JOC Article

New Synthesis, Properties, and Oxidizing Ability of 1,3-Dimethyl-5,10-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4(1,3*H*)-dionylium Tetrafluoroborate

Shin-ichi Naya, Masato Warita, Yuhki Mitsumoto, and Makoto Nitta*

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku,
Tokyo 169-8555, Japan

nitta@waseda.jp

Received August 16, 2004

A novel synthesis of 1,3-dimethyl-5,10-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4(1,3*H*)-dionylium tetrafluoroborate ($\mathbf{10}^+\cdot BF_4^-$) was accomplished by the reaction of 3,8-methano[11]-annulenone with dimethylbarbituric acid and following acidic cyclization, albeit in low yield. Remarkable structural characteristics were suggested on inspection of the spectral data and MO calculation, and it was clarified that the positive charge is largely localized at the C11. The pK_{R+} value of cation $\mathbf{10}^+$ was determined spectrophotometrically to be 4.6, which is much smaller by 4.1 pH unit than that of 1,3-dimethyl-7,12-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4(1,3*H*)-dionylium tetrafluoroborate ($pK_{R+} = 8.7$). This value is also smaller by 1.6 pH unit than that of the parent 1,6-methano[11]annulenylium ion ($pK_{R+} = 6.2$). The feature is rationalized on the basis of the perturbation derived from the bond fixation of the parent cation. The electrochemical reduction of $\mathbf{10}^+$ exhibited less negative reduction potential at −0.39 (V vs Ag/AgNO$_3$) upon cyclic voltammetry (CV). In a search for reactivity, reactions of $\mathbf{10}^+$ with some nucleophiles, hydride and diethylamine, were carried out to give mixtures of C11- and C13-adducts. In both reactions, the methano-bridge controls the nucleophilic attacks to the C13 to favor exo selectivity. The photoinduced autorecycling oxidation reactions of $\mathbf{10}^+\cdot BF_4^-$ toward some amines under aerobic conditions were carried out to give the corresponding imines (isolated by converting to the corresponding 2,4-dinitrophenylhydrazones) in 719−3286% yield (recycling number of $\mathbf{10}^+\cdot BF_4^-$: 7.2−32.9).

Introduction

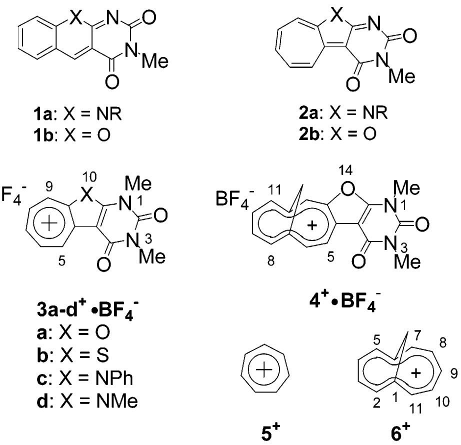


FIGURE 1.

Flavins are known to play an important role as cofactors in a wide variety of biological redox reactions.[1,2] The flavin−redox systems have been investigated extensively through synthetic model systems and theoretical calculations.[3] Among these compounds, 5-deazaflavins **1a** (Figure 1) have been studied extensively in both enzymatic[4] and model systems,[5] in the hope of providing mechanistic insight into flavin-catalyzed reactions. In this context, 5-deaza-10-oxaflavin **1b** (2*H*-chromeno[2,3-*d*]pyrimidin-2,4(3*H*)-dione), in which the nitrogen atom is replaced by an oxygen, has also been synthesized and found to possess a strong ability to oxidize alcohols to the corresponding carbonyl compounds.[6] On the basis of the above observations, we have previously studied

---

* Address correspondence to this author. Phone: +81-(0)3-5286-3236. Fax: +81-(0)3-3208-2735.

(1) Muller, F. *Chemistry and Biochemistry of Flavoenzymes*; Muller, F., Ed.; CRC Press: Boca Raton, FL, 1991; Vol. 1, pp 1−71 and references therein.

(2) Hamilton, G. A. *Progress in Bioorganic Chemistry*; Kaiser, E. T., Kezdy, F. J., Eds.; Wiley: New York, 1971; Vol. 1, p 83.

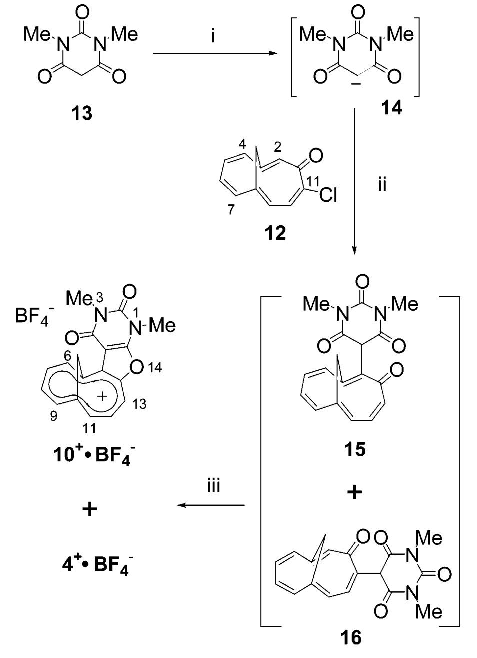
(3) (a) Chiu, C. C.; Pan, K.; Jordan, F. *J. Am. Chem. Soc.* **1995**, *117*, 7027−7028. (b) Kim, J.; Hoegy, S. E.; Mariano, P. S. *J Am. Chem. Soc.* **1995**, *117*, 100−105. (c) Murahashi, S.; Ono, S.; Imada, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 2366−2368. (d) Bergstad, K.; Jonsson, S.; Bächvall, J. *J. Am. Chem. Soc.* **1999**, *121*, 10424−10425. (e) Van Houten, K. A.; Kim, J.; Bogdan, M. A.; Ferri, D. C.; Mariano, P. S. *J. Am. Chem. Soc.* **1998**, *120*, 5864−5872. (f) Zheng, Y.; Ornstein, R. L. *J. Am. Chem. Soc.* **1996**, *118*, 9402−9408. (g) Breinlinger, E. C.; Keenan, C. J.; Rotello, V. M. *J. Am. Chem. Soc.* **1998**, *120*, 8606−8609. (h) Hasford, J. J.; Rizzo, C. J. *J. Am. Chem. Soc.* **1998**, *120*, 2251−2255. (i) Antony, J.; Medvedev, D. M.; Stuchebrukhov, A. A. *J. Am. Chem. Soc.* **2000**, *122*, 1057−1065.

(4) (a) Walsh, C. *Acc. Chem. Res.* **1986**, *19*, 216−221 and references therein. (b) Yoneda, F.; Tanaka, K. *Med. Res. Rev.* **1987**, *4*, 477−506 and references therein.

(5) Yoneda, F.; Kokel, B. *Chemistry and Biochemistry of Flavoenzymes*; Muller, F., Ed.; CRC Press: Boca Raton, FL, 1991; Vol. 1, pp 121−169 and references therein.

10.1021/jo048575s CCC: $27.50

SCHEME 1^a



^{a} Reagents and conditions: (i) base, DMF, rt, 5 min; (ii) 35 °C, 48 or 72 h; (iii) 42% aq HBF_4, Ac_2O, 0 °C, 1 h.

convenient preparations of 10-substituted 3-methylcyclohepta[4,5]pyrro[2,3-*d*]pyrimidin-2,4(3*H*)-diones[7] **2a** and 3-methylcyclohepta[4,5]furo[2,3-*d*]pyrimidin-2,4(3*H*)-dione **2b**,[8] which are the structural isomers of **1a** and **1b**, respectively, and their oxidation reactions toward some alcohols to the corresponding carbonyl compounds. In this relation, the synthesis, properties, and reactivity of **3a**$^+\cdot BF_4^-$,[9,10] and its sulfur and nitrogen analogues **3b**–**d**$^+\cdot BF_4^-$ [11,12] as well as their novel photoinduced autorecycling oxidation reactions toward some alcohols also have been studied. Thus, structural modifications of the uracil-annulated heteroazulenes such as **3a**–**d**$^+\cdot BF_4^-$ are an interesting project from the viewpoint of exploration of novel functions. Much of the motivation for studying the properties of organic molecules stems from manipulation of the primary chemical structure. One strategy for raising or lowering the HOMO and LUMO levels includes conjugation length control. On the basis of this concept, we have recently reported the synthesis of 1,3-dimethyl-7,12-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4-(1,3*H*)-dionylium tetrafluoroborate (**4**$^+\cdot BF_4^-$**,** Scheme 1),[13] which is a vinylogous compound of **3a**, to involve 1,6-methano[11]annulenylium ion **6**$^+$ instead of tropylium ion **5**$^+$. The cation **6**$^+$, which is an aromatic 10π-electron analogue of **5**$^+$, has higher thermodynamic stability (pK_{R+} = 6.2)[14] as compared with **5**$^+$ (pK_{R+} = 3.9).[15] Due to this property, cation **4**$^+\cdot BF_4^-$ exhibited higher thermodynamic stability (pK_{R+} = 8.7). Furthermore, the reactions of **4**$^+\cdot BF_4^-$ with $NaBD_4$ and diethylamine exhibit that the methano-bridge controls the nucleophilic attacks to occur with endo selectivity. Thus, study of the methano-bridged compounds is an interesting project from the viewpoint of exploration of novel chiral auxiliaries.

TABLE 1. Results for the Reactions of 12 with 13

run	base	time/h	yield/%	ratio of **10**$^+$/**4**$^+$
1	Et_3N	48	6	83:17
2	$(TMS)_2NH$	48	trace	90:10
3	$(TMS)_2NK$	72	trace	90:10
4	NaH	48	8	100:0

Furthermore, the π-conjugation mode in polycyclic conjugated π-systems containing more than one $(4n + 2)$ conjugation loop is an important subject from both theoretical and experimental viewpoints. We have recently reported that perturbations derived from benzo-annulation onto the cyclohepta[*a*]azulenylium ion are highly dependent on the annulating positions.[16] From this viewpoint, the 1,6-methano[11]annulenylium ion annulated with the furopyrimidine on a different position from that of **4**$^+\cdot BF_4^-$ seemed to be interesting. Thus, we have investigated the synthesis, properties, and reactivity of 1,3-dimethyl-5,10-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4(1,3*H*)-dionylium tetrafluoroborate (**10**$^+\cdot BF_4^-$, Scheme 1) for the first time. Its structural characteristics are deduced based on the spectral data, pK_{R+}, redox potentials, and MO calculation. The photoinduced autorecycling oxidation of amines to give the corresponding imines is studied as well. We report here the results in detail.

Results and Discussion

Synthesis. A strategy for the preparation of 1,3-dimethyl-5,10-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin-2,4(1,3*H*)-dionylium tetrafluoroborate (**10**$^+\cdot BF_4^-$) consisted of the reaction of 3,8-methano[11]annulenone (**12**)[17] with dimethylbarbituric acid (**13**) and following acidic cyclization. The reaction of **12** with **14**, which is generated by the reaction of **13** with Et_3N, proceeded at the C2 and C11 to give a mixture of **15** and **16**, as in the synthetic reaction of **17** and **18** (Figure 3).[18] Compounds **15** and **16** are unstable on TLC (SiO_2 and Al_2O_3), and thus, without further isolation and purification, cyclization was carried out by using 42% aq HBF_4 to give **10**$^+\cdot BF_4^-$ and **4**$^+\cdot BF_4^-$, respectively (Scheme 1, Table 1 run 1). Under similar conditions, $(TMS)_2NH$- and $(TMS)_2NK$-induced reactions of **12** and **13** afforded trace amounts of mixtures of **10**$^+\cdot BF_4^-$ and **4**$^+\cdot BF_4^-$ (Table 1, runs 2 and 3). In contrast, the NaH-induced reaction of **12** with **13** afforded

---

(6) Yoneda, F.; Hirayama, R.; Yamashita, M. *Chem. Lett.* **1980**, 1157–1160.

(7) Nitta, M.; Tajima, Y. *Synthesis* **2000**, 651–654.

(8) Takayasu, T.; Mizuta, Y.; Nitta, M. *Heterocycles* **2001**, *54*, 601–606.

(9) Naya, S.; Nitta, M. *Tetrahedron* **2003**, *59*, 3709–3718.

(10) Naya, S.; Miyama, H.; Yasu, K.; Takayasu, T.; Nitta, M. *Tetrahedron* **2003**, *59*, 1811–1821.

(11) Naya, S.; Miyama, H.; Yasu, K.; Takayasu, T.; Nitta, M. *Tetrahedron* **2003**, *59*, 4929–4938.

(12) Naya, S.; Nitta, M. *Tetrahedron* **2003**, *59*, 7291–7299.

(13) Naya, S.; Yamaguchi, Y.; Nitta, M. *J. Org. Chem.* **2003**, *68*, 9284–9291.

(14) (a) Grimme, W.; Hoffmann, H.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 354. (b) Vogel, E.; Feldmann, R.; Düwel, H. *Tetrahedron Lett.* **1970**, *1*, 1941.

(15) Okamoto, K.; Takeuchi, K.; Komatsu, K.; Kubota, Y.; Ohara, R.; Arima, M.; Takahashi, K.; Waki Y.; Shirai, S. *Tetrahedron* **1983**, *39*, 4011 and references therein.

(16) Yamane, K.; Yamamoto, H.; Nitta, M. *J. Org. Chem.* **2002**, *67*, 8114–8122.

(17) Vogel, E. *23rd Int. Congr. Pure Appl. Chem.* **1971**, *1*, 275.

(18) Kanomata, N.; Kamae, K.; Iino, Y.; Nitta, M. *J. Org. Chem.* **1992**, *57*, 5313–5318.

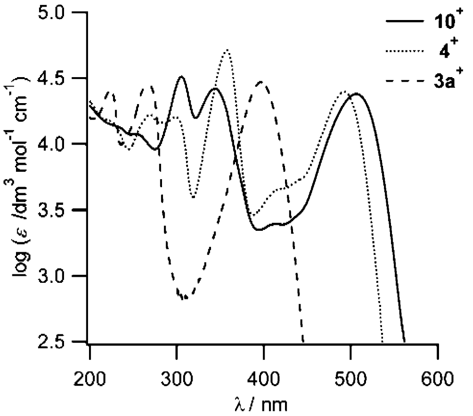


FIGURE 2. UV−vis spectra of **10**$^+$ and reference compounds **3a**$^+$ and **4**$^+$ in CH_3CN.

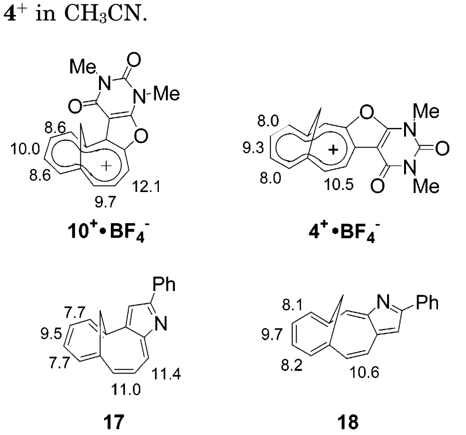


FIGURE 3. Coupling constants (*J*, in Hz) of **10**$^+$·BF_4^-, **4**$^+$·BF_4^-, **17**, and **18**.

TABLE 2. ^{13}C NMR Data and Calculated Charge Density of **10**$^+$

position	δ_c	charge	position	δ_c	charge
C2	150.6	1.106	C10	140.0	0.049
C4	164.9	0.944	C11	157.2	0.121
C4a	101.1	−0.275	C12	130.7	0.058
C4b	151.7	0.061	C13	129.3	0.052
C5	129.4	0.027	C13a	153.7	0.343
C6	139.0	0.157	C14a	158.4	0.895
C7	141.7	0.070	N1Me	31.4	0.392
C8	139.6	0.061	N3Me	29.6	0.379
C9	141.3	0.100	CH_2	31.3	0.044

a single product **15**, which is converted to **10**$^+$·BF_4^- upon treatment with 42% aq HBF_4 in Ac_2O (Table 1, run 4). Unfortunately, the yields are poor, and thus, details of these reactions cannot be discussed at this stage.

Properties. Compound **4**$^+$·BF_4^- is known[13] and compound **10**$^+$·BF_4^- was fully characterized on the basis of the ^{1}H NMR, ^{13}C NMR, IR, UV−vis, and mass spectral data, as well as elemental analysis. The mass spectrum of **10**$^+$·BF_4^- exhibited the correct $M^+ - BF_4^-$ ion peak, which is indicative of the cationic structure of the compound. The characteristic absorption band for the counterion of BF_4^- was observed at 1084 cm^{-1} in the IR spectrum. The UV−vis spectrum of **10**$^+$·BF_4^- in CH_3CN is shown in Figure 2, together with those of **3a**$^+$·BF_4^- and **4**$^+$·BF_4^-. The longest wavelength absorption maximum (λ_{max}) of **10**$^+$·BF_4^- shows a red-shift by 110 nm as compared with that of **3a**$^+$·BF_4^-, suggesting the elongated π-conjugation. In addition, a red-shift (14 nm) of λ_{max} of **10**$^+$·BF_4^- from that of **4**$^+$·BF_4^- shows a larger perturbation due to the annulating position of the furopyrimidine ring. The ^{1}H NMR spectrum of **10**$^+$·BF_4^- is noteworthy, since the chemical shifts of bridged-annulene systems are quite useful in determining such structural properties as diatropicity and bond alternation. Unambiguous proton assignment was made by analyzing ^{1}H NMR, H−H COSY, and NOE spectra and selected coupling constants of the peripheral protons of **10**$^+$·BF_4^- are shown in Figure 3 together with those of the reference compounds **4**$^+$·BF_4^-, **17**,[18] and **18**.[18] The large geminal coupling constant of the methylene protons ($J_{E,Z}$ = 12.4 Hz) supports the absence of a norcaradiene structure for **10**$^+$·BF_4^-. The bridge protons of **10**$^+$·BF_4^- appear at very high field (δ −0.53 and −1.33), and the peripheral protons appear in the aromatic region (δ 8.43 to 10.11), suggesting a large diatropic ring current.[19] The vicinal coupling constants of protons of the aromatic perimeter of **10**$^+$·BF_4^- suggest that the C6−C7−C8−C9 moiety exhibits small bond alternation [$J_{6,7}$ (8.6 Hz), $J_{7,8}$ (10.0 Hz), $J_{8,9}$ (8.6 Hz)]. This feature is similarly observed for compound **4**$^+$·BF_4^-. In contrast, it is noteworthy that the C11−C12−C13 moiety of **10**$^+$·BF_4^- exhibits large bond alternation [$J_{11,12}$ (9.7 Hz) < $J_{12,13}$ (12.5 Hz)]. While the vicinal coupling constants in the cycloheptatriene moiety of **4**$^+$·BF_4^- and **18** are similar, a large difference in the vicinal coupling constants in **10**$^+$·BF_4^- and **17** was observed. The ^{13}C NMR spectral data for **10**$^+$·BF_4^- were fully assigned by using the H−C Cosy spectra (HMQC and HMBC) as summarized in Table 2. Concerning the 11-membered ring, the chemical shift of the C13 carbon appeared at much higher field (δ_c 129.3) as compared with those of other carbons. In addition, the C11 carbon appeared at much lower field (δ_c 157.2) as compared with those of other carbons of the 11-membered ring, suggesting that the positive charge is localized largely at the C11-position. Unfortunately, a single crystal of **10**$^+$·BF_4^- was not obtained by recrystallization from various solvents; however, we have reported that the structural details of **3b**−**d**$^+$ and **4**$^+$ obtained by MO calculation show good agreement with those obtained by X-ray crystal analyses.[9,11−13] Thus, MO calculation of **10**$^+$ was carried out by the 6-31G* basis set of the MP2 levels,[20] and the results are also summarized in Table 2. The calculated charge density of the C11 (+0.121) is relatively large, which accords with the feature of the ^{13}C NMR spectrum. Thus, the canonical structures **10**$^+$**-B** and **10**$^+$**-C** would be important for **10**$^+$ (Figure 4). Furthermore, the calculated bond length of C14a−O14 (1.349 Å) is shorter than that of C13a−O14 (1.395 Å), suggesting that a contribution of **10**$^+$**-D** is less important.

---

[19] Vogel, E. *Chem. Soc. Spec. Publ.* **1967**, *21*, 113.

[20] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.11, Gaussian, Inc.: Pittsburgh, PA, 2001.

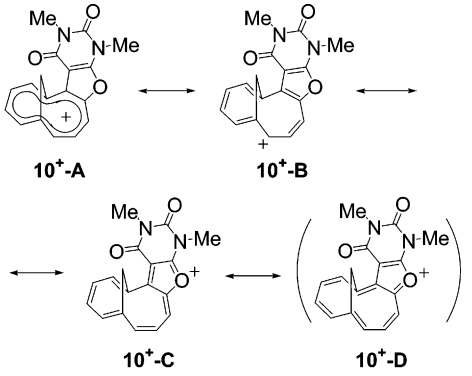


FIGURE 4.

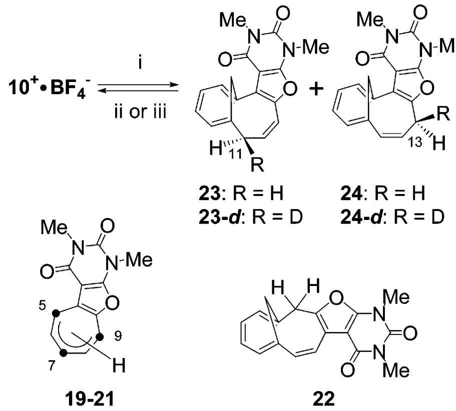
TABLE 3. pK_{R+} Values and Reduction Potentials of Cations 10^+ and Reference Compounds $3a^+$, 4^+, 5^+, and 6^+

compd	pK_{R+}	reduction potential ($E1_{red}$)[b]
10^{+} [a]	4.6	−0.39
$3a^{+}$ [c]	ca. 6.0	−0.58
4^{+} [d]	8.7	−0.43
5^{+} [e]	3.9	−0.51
6^{+} [f]	6.2	−0.42[g]

[a] Salts $10^+{\cdot}BF_4^-$ are used for the measurement. [b] V vs Ag/AgNO$_3$; cathodic peak potential. [c] Reference 10. [d] Reference 13. [e] Reference 15. [f] Reference 14. [g] This work.

The affinity of the carbocation toward hydroxide ions expressed by the pK_{R+} value is the most common criterion of carbocation stability.[21] The pK_{R+} values of cation $\mathbf{10}^+$ were determined spectrophotometrically in buffer solutions prepared in 50% aqueous CH$_3$CN and are summarized in Table 3, along with those of the reference compounds $\mathbf{3a}^+$,[9] $\mathbf{4}^+$,[13] $\mathbf{5}^+$,[15] and $\mathbf{6}^+$.[14] The pK_{R+} value of $\mathbf{10}^+$ was determined to be 4.6, which is smaller by 4.1 pH unit than that of $\mathbf{4}^+$ ($pK_{R+} = 8.7$). In the reference compounds $\mathbf{3a}^+$ and $\mathbf{4}^+$, the annulation of the electron-donating furopyrimidine ring stabilizes the parent cations $\mathbf{5}^+$ and $\mathbf{6}^+$, respectively. In contrast, the pK_{R+} value of $\mathbf{10}^+$ is smaller by 1.6 pH unit than that of $\mathbf{6}^+$ ($pK_{R+} = 6.2$), and thus, on the cation $\mathbf{10}^+$, the annulation of the furopyrimidine ring destabilizes the parent cation $\mathbf{6}^+$. The fact is quite different from those of $\mathbf{3a}^+$ and $\mathbf{4}^+$. The feature is rationalized on the basis of the perturbation derived from the bond fixation of the parent cation $\mathbf{6}^+$. We have recently clarified that perturbations derived from benzo-annulation onto the cyclohepta[*a*]azulenylium ion are highly dependent on the annulating positions.[16] While the benzo-annulation on the double bond having a large bond order of the parent cation causes smaller perturbation, the benzo-annulation on the double bond having a small bond order significantly perturbs both the original π-system and the annulating benzene ring. Regarding cation $\mathbf{6}^+$, the X-ray crystal analysis has revealed that the bond length of C7−C8 (1.416 Å) is longer than that of C8−C9 (1.375 Å).[22] Thus, the annulation of the furopyrimidine ring onto $\mathbf{6}^+$ at C7−C8 giving $\mathbf{10}^+$ would cause a larger perturbation than the annulation of the furopyrimidine ring onto $\mathbf{6}^+$ at C8−C9 giving $\mathbf{4}^+$. Due to this larger perturbation, the λ_{max} of $\mathbf{10}^+$ would show a red-shift from that of $\mathbf{4}^+$ (vide supra). In the cation $\mathbf{10}^+$, this destabilizing effect is larger than the stabilizing effect derived from the electron-donating ability of furopyrimidine, and thus the cation $\mathbf{10}^+$ would exhibit a smaller pK_{R+} value as compared with that of $\mathbf{6}^+$.

SCHEME 2[a]



[a] Reagents and conditions: (i) NaBH$_4$, CH$_3$CN, rt, 1 h; (ii) (a) DDQ, CH$_2$Cl$_2$, rt, 1 h, (b) 42% aq HBF$_4$, Ac$_2$O, 0 °C, 1 h; (iii) *hν*, aerobic, 42% aq HBF$_4$, CH$_3$CN−CH$_2$Cl$_2$, rt, 24 h.

The reduction potential of $\mathbf{10}^+$ was determined by cyclic voltammentry (CV) in CH$_3$CN. The reduction wave was irreversible under the conditions of the CV measurements; the peak potential is summarized in Table 3, together with those of the reference compounds $\mathbf{3a}$,[9] $\mathbf{4}^+$,[13] $\mathbf{5}^+$,[15] and $\mathbf{6}^+$.[14] The $E1_{red}$ of $\mathbf{10}^+$ is less negative by 0.19 V than that of $\mathbf{3a}^+$, suggesting the elongated π-conjugation of $\mathbf{10}^+{\cdot}BF_4^-$. Furthermore, the less negative $E1_{red}$ of $\mathbf{10}^+$ by 0.04 V as compared with that of $\mathbf{4}^+$ would be comparable to the lower pK_{R+} value of $\mathbf{10}^+$.[12,23] The irreversible nature is probably due to the formation of a radical species and its dimerization, as reported to be a typical property of uracil-annulated heteroazulenylium ions $\mathbf{3a}$−$\mathbf{d}^+$ [10−12] and $\mathbf{4}^+$.[13]

Reactivity. The reactions of $\mathbf{10}^+{\cdot}BF_4^-$ with some nucleophiles were investigated. While the reaction of $\mathbf{3a}^+{\cdot}BF_4^-$ with NaBH$_4$ proceeded at C5, C7, and C9 to give a mixture of three regioisomers **19**−**21** (**19**:**20**:**21** 29:12:59),[10] the reaction of $\mathbf{4}^+{\cdot}BF_4^-$ proceeded at the C13 to afford a single product **22**.[13] On the other hand, the reaction of $\mathbf{10}^+{\cdot}BF_4^-$ with NaBH$_4$ proceeded at C11 and C13 to give a mixture of **23** and **24** (in a ratio of 11:89) in quantitative yield (Scheme 2). There is a well-known tendency for double bond fixation in the methano[11]-annulene system to favor a cycloheptatriene moiety predominantly over a 1,6-dimethylenecyclohepta-2,4-diene moiety.[24] Thus, the formation of **23** and **24** would be ascribed to the stability of both the cycloheptatriene moiety and the closed furan ring. The formation of the C13-adduct predominates over the C11-adduct, although the positive charge is localized at C11 mainly (vide supra). The feature is similar to the reaction of $\mathbf{3a}^+{\cdot}BF_4^-$ with NaBH$_4$, in which the ratio of C9-adduct **21** was

---

(21) Freedman, H. H. *Carbonium Ions*; Olah, G. A., Schleyer, P., Eds.; Wiley-Insterscience: New York, 1973.

(22) Destro, R.; Simonetta, M. *Acta Crystallogr.* **1979**, *B35*, 1846−1852.

(23) Naya, S.; Nitta, M. *J. Chem. Soc., Perkin Trans. 2* **2000**, 2427−2435.

(24) (a) Paquette, L. A.; Berk, H. C.; Ley, S. V. *J. Org. Chem.* **1975**, *40*, 902 and references therein. (b) Reisdorff, J.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 218.

TABLE 4. Autorecycling Oxidation of Some Amines by 10$^+$·BF$_4^-$ under Photoirradiation[a]

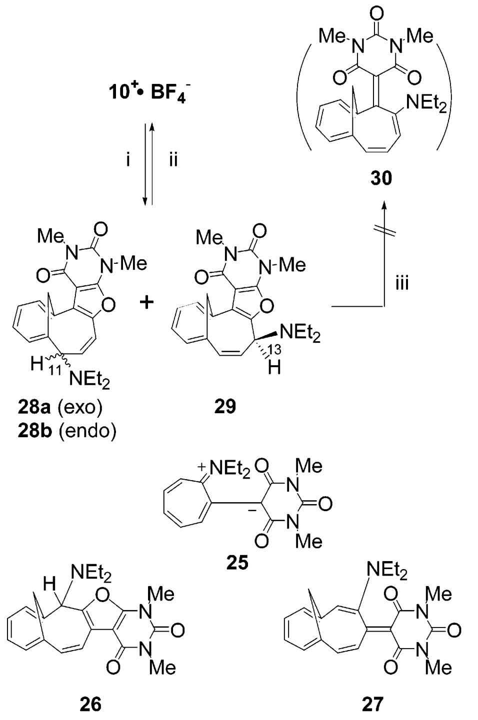
entry	compd	amine	imine	yield[b,c]/%	recycling no.[d]
1	**10**$^+$·BF$_4^-$	PhCH$_2$NH$_2$	PhCH=NCH$_2$Ph	2238	22.4
2	**10**$^+$·BF$_4^-$	PhCH(Me)NH$_2$	PhMeC=NCHMePh	1733	17.3
3	**10**$^+$·BF$_4^-$	hexylamine	*N*-hexylhexanal imine	3286	32.9
4	**10**$^+$·BF$_4^-$	cyclohexylamine	*N*-cyclohexylcyclohexanone imine	719	7.2
5	**3a**$^+$·BF$_4^-$	PhCH$_2$NH$_2$	PhCH=NCH$_2$Ph	8161	81.6
6	**4**$^+$·BF$_4^-$	PhCH$_2$NH$_2$	PhCH=NCH$_2$Ph	3007	30.1
7	**3a**$^+$·BF$_4^-$	PhCH(Me)NH$_2$	PhMeC=NCHMePh	3947	39.5
8	**4**$^+$·BF$_4^-$	PhCH(Me)NH$_2$	PhMeC=NCHMePh	2267	22.7

[a] CH$_3$CN solution was irradiated by RPR-100, 350-nm lamps under aerobic conditions. [b] Isolated by converting to the corresponding carbonyl compounds and then to 2,4-dinitrophenylhydrazones. [c] Based on **10**$^+$·BF$_4^-$, **3a**$^+$·BF$_4^-$, and **4**$^+$·BF$_4^-$ used; the yield is calculated by subtraction of the "blank" yield from the total yield of imine in the presence of **10**$^+$·BF$_4^-$, **3a**$^+$·BF$_4^-$, and **4**$^+$·BF$_4^-$. [d] Recycling number of **10**$^+$·BF$_4^-$, **3a**$^+$·BF$_4^-$, and **4**$^+$·BF$_4^-$.

larger than those of C5- and C7-adducts, **19** and **20**.[10] Recrystallization of a mixture of **23** and **24** from CH$_3$CN gave a pure sample of major product **24**. To clarify the endo–exo selectivity, a reaction of **10**$^+$·BF$_4^-$ with NaBD$_4$ was carried out in an NMR tube to give a mixture of C11-adduct **23**-*d* and C13-adduct **24**-*d* and **24**. Since NaBD$_4$ used for the reaction is of 96% deuterium content, the reaction of **10**$^+$·BF$_4^-$ with the remaining hydride would give also compound **24**. The ratio of **23**-*d*, **24**-*d*, and **24** was determined to be 16:76:10 by the ^{1}H NMR spectrum of the mixture. The structural assignment of **23**, **24**, **23**-*d*, and **24**-*d* was based on the NMR, IR, and mass spectral data. Furthermore, compounds **23**-*d* and **24**-*d* were determined to be the exo adduct by the H–H COSY and NOE spectra. Upon hydride abstraction with DDQ and subsequent anion exchange reaction, a mixture of compounds **23** and **24** regenerated **10**$^+$·BF$_4^-$ in quantitative yield. Furthermore, photoirradiation of a mixture of compounds **23** and **24** in CH$_3$CN and (CH$_2$Cl)$_2$ solution containing 42% aquaous HBF$_4$ under aerobic conditions for 24 h afforded **10**$^+$·BF$_4^-$ mainly in addition to unidentified materials.

The reaction of **3a**$^+$·BF$_4^-$ with diethylamine has been shown to give a C9a-adduct, which underwent ring-opening reaction to give **25** (Scheme 3).[10] In contrast, the diethylamine addition of **4**$^+$·BF$_4^-$ occurred at low temperature (−65 °C) to give C13-adduct **26**, which isomerized to **27** (Scheme 3) at higher temperature (>−35 °C).[13] In the reaction of **10**$^+$·BF$_4^-$ with diethylamine, a mixture of **28a**,**b** and **29** was obtained in quantitative yield. Since the products were unstable on SiO$_2$ and Al$_2$O$_3$, isomers **28a**,**b** and **29** could not be separated. Thus, the structural assignment of **28a**,**b** and **29** was based on the ^{1}H NMR, IR, and HRMS spectra. The ^{1}H NMR spectra of **28a**,**b** and **29** are unequivocally assigned by using the H–H COSY and NOE spectra, and the ratio of **28a**,**b** and **29** was determined to be 22:14:64 by the ^{1}H NMR spectrum of the mixture; exo adduct **28a** predominates slightly. On the other hand, the addition reaction at the C13 proceeded selectively to give only exo adduct **29**. This exo selectivity is similar to the reaction of **10**$^+$·BF$_4^-$ with NaBD$_4$ (vide supra). The results show the feasibility of the methano[11]annulene system for the exploration of a novel chiral auxiliary. Unlike in the case of **26**,[13] heating of **28a**,**b** and **29** in CH$_3$CN did not undergo any isomerization, such as a reaction giving **30**. Upon treatment with aq HBF$_4$ in Ac$_2$O, a mixture of compounds **28a**,**b** and **29** regenerated **10**$^+$·BF$_4^-$ in good yield.

SCHEME 3[a]



[a] Reagents and conditions: (i) Et$_2$NH, CH$_3$CN, rt, 1 h; (ii) 42% aq HBF$_4$, Ac$_2$O, 0 °C, 1 h; (iii) CH$_3$CN, reflux, 24 h.

Autorecycling Oxidation. Compounds **3a**–**d**$^+$·BF$_4^-$ act as a catalyst for oxidation of some alcohols under photoirradiation.[10−12] Moreover, compounds **2a** and **4**$^+$·BF$_4^-$ have also been reported to undergo autorecycling oxidation toward some amines under photoirradiation.[13,25] In this context, we examined the oxidation of some amines by using **10**$^+$·BF$_4^-$. We found that compounds **10**$^+$·BF$_4^-$ have an oxidizing ability toward benzylamine, 1-phenylethylamine, hexylamine, and cyclohexylamine to give the corresponding imines under aerobic and photoirradiation conditions. The results are summarized in Table 4, together with the results obtained by using reference compounds **3a**$^+$·BF$_4^-$ and **4**$^+$·BF$_4^-$. The reactions with **10**$^+$·BF$_4^-$ gave lower yields as compared with those of **3a**$^+$·BF$_4^-$ and **4**$^+$·BF$_4^-$. Direct irradiation of the amines in the absence of **10**$^+$·BF$_4^-$ (named "blank") gives the corresponding imines in small amounts. Thus, the yield in Table 4 is calculated by subtraction of the "blank" yield from the yield of the imine in the presence of **10**$^+$·BF$_4^-$. Imines are obtained in more

---

(25) Naya, S.; Iida, Y.; Nitta, M. *Tetrahedron* **2004**, *60*, 459–467.

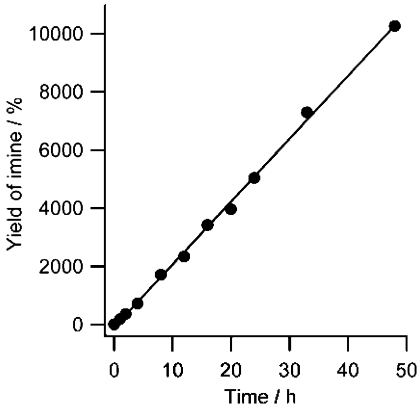


FIGURE 5. Time dependency of autorecycling oxidation of benzylamine by using $\mathbf{10}^+\cdot BF_4^-$.

than 100% yield [based on compound $\mathbf{10}^+\cdot BF_4^-$] under photoirradiation, and thus, autorecycling oxidation clearly proceeds. To clarify the time dependency of the oxidizing reaction, ^1H NMR monitoring of the photooxidation reaction of $\mathbf{10}^+\cdot BF_4^-$ toward benzylamine was carried out. By using mesitylene as an internal standard, the yield of imine is recorded by using the ^1H NMR spectra at selected intervals. The results are summarized in Figure 5. The yield of benzaldimine was increased linearly as the irradiation time was prolonged to 48 h, suggesting that $\mathbf{10}^+\cdot BF_4^-$ would be stable under these conditions. Attempted detection of the intermediate such as reduced compounds **23** and **24** in the oxidation reaction of amines is unsuccessful at this stage. We propose that the present autorecycling oxidation proceeds via electron transfer from amines to the excited cation $\mathbf{10}^+\cdot BF_4^-$;[10,25] however, further studies will be required to clarify the detailed mechanistic aspect.

Summary

Novel synthesis of 1,3-dimethyl-5,10-methanocycloundeca[4,5]furo[2,3-*d*]pyrimidin- 2,4(1,3*H*)-dionylium tetrafluoroborate ($\mathbf{10}^+\cdot BF_4^-$) was accomplished albeit in low yield. The structural characteristics were clarified by the inspection of the spectral data and the MO calculation. The physical properties of $\mathbf{10}^+\cdot BF_4^-$ were studied by measurement of the UV−vis spectra, the pK_{R+} values, and the reduction potentials. Reactions of $\mathbf{10}^+\cdot BF_4^-$ with hydride and diethylamine afforded mixures of C11- and C13-adducts. In both reactions, the methano-bridge controls the nucleophilic attacks to the C13 to prefer exo selectivity. The results show that the methano[11]-annulene system shows promise for the novel chiral auxiliary. The photoinduced oxidation reactions of $\mathbf{10}^+\cdot BF_4^-$ toward some amines under aerobic conditions were carried out to give the corresponding imines in 719−3286% yields (7.2−32.9 cycles).

Experimental Section

Preparation of 1,3-Dimethyl-5,10-methanocycloundeca-[4,5]furo[2,3-*d*]pyrimidin- 2,4(1,3*H*)-dionylium Tetrafluoroborate ($\mathbf{10}^+\cdot BF_4^-$). A solution of dimethylbarbituric acid **13** (780 mg, 5 mmol) and base (4 mmol) in DMF (2 mL) was stirred at room temperature for 5 min. To the solution was added **12** (204 mg, 1 mmol) and the mixture was stirred at 35 °C for the period indicated in Table 1. To the mixture was added saturated 3% HCl, and the mixture was extracted with AcOEt. The extract was dried over Na_2SO_4 and concentrated in vacuo. The residue was dissolved in a mixture of Ac_2O (10 mL) and 42% HBF_4 (2 mL) at 0 °C, and the mixture was stirred for another 1 h. To the mixture was added Et_2O (50 mL) and the precipitates were collected by filtration to give $\mathbf{4}^+\cdot BF_4^-$ and/or $\mathbf{10}^+\cdot BF_4^-$. The results are summarized in Table 1 (run 1, 23.6 mg, 6%; run 4, 31.5 mg, 8%).

Determination of $\mathbf{p}\boldsymbol{K}_{\mathbf{R+}}$ Value of Cation $\mathbf{10}^+$. Buffer solutions of slightly different acidities were prepared by mixing aqueous solutions of potassium hydrogen phthalate (0.1M) and HCl (0.1 M) (for pH 2.2−4.0), potassium hydrogen phthalate (0.1M) and NaOH (0.1 M) (for pH 4.1−5.9), and KH_2PO_4 (0.1M) and NaOH (0.1 M) (for pH 6.0−8.0) in various portions. For the preparation of sample solutions, 1 mL portions of the stock solution, prepared by dissolving 4 mg of compound $\mathbf{10}^+\cdot BF_4^-$ in CH_3CN (20 mL), were diluted to 10 mL with the buffer solution (8 mL) and CH_3CN (1 mL). The UV−vis spectrum was recorded for cation $\mathbf{10}^+$ in 20 different buffer solutions. Immediately after recording the spectrum, the pH of each solution was determined on a pH meter calibrated with standard buffers. The observed absorbance at the specific absorption wavelength (500 nm) of cation $\mathbf{10}^+$ was plotted against pH to give a classical titration curve, whose midpoint was taken as the pK_{R+} value.

Cyclic Voltammetry of $\mathbf{10}^+$. The reduction potential of $\mathbf{10}^+\cdot BF_4^-$ was determined by means of CV-27 voltammetry controller (BAS Co). A three-electrode cell was used, consisting of Pt working and counter electrodes and a reference Ag/$AgNO_3$ electrode. Nitrogen was bubbled through an acetonitrile solution (4 mL) of $\mathbf{10}^+\cdot BF_4^-$ (0.5 mmol dm^{-3}) and Bu_4NClO_4 (0.1 mol dm^{-3}) to deaerate it. The measurements were made at a scan rate of 0.1 V s^{-1} and the voltammograms were recorded on a WX-1000-UM-019 (Graphtec Co) X−Y recorder. Immediately after the measurements, ferrocene (0.1 mmol) ($E_{1/2} = +0.083$) was added as the internal standard, and the observed peak potentials were corrected with reference to this standard. Compound $\mathbf{10}^+\cdot BF_4^-$ exhibited an irreversible reduction wave, which is summarized in Table 3.

Reaction of $\mathbf{10}^+\cdot BF_4^-$ with $NaBH_4$. A solution of $\mathbf{10}^+\cdot BF_4^-$ (19.7 mg, 0.05 mmol) and $NaBH_4$ (8 mg, 0.20 mmol) in CH_3CN (3 mL) was stirred at room temperature for 1 h. To the mixture was added saturated aqueous NH_4Cl solution, and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and concentrated in vacuo to give a mixture of **23** and **24** (15.5 mg, 100%).

^1H NMR Monitoring of the Reaction of $\mathbf{10}^+\cdot BF_4^-$ with $NaBD_4$. To a solution of compound $\mathbf{10}^+\cdot BF_4^-$ (3.9 mg, 0.01 mmol) in CD_3CN (0.5 mL) was added $NaBD_4$ (2.1 mg, 0.05 mmol) at room temperature in an NMR tube. After 1 h, the NMR measurement was carried out.

Oxidation of a Mixture of 23 and 24. To a stirred solution of **23** and **24** (15.4 mg, 0.05 mmol) in CH_2Cl_2 (2 mL) was added DDQ (17.6 mg, 0.075 mmol), and the mixture was stirred at room temperature for 1 h. After evaporation of the CH_2Cl_2, the residue was dissolved in a mixture of Ac_2O (2 mL) and 42% HBF_4 (0.4 mL) at 0 °C, and the mixture was stirred for another 1 h. To the mixture was added Et_2O (10 mL) and the precipitates were collected by filtration to give $\mathbf{10}^+\cdot BF_4^-$ (20 mg, 100%).

Oxidation of a Mixture of 23 and 24 by Photoirradiation. A solution of a mixture of **23** and **24** (16.7 mg, 0.054 mmol) and 42% aq HBF_4 (0.1 mL) in CH_3CN (1 mL) and CH_2Cl_2 (2 mL) in a Pyrex tube was irradiated by RPR-100, 350-nm lamps under aerobic conditions for 24 h until the reaction was complete. The mixture was concentrated in vacuo, and the resulting residue was dissolved in a mixture of acetic anhydride (2 mL) and 42% aq HBF_4 (0.4 mL) at 0 °C. The mixture was stirred for 1 h. To the mixture was added Et_2O (20 mL) and the precipitate was collected by filtration to give $\mathbf{10}^+\cdot BF_4^-$ mainly in addition to unidentified materials (13.5 mg).

Reaction of $10^+\cdot BF_4^-$ with Diethylamine. To a solution of **10**$^+\cdot BF_4^-$ (19.7 mg, 0.05 mmol) in CH_3CN (2 mL) was added diethylamine (11 mg, 0.15 mmol), and the mixture was stirred at room temperature for 1 h. To the mixture was added saturated aqueous NH_4Cl solution, and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and concentrated in vacuo to give a mixture of **28a**,**b** and **29** (19.0 mg, 100%).

Reaction of a Mixture of 28a,b and 29 with HBF_4. To a solution of a mixture of **28a**,**b** and **29** (19.0 mg, 0.05 mmol) in Ac_2O (2 mL) was added 42% aq HBF_4 (0.4 mL) at 0 °C. The mixture was stirred for 1 h. To the mixture was added Et_2O (10 mL) and the precipitate was collected by filtration to give **10**$^+\cdot BF_4^-$ (20 mg, 100%).

General Procedure for Autorecycling Oxidation of Amines in the Presence of $10^+\cdot BF_4^-$. A CH_3CN (16 mL) solution of compound **10**$^+\cdot BF_4^-$ (1.97 mg, 0.005 mmol) and amines (2.5 mmol, 500 equiv) in a Pyrex tube was irradiated by RPR-100, 350-nm lamps under aerobic conditions for 16 h. The reaction mixture was concentrated in vacuo and diluted with Et_2O and filtered. The filtrate was treated with a saturated solution of 2,4-dinitrophenylhydrazine in 6% HCl to give 2,4-dinitrophenylhydrazone. The results are summarized in Table 4.

^1H NMR Monitoring of the Photooxidation of Benzylamine by Using $10^+\cdot BF_4^-$. A CD_3CN (0.5 mL) solution of compound **10**$^+\cdot BF_4^-$ (0.197 mg, 0.0005 mmol), benzylamine (18.73 mg, 0.175 mmol), and mesitylene (internal standard; 3.6 mg, 0.03 mmol) in an NMR tube was irradiated by RPR-100, 350-nm lamps under aerobic conditions. The NMR measurement was carried out at intervals, and the yield of benzaldimine calculated by the ratio of the ^1H signal of benzaldimine and mesitylene was plotted against them (Figure 5).

Acknowledgment. Financial support from a Waseda University Grant for Special Research Project and 21COE "Practical Nano-chemistry" from MEXT, Japan, is gratefully acknowledged. We thank the Materials Characterization Central Laboratory, Waseda University, for technical assistance with the spectral data and elemental analyses.

Supporting Information Available: Physical, analytical, and spectroscopic data for **10**$^+\cdot BF_4^-$, **23**, **24**, **23**-*d*, **24**-*d*, **28a**,**b,** and **29** and ^1H and ^{13}C NMR spectra of **10**$^+\cdot BF_4^-$, **23**, **24**, **23**-*d*, **24**-*d*, **28a**,**b**, and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO048575S