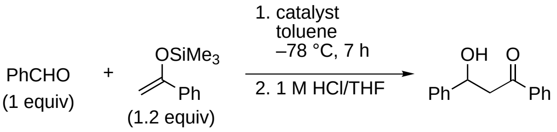
(3)



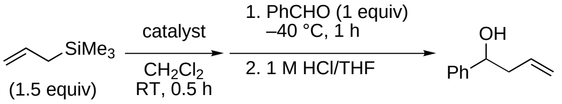
(4)



(5)



(6)



(7)

Table 4. Comparison of catalytic activities of **3** and Nafion SAC-13.

Reaction	**3** [g mol^{-1} (mol% Tf$_2$CH)]	Yield [%]	Nafion SAC-13 [g mol^{-1}]	Yield [%]
Eq. (3)	10 (1)	94	10	39
Eq. (4)	30 (3)	> 99	–	–
Eq. (4)	10 (1)	54	10	25
Eq. (5)	5 (0.5)	> 99	5	16
Eq. (6)	30 (3)	> 99	30	> 99
Eq. (7)	30 (3)	89	30	2

(0.1 mol% Tf$_2$CH units) was reused for acetalization [Eq. (5)] more than ten times, and no loss of activity was observed for the recovered catalyst.[21] This means that the turnover number (TON) is greater than 10000 and the turnover frequency (TOF) exceeds 1000 h^{-1}.

In conclusion, a practical method for preparing a novel carbon Brønsted superacid **2** was developed and a resin-bound strong Brønsted acid **3** was obtained by *para* substitution of the lithium salt of **2** with lithiated polystyrenes. To the best of our knowledge, this is the first example of a highly acidic heterogeneous Brønsted acid catalyst that is effectively swollen by nonpolar organic solvents, and its catalytic activity is superior to that of Nafion SAC-13. Such superacids could make a major contribution to green chemistry.

Received: June 7, 2001 [Z17241]

---

[1] G. A. Olah, P. S. Iyer, G. K. S. Prakash, *Synthesis* **1986**, 513.

[2] a) S. Kobayashi, S. Nagayama, *J. Org. Chem.* **1996**, *61*, 2256; b) S. Nagayama, S. Kobayashi, *Angew. Chem.* **2000**, *112*, 578; *Angew. Chem. Int. Ed.* **2000**, *39*, 567, and references therein; c) S. Murata, R. Noyari, *Tetrahedron Lett.* **1980**, *21*, 767.

[3] A. Corma, *Chem. Rev.* **1995**, *95*, 559.

[4] a) J. B. Hendrickson, A. Giga, J. Wareing, *J. Am. Chem. Soc.* **1974**, *96*, 2275; b) R. Goumont, N. Faucher, G. Moutiers, M. Tordeux, C. Wakselman, *Synthesis* **1997**, 691; c) F. Eugene, B. Langlois, E. Laurent, *J. Fluorine Chem.* **1994**, *66*, 301.

[5] A. R. Siedle, R. A. Newmark, L. H. Pignolet, R. D. Howells, *J. Am. Chem. Soc.* **1984**, *106*, 1510.

[6] I. Leito, I. Kaljurand, I. A. Koppel, L. M. Yagupolskii, V. M. Vlasov, *J. Org. Chem.* **1998**, *63*, 7868.

[7] I. A. Koppel, R. W. Taft, F. Anvia, S.-Z. Zhu, L.-Q. Hu, K.-S. Sung, D. D. DesMarteau, L. M. Yagupolskii, Y. L. Yagupolskii, N. V. Ignat'ev, N. V. Kondratenko, A. Y. Volkonskii, V. M. Vlasov, R. Notario, P.-C. Maria, *J. Am. Chem. Soc.* **1994**, *116*, 3047.

[8] To the best of our knowledge, there are only two reported methods for the synthesis of **1**:[9] the reaction of benzylmagnesium chloride with triflyl fluoride and the photochemical reaction of phenyliodonium bis(triflyl) methide with benzene give **1** in yields of 40 and 61%, respectively.[9a,b] The former method requires gaseous triflyl fluoride (b.p. −21 °C), which is not commercially available, as an electrophilic triflyl source, while the latter requires a large amount of benzene as solvent, and upon photochemical reaction with arenes bearing electron-withdrawing groups such as fluorobenzene, no corresponding arylbis(triflyl)methanes are formed.

[9] a) R. J. Koshar, R. A. Mitsch, *J. Org. Chem.* **1973**, *38*, 3358; b) S.-Z. Zhu, *Heteroat. Chem.* **1994**, *5*, 9; c) S.-Z. Zhu, *J. Fluorine Chem.* **1993**, *64*, 47; d) According to Zhu,[9c] **1a** can be prepared in 73% yield by the pyrolysis of benzenediazonium bis(triflyl)methide. However, we obtained the *O*-phenylation product PhO(CF$_3$)S(O)=CHTf in 71% yield instead of **1a** by following his procedure. K. Ishihara, A. Hasegawa, H. Yamamoto, *J. Fluorine Chem.* **2000**, *106*, 139.

[10] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-165028 (**6c**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[11] In contrast, the ^{13}C NMR signal ($\delta = 104.7$) for C4 of BnLi was observed at lower field than that of toluene ($\delta = 126.1$). G. Vanermen, S. Toppet, M. Van Beylen, P. Geerlings, *J. Chem. Soc. Perkin Trans. 2* **1986**, 707.

[12] The frontier electron density was calculated to be twice the square of the coefficient of the NLUMO. Analysis of the orbitals reveals that the LUMO mainly participates in the unoccupied 2s orbital of the lithium atom.

[13] Geometry optimizations were performed with Gaussian98 (Revision A.5), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.

[14] The nucleophilic substitution reaction of pentafluorobenzenes C$_6$F$_5$X with weakly deactivating, nonactivating, and activating X (H, Me, CH(C$_6$F$_5$)$_2$, halogens, CF$_3$, etc.) is *para*-selective, while the reaction of compounds with strongly deactivating X (O$^-$, NH$_2$, etc.) is *meta*-selective. L. S. Kobrina, *Fluorine Chem. Rev.* **1974**, *7*, 1.

[15] B. M. Rode, A. Engelbrecht, J. Z. Schantl, *J. Prakt. Chem. (Leipzig)* **1973**, *253*, 17.

[16] a) M. J. Farrall, J. M. Fréchet, *J. Org. Chem.* **1976**, *41*, 3877; b) R. Santini, M. C. Griffith, M. Qi, *Tetrahedron Lett.* **1998**, *39*, 8951.

[17] Purchased from Tokyo Kasei Kogyo Co., Ltd.

[18] K. Ishihara, M. Kubota, H. Yamamoto, *Synlett* **1996**, 265.

[19] Purchased from Aldrich. B. Török, I. Kiricsi, A. Molnár, G. A. Olah, *J. Catal.* **2000**, *193*, 132.

[20] The aromatic polymer backbone of **3**, which was prepared by nucleophilic substitution at the active surface of **7**, was inert to electrophilic attack.

[21] Reaction conditions: **3** (0.1 mol%), benzylacetone (1 equiv), trimethyl orthoformate (1.2 equiv), toluene, 0 °C, 1–2 h. After the reaction, the solution was decanted and the residual catalyst **3** was reused without drying.