doi:10.1246/cl.121273

Synthesis of Substituted Sumanenes by Aromatic Electrophilic Substitution Reactions

Binod Babu Shrestha,[1] Sangita Karanjit,[1] Gautam Panda,[2] Shuhei Higashibayashi,*[1,2,3] and Hidehiro Sakurai*[1,2]
[1]*Department of Functional Molecular Science, School of Physical Sciences, The Graduate University for Advanced Studies, Myodaiji, Okazaki, Aichi 444-8787*
[2]*Research Center for Molecular Scale Nanoscience, Institute for Molecular Science, Myodaiji, Okazaki, Aichi 444-8787*
[3]*Japan Science and Technology Agency, ACT–C, 4-1-8 Honcho, Kawaguchi, Saitama 332-0012*

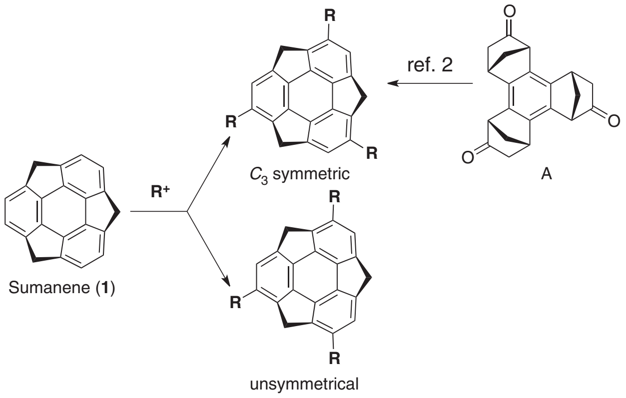
(Received December 26, 2012; CL-121273; E-mail: higashi@ims.ac.jp, hsakurai@ims.ac.jp)

Electrophilic substitution reactions of sumanene were studied. Mono-, di-, and trisubstituted sumanenes were selectively prepared with the separation of all regioisomers. The regioselectivity was predicted well by the HOMO density values determined by DFT calculations.

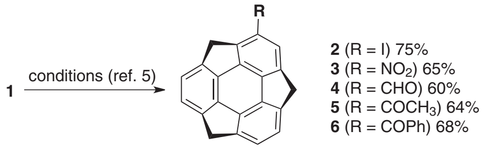
The regioselective synthesis of aromatic compounds, including sumanene derivatives, is very important in order to explore their physical properties.[1] For example, two sumanene derivatives trisubstituted at the benzene rings, C_3 symmetric and unsymmetrical, are possible if *ortho*-substituted derivatives are excluded. Previously, we developed the functionalization of C_3 symmetric derivatives from precursor A (Scheme 1).[2] However, direct preparation of both isomers from sumanene (**1**)[3] is also beneficial if these isomers can be easily separated or one isomer can be selectively obtained. A more complicated situation is encountered in the case of disubstituted sumanene synthesis; three possible isomers may be produced (Table 1).

Electrophilic aromatic substitution (S_EAr) is one of the most reliable methods for the direct functionalization of aromatic compounds. However, due to the lack of regioselectivity and the difficulty in separation of the regioisomers, the S_EAr route has rarely been applied to sumanene derivatization.[4] The purpose of this study involves the development of regioselective electrophilic substitution reactions of sumanene, and prediction of their regioselectivity by DFT calculations.

Selective syntheses of monosubstituted sumanenes were first investigated as summarized in Scheme 2.[5] Iodosumanene (**2**) was selectively prepared in 75% yield by $AuCl_3$-catalyzed iodination[6] with *N*-iodosuccinimide (NIS) with recovery of **1**. Nitrosumanene (**3**) was obtained in 65% yield by nitration using trifluoroacetyl nitrate, generated in situ from trifluoroacetic anhydride and concd nitric acid.[7] **1** was completely consumed and dinitrosumanenes were not formed. However, some amount of degradation was observed due to the harsh conditions. Formylation was achieved using triflic anhydride and DMF[8] under microwave-assisted heating conditions to afford formylsumanene (**4**) in 60% yield. Because of the low reactivity of the reagent, high temperature (130 °C) was required to complete the reaction. Although diformylsumanenes were also formed in 20% yield with **4**, these compounds were easily separated from **4** by preparative thin layer chromatography (PTLC). Acetylation was achieved by adopting similar conditions as the formylation in the presence of DMA to afford acetylsumanene (**5**) in 64% yield and diacetylsumanenes in 10% yield. Benzoylsumanene (**6**) was also prepared in 68% yield using triflic acid and PhCOCl with complete consumption of **1**.[9] They were easily purified by PTLC as well.

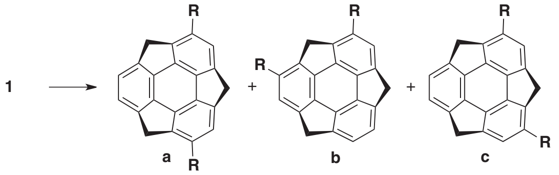


Scheme 1.



Scheme 2.[5]

Table 1. Synthesis of disubstituted sumanenes



Compounds	Isolated yield/%		
	a	b	c
7 (R = I)	30	15	23
8 ($R = NO_2$)	0	27	30
9 (R = CHO)	<1	20	25
10 ($R = COCH_3$)	5	10	25
11 (R = COPh)	0	26	41

The thus-employed reaction conditions were further applied to the syntheses of disubstituted sumanenes (Table 1).[10] Preparation of diiodosumanenes **7**, dinitrosumanenes **8**, diformylsumanenes **9**, diacetylsumanenes **10**, and dibenzoylsumanenes **11** were achieved by increasing the amount of reagents. Diiodination of **1** afforded a mixture of three regioisomers, which were successfully separated by gel permeation chromatography (GPC) to give **7a** (30%), **7b** (15%), and **7c** (23%).[11] Isomer

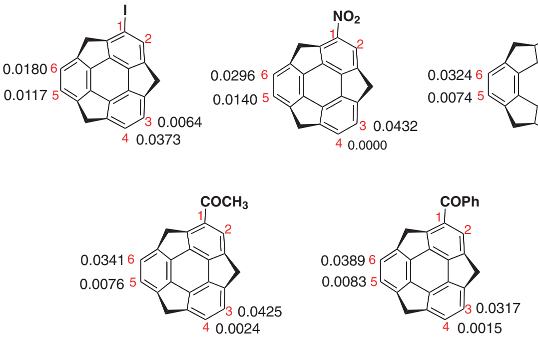


Figure 1.

7a was the major product in the case of iodination. In contrast, nitration, formylation, acetylation, and benzoylation showed different regioselectivities from that of iodination. Dinitrosumanenes **8b** (27%), **8c** (30%), diformylsumanenes **9b** (20%), **9c** (25%), diacetylsumanenes **10a** (5%), **10b** (10%), **10c** (25%), and dibenzoylsumanenes **11b** (26%), **11c** (41%) were formed with similar ratios of regioisomers.[11] It should be pointed out that these regioisomers of **8**–**11** were easily separated by PTLC.

Predictability of the regioselectivity is the key issue in designing the reaction. Since different regioselectivities were observed between iodination and other functionalizations, we conducted DFT calculations [B3LYP/6-31G(d,p)] for monosubstituted sumanenes to determine Fukui function,[12,13] HOMO density,[12,14] and spin density[12] as shown in Table S6 (Supporting Information).[20] Among the calculated parameters, the HOMO density of monosubstituted sumanenes (Figure 1) is consistent with the observed regioselectivity to give disubstituted sumanenes. In contrast, Fukui function and spin density are not consistent with the observed regioselectivities. This may be due to soft nature of bowl-shaped polyaromatic hydrocarbon. In this case, orbital contribution (HOMO density) predominated over charge contribution (Fukui function).[13b]

Single crystals of **7b** and **10b** for X-ray crystallographic analysis were obtained by crystallization from $CHCl_3$ and THF, respectively.[15] Their packing structures are shown in Figure 2. The bowl depth of **7b** is 1.18 Å, which is deeper than those of sumanene (1.11 Å)[16] and trimethylsumanene (1.11 Å).[2c] In contrast, **10b** shows a more shallow bowl depth (1.10 Å). The packing structure of **7b** adopts a *quasi* convex–convex and concave–concave stacking model, which is similar to that of tris(methylsulfonyl)triazasumanene.[17] At the convex face, the benzylic *exo*-hydrogens and the non-iodinated benzene rings of two molecules are located within the distance (2.88 Å) of CH–π interaction. The benzene rings substituted by iodine are also stacked at a distance of 3.29 Å at the convex face. At the concave face, the iodine atoms face the central benzene ring of the bowl structure at a distance of 3.42 Å. Similar interactions between the oxygen atoms of the sulfonyl groups and the central benzene rings at the concave face are observed in the crystal packing of tris(methylsulfonyl)triazasumanene.[17] These two examples may suggest a lone pair–π interaction between iodine or oxygen and the bowl at the concave face.[18] On the other hand, **10b** adopts a convex–concave stacking model with neighboring columns in opposite directions, which is similar to that of trimethylsumanene.[2c] However, the bowls of **10b** in a column are slipped from side to side, while those of sumanene and trimethylsumanene are not. As a result of the slipping, the convex faces of a central benzene ring and a peripheral benzene ring with an acetyl group stack with the concave faces of peripheral benzene rings with and without acetyl groups with distances of 3.71 and 3.63 Å, respectively.

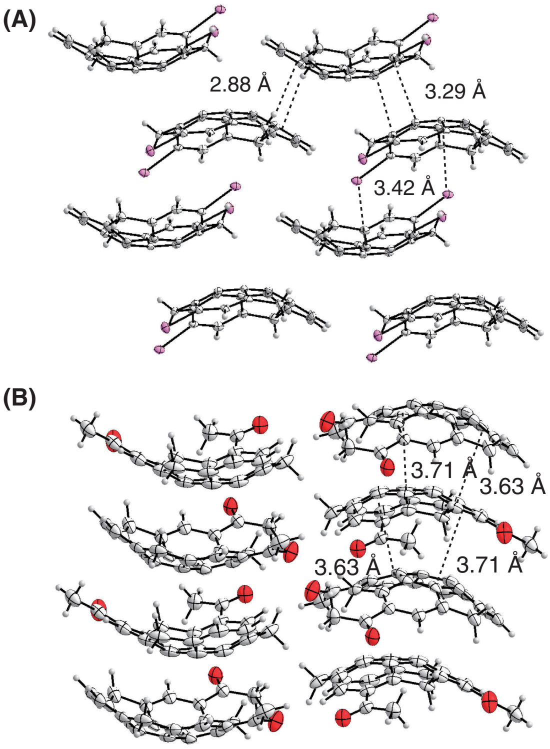
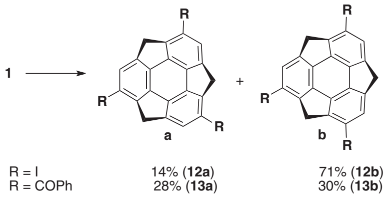
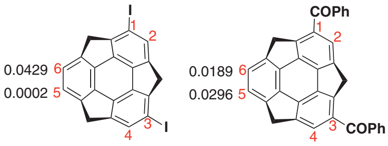


Figure 2. ORTEP drawings of (A) **7b** and (B) **10b** with 50% probability ellipsoids.



Scheme 3.

Finally, syntheses of trisubstituted sumanenes are demonstrated in Scheme 3.[19] Triiodosumanenes **12a** and **12b** were obtained in 14% yield and 71% yield, respectively, after separation by GPC.[11] Unsymmetrical **12b** was formed as the major isomer of iodination. In contrast, tribenzoylation afforded **13a** in 28% yield and **13b** in 30% yield.[11] The regioisomers of **12** and **13** were separable by GPC. As observed in disubstituted sumanenes, different regioselectivities between iodination and benzoylation were observed in trisubstituted sumanenes as well. The regioselectivity is also explained well by the HOMO densities of disubstituted sumanenes (Figure 3). Since diiodosumanenes **7a** and **7b** were converted to only triiodosumanene **12b**, the selectivity of **7c** to **12a** and **12b** was examined. The lower HOMO density of **7c** at C5 (0.0002) compared to C6 (0.0429) leads to less formation of **12a**, which agrees with the



7c **11c**

Figure 3.

experimental results. On the other hand, the higher HOMO density of **11c** at C5 (0.0296) compared to C6 (0.0189) causes greater formation of **13a**. The sum of the conversion from **11b** to **13b** and **11c** to **13a** and **13b** afford the observed fair yield of **13a** and **13b**.

In summary, we have succeeded in the selective preparation of mono-, di-, and trisubstituted sumanenes from sumanene and the separation of regioisomers by employing $\mathrm{S_EAr}$ reactions: iodination, nitration, formylation, acetylation, and benzoylation. The observed regioselectivities for di- and trisubstituted sumanenes were explained well by the HOMO densities calculated by the DFT method. In order to study the physical properties of sumanene derivatives with various substituents, these prepared compounds are useful precursors for further transformation. They could also be potential components for synthesizing three-dimensionally π-conjugated compounds.

This work was funded by MEXT and JST (ACT–C). B. B. S. thanks the Daiko Foundation for financial support. G.P. acknowledges the support from JSPS as a long-term Invitation Fellowship Program from Central Drug Research Institute, India. We thank Ms. Sachiko Nakano for technical contributions.

References and Notes

1 For recent reviews: a) S. Higashibayashi, H. Sakurai, *Chem. Lett.* **2011**, *40*, 122. b) T. Amaya, T. Hirao, *Chem. Commun.* **2011**, *47*, 10524.

2 a) S. Higashibayashi, H. Sakurai, *J. Am. Chem. Soc.* **2008**, *130*, 8592. b) R. Tsuruoka, S. Higashibayashi, T. Ishikawa, S. Toyota, H. Sakurai, *Chem. Lett.* **2010**, *39*, 646. c) S. Higashibayashi, R. B. N. Baig, Y. Morita, H. Sakurai, *Chem. Lett.* **2012**, *41*, 84. d) S. Higashibayashi, R. Tsuruoka, Y. Soujanaya, U. Purushotham, G. N. Sastry, S. Seki, T. Ishikawa, S. Toyota, H. Sakurai, *Bull. Chem. Soc. Jpn.* **2012**, *85*, 450.

3 H. Sakurai, T. Daiko, T. Hirao, *Science* **2003**, *301*, 1878.

4 a) T. Amaya, S. Seki, T. Moriuchi, K. Nakamoto, T. Nakata, H. Sakane, A. Saeki, S. Tagawa, T. Hirao, *J. Am. Chem. Soc.* **2009**, *131*, 408. b) T. Amaya, T. Nakata, T. Hirao, *J. Am. Chem. Soc.* **2009**, *131*, 10810.

5 Conditions (for monosubstitution): R = I, $\mathrm{AuCl_3}$ (10 mol %), NIS (120 mol %), $\mathrm{CH_2ClCH_2Cl}$, rt, 22 h; R = $\mathrm{NO_2}$, $\mathrm{(CF_3CO)_2O}$ (200 mol %), 60% $\mathrm{HNO_3}$ (200 mol %), $\mathrm{CH_2Cl_2}$, −10 °C, 0.5 h; R = CHO, $\mathrm{(CF_3SO_2)_2O}$ (1000 mol %), DMF (1000 mol %), $\mathrm{CH_2ClCH_2Cl}$, Microwave, 130 °C, 3 h; R = $\mathrm{COCH_3}$, $\mathrm{(CF_3SO_2)_2O}$ (500 mol %), DMA (500 mol %), $\mathrm{CH_2ClCH_2Cl}$, Microwave, 130 °C, 3 h; R = COPh, $\mathrm{CF_3SO_3H}$ (500 mol %), PhCOCl (250 mol %), $\mathrm{CH_2ClCH_2Cl}$, −40 °C, 0.5 h, 80 °C, 1 h.

6 a) F. Mo, J. M. Yan, D. Qiu, F. Li, Y. Zhang, J. Wang, *Angew. Chem., Int. Ed.* **2010**, *49*, 2028. b) B. Topolinski, B. M. Schmidt, M. Kathan, S. I. Troyanov, D. Lentz, *Chem. Commun.* **2012**, *48*, 6298.

7 K. Smith, T. Gibbins, R. W. Millar, R. P. Claridge, *J. Chem. Soc., Perkin Trans. 1* **2000**, 2753.

8 A. G. Martínez, R. M. Alvarez, J. O. Barcina, S. de la Moya Cerero, E. T. Vilar, A. G. Fraile, M. Hanack, L. R. Subramanian, *J. Chem. Soc., Chem. Commun.* **1990**, 1571.

9 F. Effenberger, J. K. Eberhard, A. H. Maier, *J. Am. Chem. Soc.* **1996**, *118*, 12572.

10 Conditions (for disubstitution): R = I, $\mathrm{AuCl_3}$ (30 mol %), NIS (300 mol %), $\mathrm{CH_2ClCH_2Cl}$, rt, 1 h; R = $\mathrm{NO_2}$, $\mathrm{(CF_3CO)_2O}$ (500 mol %), 60% $\mathrm{HNO_3}$ (500 mol %), $\mathrm{CH_2Cl_2}$, −10 °C, 1 h, rt, 6 h; R = CHO, $\mathrm{(CF_3SO_2)_2O}$ (5000 mol %), DMF (5000 mol %), $\mathrm{CH_2ClCH_2Cl}$, Microwave, 130 °C, 3 h; R = $\mathrm{COCH_3}$, $\mathrm{(CF_3SO_2)_2O}$ (2500 mol %), DMA (2500 mol %), $\mathrm{CH_2ClCH_2Cl}$, Microwave, 130 °C, 3 h; R = COPh, $\mathrm{CF_3SO_3H}$ (1000 mol %), PhCOCl (500 mol %), $\mathrm{CH_2ClCH_2Cl}$, −40 °C, 0.5 h, 80 °C, 2 h.

11 The regioisomers were assigned by NMR and X-ray analysis. See the Supporting Information for details.[20]

12 a) R. K. Roy, S. Saha, *Annu. Rep. Prog. Chem., Sect. C: Phys. Chem.* **2010**, *106*, 118. b) K. Shopsowitz, F. Lelj, M. J. MacLachlan, *J. Org. Chem.* **2011**, *76*, 1285.

13 a) P. Fuentealba, E. Florez, W. Tiznado, *J. Chem. Theory Comput.* **2010**, *6*, 1470. b) P. Geerlings, F. De Proft, W. Langenaeker, *Chem. Rev.* **2003**, *103*, 1793.

14 a) G. Gayatri, G. N. Sastry, *J. Chem. Sci.* **2005**, *117*, 573. b) M. Gonzalez-Suarez, A. Aizman, J. Soto-Delgado, R. Contreras, *J. Org. Chem.* **2012**, *77*, 90.

15 See Supporting Information for details.[20]

16 a) H. Sakurai, T. Daiko, H. Sakane, T. Amaya, T. Hirao, *J. Am. Chem. Soc.* **2005**, *127*, 11580. b) S. Mebs, M. Weber, P. Luger, B. M. Schmidt, H. Sakurai, S. Higashibayashi, S. Onogi, D. Lentz, *Org. Biomol. Chem.* **2012**, *10*, 2218.

17 Q. Tan, S. Higashibayashi, S. Karanjit, H. Sakurai, *Nat. Commun.* **2012**, *3*, 891.

18 M. Egli, S. Sarkhel, *Acc. Chem. Res.* **2007**, *40*, 197.

19 Conditions (for trisubstitution): R = I, $\mathrm{AuCl_3}$ (30 mol %), NIS (500 mol %), $\mathrm{CH_2ClCH_2Cl}$, rt, 1 h; R = COPh, $\mathrm{CF_3SO_3H}$ (1000 mol %), PhCOCl (1000 mol %), $\mathrm{CH_2ClCH_2Cl}$, −40 °C, 0.5 h, 80 °C, 2 h.

20 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.