JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

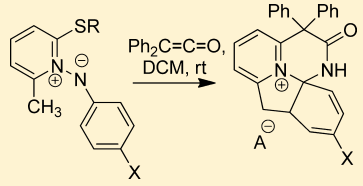
# Transformation of Zwitterionic Pyridine Derivatives to a Spiro-Fused Ring System: Azoniabenzo[*de*]fluorine. Synthesis and Mechanistic Rationalization

Roberta Palkó, Orsolya Egyed, Tibor András Rokob, Petra Bombicz, Zsuzsanna Riedl, and György Hajós*

Research Centre for Natural Sciences, Institute of Organic Chemistry, Hungarian Academy of Sciences, Magyar tudósok körútja 2, H-1117 Budapest, Hungary

Supporting Information

**ABSTRACT:** Reaction of aryl- and benzylsulfanopyridinium amidates bearing a methyl group in position 6 with 2 equiv of diphenylketene afforded a spiro-fused ring system: azoniabenzo[*de*]fluorine. By use of an excess amount of ketene, a distinct reaction was observed via which a 1*H*-pyrrolo[3,2-*b*]pyridin-2(3*H*)-one derivative was furnished. The structure of the tetracyclic spiro-fused ring system was unambiguously confirmed by X-ray diffraction, and its formation was rationalized by DFT calculations.



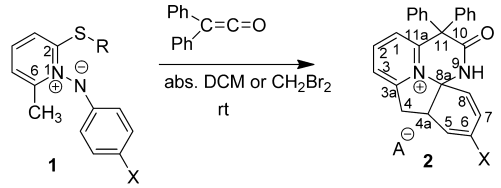

## INTRODUCTION

Recently we have found that arylsulfanopyridinium amidates (**1**) as reactive mesomeric betaines can serve as valuable starting materials for 1,3-dipolar cycloadditions and subsequent transformations. Thus, syntheses of triazolo[2,3-*a*]pyridinium salts,[1] pyrrolo[3,2-*b*]pyiridines,[2] imidazo[4,5-*b*]pyridines,[1] 4-azaindoles,[2,3] and 7-azaindoles[3] have been elaborated.

## RESULTS AND DISCUSSION

Herein, as a continuation of these research activities, we report on transformation of mesomeric betaine **1** with diphenylketene (Scheme 1.). When a dichloromethane solution of **1a** was treated with diphenylketene (prepared by literature procedures[4,5]) at room temperature, formation of a white precipitate was observed after 7 days. Detailed NMR studies of this product revealed that a derivative of a spiro-fused ring system, azoniabenzo[*de*]fluorine (**2a**, A = Cl), was formed. Similarly, reaction of the benzylsulfano mesomeric betaine **1c** also resulted in formation of the tetracyclic compound **2a**, A = Cl, whereas **1b** and **1d** gave **2b** and **2c**, A = Cl, respectively.

**Scheme 1. Reaction of Mesomeric Betaine 1 with Diphenylketene**




| | X | R |
|---|---|---|
| **1a** | $CH_3$ | 4-$CH_3$-$C_6H_4$ |
| **1b** | Cl | Bn |
| **1c** | $CH_3$ | Bn |
| **1d** | $OCH_3$ | Bn |

| | X | Starting compound | Yield (%) A=Cl or Br |
|---|---|---|---|
| **2a** | $CH_3$ | **1a or 1c** | 21 |
| **2b** | Cl | **1b** | 20 |
| **2c** | $OCH_3$ | **1d** | 26 |

The NMR peak assignments were performed on the basis of one- ($^1$H, $^{13}$C NMR) and two-dimensional ($^1$H−$^{13}$C-gHSQC, $^1$H−$^{13}$C-gHMBCAD) experiments. The coherence transfer delays in the $^1$H−$^{13}$C-gHSQC measurements were set to $^1/_4$ *J*, where the one-bond *J* coupling was 140 Hz. The delay times of $^1$H−$^{13}$C-gHMBCAD experiments were set to $^1/_4$ *J* and $^1/_2$ *J*, controlled by the parameters *j1xh* = 140 Hz and *jnxh* = 8 Hz.

The NMR spectral data of the new products could be interpreted by assuming the formation of the spiro-fused ring system **2a**,**b**,**c** for the following reasons:

(i) The $^1$H and $^{13}$C resonances characteristic for the arylthio group of the starting materials **1a**,**b**,**c**,**d** completely disappeared from the spectra of the products **2a**,**b**,**c**.

(ii) New signals referring to a methylene group appeared at appr. $\delta_H$ = 3.0−4.0 ppm and $\delta_C$ = 38.0 ppm in the spectra of each product (**2a**,**b**,**c**).

(iii) The *para* disubstituted aromatic ring system of the starting materials was transformed into a cyclohexadiene moiety consisting of sp$^2$ ($\delta_C$ between 118 and 130 ppm) and sp$^3$ ($\delta_C$ between 40 and 80 ppm) carbon atoms.

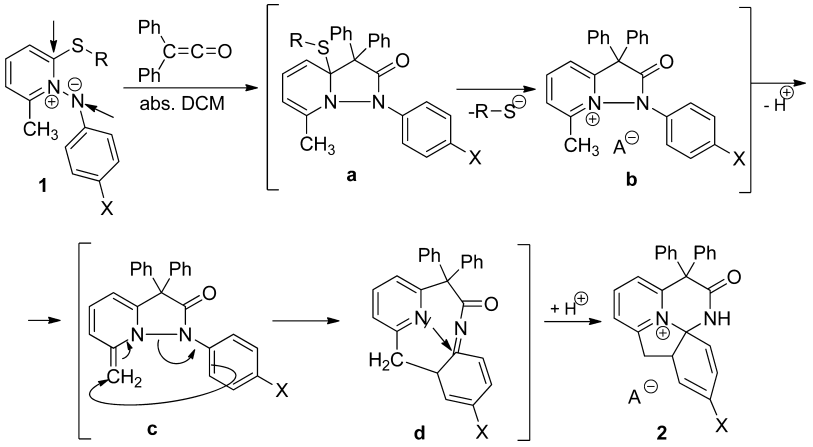
(iv) The HMBC crosspeaks corresponding to the three bond connections between H($4_x$,$4_y$)−C(3), H($4_x$,$4_y$)−C(5), H($4_x$)−C(8a); H(5)−C(8a) and H(7)−C(8a) (for 2D spectra of **2c**, see S5 in the Supporting Information; numbering is shown in Scheme 1.) provided evidence for the proposed spiro-fused ring system.

Single-crystal X-ray structure determination of **2a** (A = Br) confirmed the formation of this unusual structure. The obtained ORTEP diagram[43] is depicted in Figure S1 (Supporting Information); the summary of crystallographic

**Received:** October 3, 2014
**Published:** November 19, 2014

   dx.doi.org/10.1021/jo5022663 | *J. Org. Chem.* 2015, 80, 174−179

**Scheme 2. Mechanistic Proposal for Transformation of Mesomeric Betaine 1 to the Spiro-Fused Azoniabenzo[*de*]fluorine Ring System 2**




data and structure determination for crystal **2a** can be found in Table S1 (Supporting Information).

The crystal of **2a** A = Br is racemic, comprising SS and RR stereoisomers regarding C4a and C8a atoms. The crystal lattice is completed with acetonitrile solvent molecules in a 1:1 stoichiometric ratio (Figure S2, Supporting Information).[44] The N11B–C8A bond length is 1.502(2) Å. The hydrogen atom on the C4A carbon is in the axial position. The intra- and intermolecular interactions are presented in Table S2, and the packing diagrams are shown in Figure S3 (see the Supporting Information).

The possible reaction mechanism of the transformation of **1a** to **2a**, A = Cl, is shown in Scheme 2. It has been assumed that the first step is a 1,3-dipolar cyclization between the C=C bond of the ketene and the two strongly polarized centers of **1a** shown by the arrows to afford a regular cycloadduct (**a**), followed by spontaneous elimination of the mercaptide anion to yield an intermediate pyridinium salt (**b**).[6−10] These two steps (i.e., **1** → **a** → **b**) are strongly reminiscent of transformation of **1** with isocyanates and isothiocyanates.[11]

When **b** is deprotonated by the mercaptide anion being present in the reaction mixture, a methenopyridine moiety can be formed (**c**), which can undergo a diaza-Cope rearrangement to **d** shown by the three arrows.[12] As a result, a new $\sigma$ bond is formed between the $CH_2$ group and the *N*-phenyl ring and, simultaneously, a N–N fission occurs to result in a nine-membered ring. Ring enlargement by Cope-type rearrangement has been observed by us earlier,[2] and it can also be brought about by other rearrangements as reported recently.[13] This intermediate (**d**) can be stabilized by an intramolecular cyclization (attack of the pyridine ring-nitrogen atom on the imino carbon atom), transforming the nine-membered ring to a 5 + 6 fused system, which is *peri* fused to the pyridine ring and spiro-fused to the benzene moiety.

An especially interesting feature of this reaction sequence is that a chloride ion is present in the final product (**2**). Some literature works[14−18] as well as one of our earlier findings[12] reveal that the source of the chloride anion is the nucleophilic attack of the mercaptide anion on the solvent dichloromethane.

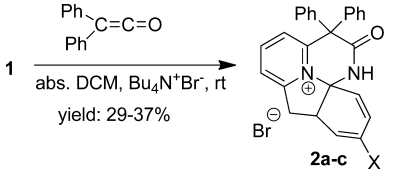
As the salts (**2a–c**) could only be isolated by filtration from the reaction mixture, one reason for the experienced poor yield might be the relative good solubility of the chloride salt in dichloromethane. Thus, change of the anion for a bromide ion seemed to be a possible tool to increase the yield.

To this end, two modifications have been done:

(i) The reaction was carried out in dibromomethane. Unfortunately, with this change, the yields remained basically at the same low level (10–20%).

(ii) Dichloromethane solvent was maintained and tetrabutylammonium bromide was added to the reaction mixture in order to ensure sufficient bromide anion concentration. The yields in this case significantly increased, and **2a**, **2b**, and **2c** (A = Br) have been obtained in 30, 29, and 37%, respectively (Scheme 3). Besides formation of the main products, only decomposition could be detected by chromatography.

**Scheme 3. Formation of Bromide Salts of 2 in the Presence of Tetrabutylammonium Bromide**




Our efforts to improve the yield by using microwave irradiation failed. Under these conditions, formation of the nondesired side product **3** as discussed below was accelerated.

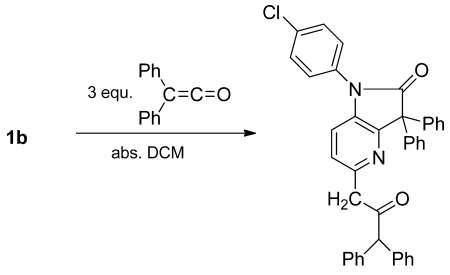
Further considerations of possible reasons for the poor yields prompted us to attempt employing an excess amount of ketene, as this might be beneficial for the outcome of the reactions. Thus, the reactions have been repeated using 3 instead of 2 equiv of diphenylketene (Scheme 4.).

Unfortunately, these reaction conditions lead to profound change: the expected spiro-fused product was not detected, and instead, a complex mixture containing 1*H*-pyrrolo[3,2-*b*]-pyridin-2(3*H*)-one derivative **3b** as the only isolable component implying 2 equiv of the elements of the ketene reagent was formed in poor yield (13–15%), similar to our observations with analogous transformations with isocyanates.[12]

In order to rationalize the pathway from **1** to **2** and to further elucidate the possible reasons for the modest product yields, we carried out density functional theory calculations. The computed solvent-phase free energy profile for the transformation of **1a**, obtained for dichloromethane solution using


dx.doi.org/10.1021/jo5022663 | *J. Org. Chem.* 2015, 80, 174–179

**Scheme 4. Formation of 1*H*-Pyrrolo[3,2-*b*]pyridin-2(3*H*)-one Derivative 3b with an Excess of Diphenylketene**




the M05-2X exchange-correlation functional and the SMD continuum solvation model, is shown in Figure 1. The reaction commences with a [3 + 2] cycloaddition of the 1,3-dipole **1a** and diphenylketene. On the basis of experimental data[19,20] or computational mechanistic analyses,[21] ketenes have been suggested to react with various 1,3-dipoles in a stepwise fashion, but the situation is less clear for the closely related keteneimines where concerted[22] and stepwise[23] reactions with 1,3-dipoles have both been proposed. For the present cyclization, we found that the reaction takes place in two steps. First, a zwitterionic adduct **zwad** is formed via the attack of the negatively charged nitrogen on the ketene carbon. The adduct then undergoes ring closure to form cycloadduct **a**. The latter step formally corresponds to a $6e^-$ electrocyclization, but the absence of delocalization of HOMO and LUMO of **zwad** along the forming ring points to an intramolecular nucleophilic attack instead. The overall addition reaction has a large thermodynamic driving force ($\Delta G$ = −7.5 kcal/mol), and the involved barriers are modest, pointing to an essentially instantaneous reaction at room temperature.

After the cyclization, we hypothesized the elimination of the mercaptide anion. This step, resulting in intermediate **b**, is calculated to be indeed feasible. It is a direct dissociation with a modest endothermicity of $\Delta H$ = +5.6 kcal/mol, but the favorable entropy contribution renders it exergonic. Following the dissociation, the mercaptide ion can deprotonate the 2-methyl group in an almost isoergonic step, yielding neutral intermediate **c**. We have not calculated the transition state of this proton transfer step, but we do not expect it to be rate-determining.

The supposed key step of the reaction, a [3,3]-sigmatropic rearrangement[24−27] of **c** to **c′**, was computed to proceed in a concerted way, and it represents the highest barrier along the reaction route (**TScc′**). The computed large free energy of activation ($\Delta G^{\ddagger}$ = +28.0 kcal/mol) suggests that a reason behind the observed low yields might also be the sluggish reaction rate. The geometry of the transition state **TScc′** is depicted in Figure 2, featuring a chairlike arrangement of the reacting atoms as expected.[24−27]

The obtained isomer **c′** lies marginally higher in free energy than **c**, but it can very quickly react further via the low-barrier, exergonic intramolecular nucleophilic attack of the pyridine nitrogen atom onto the C═N double bond. The attack yields intermediate **d**, already containing the four-ring skeleton. The reaction sequence is closed by transferring the proton back to the amide nitrogen. This last step leads to $\mathbf{2a}^{S}$, which is identical to the observed product **2a** but has mercaptide as counterion. The proton transfer is computed to be slightly endergonic. Nevertheless, this endergonicity is within the error bar of our computational method, and ion exchange or crystallization of the product may also shift the equilibrium toward the protonated form.

## CONCLUSION

The above findings reveal that derivatives of the earlier unprecedented tetracyclic spiro-fused azoniabenzo[*de*]fluorine ring system **2** can be prepared by one single reaction step: by reaction of the relatively easily available zwitterionic pyridinium amidate **1** and diphenylketene. DFT calculations suggest that the cycloaddition proceeds by a two-step mechanism.

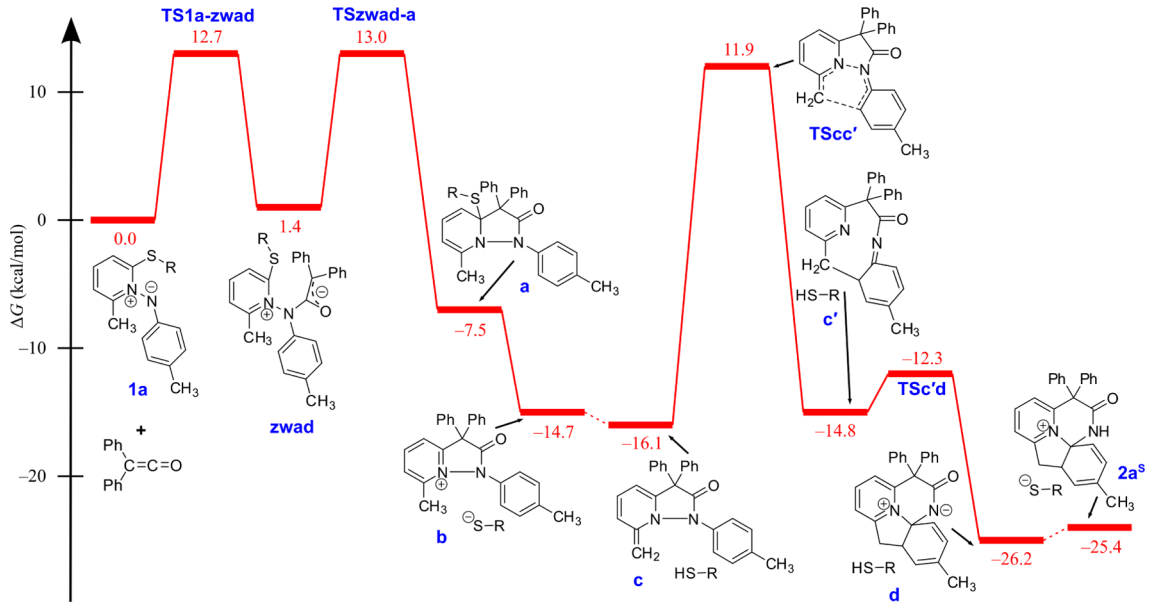



**Figure 1.** Computed solvent-phase Gibbs free energy profile for the reaction of **1a** with diphenylketene. Energies are relative to the isolated starting materials. Barriers for the proton transfer steps were not calculated; these steps are denoted by dashed lines in the profile. R = 4-$CH_3$-$C_6H_4$.


dx.doi.org/10.1021/jo5022663 | *J. Org. Chem.* 2015, 80, 174−179

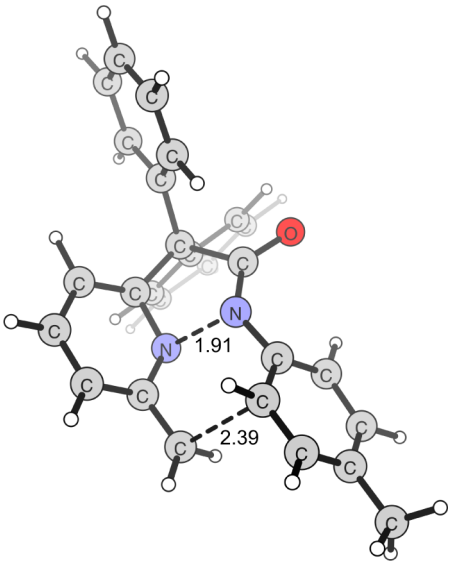



**Figure 2.** Computed geometry of the transition state of the [3,3]-sigmatropic rearrangement (**TScc′**). Lengths of partially formed bonds are given in angstroms.

## EXPERIMENTAL SECTION

**Materials and Methods.** All reagents and solvents were purchased from commercial vendors and used without further purification. Concentration of reaction mixtures refers to rotary evaporation under reduced pressure carried out at 40 °C. Thin layer chromatography (TLC) was performed on aluminum oxide 60 $F_{254}$-precoated TLC plates (0.25 mm thickness) and visualized at 254 nm. NMR spectral data were obtained at ambient temperature unless otherwise specified. $^{1}$H ($^{13}$C) NMR spectra were recorded at 400 (100) MHz in $CDCl_3$ or DMSO. Chemical shifts are reported and shown in parts per million (ppm) and referenced against $CDCl_3$ (7.26 ppm for $^{1}$H and 77.0 ppm for $^{13}$C) or DMSO (2.50 ppm for $^{1}$H and 39.5 ppm for $^{13}$C), and $J$ coupling values are listed in Hz. Infrared spectral data were obtained on an FT-IR spectrometer with major peaks listed. Melting points are uncorrected. Synthesis of 2-benzylthio or 2-arylthio-6-methylpyridinium imides (**1a−d**) has been published earlier and has been carried out according to these literature procedures.[12]

**Computational Details.** Geometries of all involved species were optimized using the M05-2X density functional level of theory[28] in conjunction with the 6-31G(d) basis set[29−32] in vacuo. Harmonic frequency calculations at the same level of theory were carried out to confirm the nature of the stationary points as true minima or saddle points, having zero and one imaginary frequency, respectively, and to derive zero-point energies and thermal corrections to the Gibbs free energy using the ideal gas−rigid rotor−harmonic oscillator approximation for 298 K and 1 mol/L concentration. Solvation free energies for dichloromethane were calculated in single-point calculations using the SMD model[33] and the same functional and basis set. More accurate electronic energies were computed using the larger 6-311++G(2df,2pd) basis set[34−37] on the above geometries. The "ultrafine" integration grid consisting of 99 radial shells and 590 angular points per shell was employed for DFT. All calculations were carried out using the Gaussian 09 package.[38] Molecular graphics were drawn using XYZ Viewer.[39]

*Crystal Data.* $C_{27}H_{23}N_2OBr \times C_2H_3N$, *Fwt.*: 512.44, colorless, prism, size: 0.2 × 0.15 × 0.1 mm, triclinic, space group $P\bar{1}$, $a$ = 8.9351(3) Å, $b$ = 10.5522(3) Å, $c$ = 14.2075(4) Å, $\alpha$ = 91.2659(9)°, $\beta$ = 104.1456(14)°, $\gamma$ = 104.6546(14)°, $V$ = 1251.64(7) Å$^3$, $T$ = 294(1) K, $Z$ = 2, $Z'$ = 1, $F(000)$ = 528, $D_x$ = 1.360 Mg/m$^3$, $\mu$ = 1.677 mm$^{-1}$.

A crystal of **2a** A = Br was mounted on a loop. Cell parameters were determined by least-squares using 9878 (2.4389 ≤ $\theta$ ≤ 35.8736°) reflections. Intensity data were collected on a diffractometer (monochromator; molybdenum−K$\alpha$ radiation, $\lambda$ = 0.71073 Å) at 293(1) K in the range 3.173 ≤ $\theta$ ≤ 27.481. A total of 59 698 reflections were collected,[40] of which 5714 were unique [$R$(int) = 0.0339, $R(\sigma)$ = 0.0156]; intensities of 5082 reflections were greater than 2$\sigma(I)$. Completeness to $\theta$ = 0.998. A numerical absorption[41] correction was applied to the data (the minimum and maximum transmission factors were 0.4344 and 0.6603).

The structure was solved by direct methods.[42] Anisotropic full-matrix least-squares refinement[42] on $F^2$ for all non-hydrogen atoms yielded $R1$ = 0.0327 and $wR2$ = 0.0810 for 1332 [$I > 2\sigma(I)$] and $R1$ = 0.0384 and $wR2$ = 0.0839 for all (5714) intensity data, (number of parameters = 309, goodness-of-fit = 1.027, the maximum and mean shift/esd is 0.000 and 0.000). The maximum and minimum residual electron density in the final difference map was 0.310 and −0.217e·Å$^{-3}$. The weighting scheme applied was $w = 1/[\sigma^2(F_o^2) + (0.04090.5850P)^2 + 0.5850P]$, where $P = (F_o^2 + 2F_c^2)/3$.

Hydrogen atomic positions were located in difference Fourier maps, except for the terminal $CH_3$ of the acetonitrile that were calculated from assumed geometries combined with a rotating group maximum electron density refinement. Hydrogen atoms were included in structure factor calculations, but they were not refined. The isotropic displacement parameters of the hydrogen atoms were approximated from the $U$(eq) value of the atom they were bonded to.

**General Procedure for the Synthesis of 6-Substituted-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Chloride (2a−c, A = Cl).** To a solution of the appropriate 2-benzylthio or 2-arylthio-6-methylpyridinium imides (**1a−d**) (1 mmol) in dichloromethane (11 mL) was added 0.388 g (2 mmol) of diphenylketene and was stirred at room temperature for 7 days. The obtained precipitate was filtered off, washed with diethyl ether, and crystallized from acetonitrile.

**6-Methyl-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Chloride (2a, A = Cl).** This compound was obtained from **1a** or **1c** as white crystals; (0.09 g, 21% in both cases); mp 212−220 °C; IR (KBr) $\nu_{max}$: 3478, 3278, 2997, 2835, 1684, 1657, 1619, 1490, 1449, 1345, 1319, 1198, 813 cm$^{-1}$; $^{1}$H NMR (400 MHz, DMSO) $\delta$ 1.78 (3H, s, C$\underline{H}_3$), 3.07 (1H, dd, $J$ = 17.6, 11.2 Hz, H4$_y$), 3.66 (1H, ddd, $J$ = 11.2, 7.8, 5.6 Hz, H4a), 4.00 (1H, dd, $J$ = 17.6, 7.8 Hz, H4$_x$), 4.52 (1H, d, $J$ = 9.8 Hz, H8), 5.92 (1H, dd, $J$ = 9.8, 1.2 Hz, H7), 6.02 (1H, dd, $J$ = 5.6, 1.2 Hz, H5), 6.83 (2H, m, H2″ + H6″), 7.27 (1H, d, $J$ = 8.1 Hz, H1), 7.30−7.40 (5H, m, H3″ + H4″ + H5″ +H2′ + H6′), 7.57 (3H, m, H3′ + H4′ + H5′), 8.21 (1H, d, $J$ = 8.1 Hz, H3), 8.55 (1H, t, $J$ = 8.1 Hz, H2), 10.70 (1H, s, H9); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 20.3 (C$\underline{H}_3$), 37.7 (C4), 44.2 (C4a), 61.2 (C11), 82.2 (C8a), 118.5 (C8), 122.2 (C5), 123.3 (C3), 128.1 (C3″ + C4″ + C5″), 128.3 (C2′ + C6′), 128.6 (C1 + C6), 129.3 (C4′), 129.9 (C3′ + C5′), 130.1 (C2″ + C6″), 130.8 (C7), 136.4 (C1′), 141.7 (C1″), 145.8 (C2), 152.9 (C11a), 156.8 (C3a), 166.7 (C10); $^{15}$N NMR (DMSO): −265.0 (N9), −180.1 (N11b). Anal. Calcd for $C_{27}H_{23}ClN_2O$: C, 75.96; H, 5.43; N, 6.56. Found: C, 75.62; H, 5.21; N, 6.44.

**6-Chloro-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Chloride (2b, A = Cl).** This compound was obtained from **1b** as white crystals; (0.09 g, 20%); mp 246−252 °C; IR (KBr) $\nu_{max}$: 3374, 2994, 2826, 1695, 1618, 1491, 1449, 1312, 1198, 1048, 811 cm$^{-1}$; $^{1}$H NMR (400 MHz, DMSO) $\delta$ 3.24 (1H dd, $J$ = 17.6, 11.7 Hz, H4$_y$), 3.86 (1H, ddd, $J$ = 11.7, 7.8, 6.4 Hz, H4a), 4.03 (1H, dd, $J$ = 17.6, 7.8 Hz, H4$_x$), 4.64 (1H, d, $J$ = 10.2 Hz, H8), 6.09 (1H, dd, $J$ = 10.2, 1.4 Hz, H7), 6.51 (1H, dd, $J$ = 6.4, 1.4 Hz, H5), 6.83 (2H, m, H2″+ H6″), 7.28 (1H, d, $J$ = 7.9 Hz, H1), 7.30−7.60 (8H, m, H2′ + H3′ + H4′ + H5′ + H6′ + H3″ + H4″ +H5″), 8.24 (1H, d, $J$ = 8.1 Hz, H3), 8.55 (1H, dd, $J$ = 8.1, 7.9 Hz, H2), 10.90 (1H, br. s, H9); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 37.1 (C4), 45.3 (C4a), 61.2 (C11), 81.1 (C8a), 121.6 (C8), 123.5 (C3), 124.5 (C5), 125.3 (C7), 128.1 (C3″ + C4″ + C5″), 128.3 (C2′ + C6′), 128.7 (C1), 129.5 (C6), 130.0 (C3′ + C5′), 130.1 (C2″ + C6″), 136.2 (C1′), 141.6 (C1″), 146.2 (C2), 152.9 (C11a), 156.6 (C3a), 166.6 (C10). Anal. Calcd for $C_{26}H_{20}Cl_2N_2O$: C, 69.81; H, 4.51; N, 6.26. Found: C, 69.57; H, 4.36; N, 5.95.


dx.doi.org/10.1021/jo5022663 | J. Org. Chem. 2015, 80, 174−179

**6-Methoxy-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Chloride (2c, A = Cl).** This compound was obtained from **1d**, as white crystals; (0.116 g, 26%); mp 224−228 °C; IR (KBr) $\nu_{max}$: 3389, 2998, 2833, 1690, 1660, 1618, 1489, 1239, 703 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO) $\delta$ 3.11 (1H, dd, J = 18.2, 11.0 Hz, $H4_y$), 3.55 (3H, s, $OCH_3$), 3.79 (1H, ddd, *J* = 11.0, 7.8, 6.5 Hz., H4a), 4.00 (1H, dd, *J* = 18.2, 7.8 Hz, $H4_x$),), 4.60 (1H, d, *J* = 10.0 Hz, H8), 5.25 (1H, dd, *J* = 6.5, 2.5 Hz, H5), 5.92 (1H, d,d *J* = 10.0, 2.5 Hz, H7), 6.83 (2H, m, H2″ + H6″), 7.26 (1H, d, *J* = 7.8 Hz, H1), 7.32 (2H, m, H2′ + H6′), 7.35 (3H, m, H3″ + H4″ + H5″), 7.56 (1H, m, H4′), 7.57 (2H, m, H3′ + H5′), 8.21 (1H, d, *J* = 7.8 Hz, H3), 8.54 (1H, t, *J* = 7.8 Hz, H2), 10.8 (1H, br. s, H9); $^{13}C$ NMR (100 MHz, DMSO) $\delta$ 38.6 (C4), 44.1 (C4a), 54.6 ($OCH_3$), 61.2 (C11), 82.1 (C8a), 93.6 (C5), 121.1 (C8), 123.4 (C3), 127.2 (C7), 128.1 (C3″ +C4″ + C5″), 128.3 (C2′ + C6′), 128.6 (C1), 129.4 (C4′), 129.9 (C3′ + C5′), 130.1 (C2″ + C6″), 136.3 (C1′), 141.7 (C1″), 146.0 (C2), 150.0 (C6), 152.9 (C11a), 156.9 (C3a), 166.9 (C10). Anal. Calcd for $C_{27}H_{23}ClN_2O_2$: C, 73.21; H, 5.23; N, 6.32. Found: C, 73.01; H, 5.04; N, 6.12.

**General Procedure for the Synthesis of 6-Substituted-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Bromide (2a−d, A = Br).** A solution of the appropriate 2-benzylthio or 2-arylthio-6-methylpyridinium imides (**1a−d**) (1 mmol) in dibromomethane (11 mL) was added 0.388 g (2 mmol) of diphenylketene and was stirred at room temperature for 7 days. The obtained precipitate was filtered off, washed with diethyl ether, and crystallized from acetonitrile.

**General Procedure for Reaction of 2-Benzylthio or 2-Arylthio-6-methylpyridinium imides (1a−d) with Diphenylketene in the Presence of Tetrabutylammonium Bromide.** To a solution of the appropriate 2-arylthio-6-methylpyridinium imides (**1a−d**) (1 mmol) in dichloromethane (11 mL) was added 0.644 g (2 mmol) of tetrabutylammonium bromide and 0.388 g (2 mmol) of diphenylketene, and the mixture was stirred at room temperature for 7 days. The obtained precipitate was filtered off, washed with diethyl ether, and crystallized from acetonitrile.

**6-Methyl-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Bromide (2a, A = Br).** This compound was obtained from **1a** or **1c** as white crystals (0.141 g, 30%); mp 212−220 °C; IR (KBr) $\nu_{max}$: 3478, 3278, 2997, 2835, 1684, 1657, 1619, 1490, 1449, 1345, 1319, 1198, 813 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO) $\delta$ 1.78 (3H, s, $C\underline{H}_3$), 3.07 (1H, dd, *J* = 17.6, 11.2 Hz, $H4_y$), 3.66 (1H, ddd, *J* = 11.2, 7.8, 5.6 Hz, H4a), 4.00 (1H, dd, *J* = 17.6, 7.8 Hz, $H4_x$), 4.52 (1H, d, *J* = 9.8 Hz, H8), 5.92 (1H, dd, *J* = 9.8, 1.2 Hz, H7), 6.02 (1H, dd, *J* = 5.6, 1.2 Hz, H5), 6.83 (2H, m, H2″ + H6″), 7.27 (1H, d, *J* = 8.1 Hz, H1), 7.30−7.40 (5H, m, H3″ + H4″ + H5″ +H2′ + H6′), 7.57 (3H, m, H3′ + H4′ + H5′), 8.21 (1H, d, *J* = 8.1 Hz, H3), 8.55 (1H, t, *J* = 8.1 Hz, H2), 10.70 (1H, s, H9); $^{13}C$ NMR (100 MHz, DMSO) $\delta$ 20.3 ($\underline{C}H_3$), 37.7 (C4), 44.2 (C4a), 61.2 (C11), 82.2 (C8a), 118.5 (C8), 122.2 (C5), 123.3 (C3), 128.1 (C3″ + C4″ + C5″), 128.3 (C2′ + C6′), 128.6 (C1 + C6), 129.3 (C4′), 129.9 (C3′ + C5′), 130.1 (C2″ + C6″), 130.8 (C7), 136.4 (C1′), 141.7 (C1″), 145.8 (C2), 152.9 (C11a), 156.8 (C3a), 166.7 (C10); $^{15}N$ NMR (DMSO): −265.0 (N9), −180.1 (N11b). Anal. Calcd for $C_{27}H_{23}BrN_2O$: C, 68.79; H, 4.92; N, 5.94. Found: C, 68.58; H, 4.93; N, 5.91.

**6-Chloro-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Bromide (2b, A = Br).** This compound was obtained from **1b** as white crystals (0.142 g, 29%); mp 236−242 °C; IR (KBr) $\nu_{max}$: 3374, 2994, 2826, 1695, 1618, 1491, 1449, 1312, 1198, 1048, 811 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO) $\delta$ 3.24 (1H dd, *J* = 17.6, 11.7 Hz, $H4_y$), 3.86 (1H, ddd, *J* = 11.7, 7.8, 6.4 Hz., H4a), 4.03 (1H, dd, *J* = 17.6, 7.8 Hz, $H4_x$), 4.64 (1H, d, *J* = 10.2 Hz, H8), 6.09 (1H, dd, *J* = 10.2, 1.4 Hz, H7), 6.51 (1H, dd, *J* = 6.4, 1.4 Hz, H5), 6.83 (2H, m, H2″+ H6″), 7.28 (1H, d, *J* = 7.9 Hz, H1), 7.30−7.60 (8H, m, H2′ + H3′ + H4′ + H5′ + H6′ + H3″ + H4″ +H5″), 8.24 (1H, d, *J* = 8.1 Hz, H3), 8.55 (1H, dd, *J* = 8.1, 7.9 Hz, H2), 10.90 (1H, br. s, H9); $^{13}C$ NMR (100 MHz, DMSO) $\delta$ 37.1 (C4), 45.3 (C4a), 61.2 (C11), 81.1 (C8a), 121.6 (C8), 123.5 (C3), 124.5 (C5), 125.3 (C7), 128.1 (C3″ + C4″ + C5″), 128.3 (C2′ + C6′), 128.7 (C1), 129.5 (C6), 130.0 (C3′ + C5′), 130.1 (C2″ + C6″), 136.2 (C1′), 141.6 (C1″), 146.2 (C2), 152.9 (C11a), 156.6 (C3a), 166.6 (C10). Anal. Calcd for $C_{26}H_{20}BrClN_2O$: C, 63.50; H, 4.10; N, 5.70. Found: C, 63.62; H, 4.31; N, 5.57.

**6-Methoxy-10-oxo-11,11-diphenyl-4,4a,10,11-tetrahydro-9*H*-9-aza-11b-azoniabenzo[*de*]fluorene Bromide (2c, A = Br).** This compound was obtained from **1d** as white crystals (0.180 g, 37%); mp 266−271 °C; IR (KBr) $\nu_{max}$: 3389, 2998, 2833, 1690, 1660, 1618, 1489, 1239, 703 $cm^{-1}$. $^1H$ NMR (400 MHz, DMSO) $\delta$ 3.11 (1H, dd, *J* = 18.2, 11.0 Hz, $H4_y$), 3.55 (3H, s, $OCH_3$), 3.79 (1H, ddd, *J* = 11.0, 7.8, 6.5 Hz., H4a), 4.00 (1H, dd, *J* = 18.2, 7.8 Hz, $H4_x$), 4.60 (1H, d, *J* = 10.0 Hz, H8), 5.25 (1H, dd, *J* = 6.5, 2.5 Hz, H5), 5.92 (1H, d,d *J* = 10.0, 2.5 Hz, H7), 6.83 (2H, m, H2″ + H6″), 7.26 (1H, d, *J* = 7.8 Hz, H1), 7.32 (2H, m, H2′ + H6′), 7.35 (3H, m, H3″ + H4″ + H5″), 7.56 (1H, m, H4′), 7.57 (2H, m, H3′ + H5′), 8.21 (1H, d, *J* = 7.8 Hz, H3), 8.54 (1H, t, *J* = 7.8 Hz, H2), 10.8 (1H, br. s, H9); $^{13}C$ NMR (100 MHz, DMSO) $\delta$ 38.6 (C4), 44.1 (C4a), 54.6 ($OCH_3$), 61.2 (C11), 82.1 (C8a), 93.6 (C5), 121.1 (C8), 123.4 (C3), 127.2 (C7), 128.1 (C3″ +C4″ + C5″), 128.3 (C2′ + C6′), 128.6 (C1), 129.4 (C4′), 129.9 (C3′ + C5′), 130.1 (C2″ + C6″), 136.3 (C1′), 141.7 (C1″), 146.0 (C2), 150.0 (C6), 152.9 (C11a), 156.9 (C3a), 166.9 (C10). Anal. Calcd for $C_{27}H_{23}BrN_2O_2$: C, 66.54; H, 4.76; N, 5.75. Found: C, 66.23; H, 4.46; N, 5.46.

**Synthesis of 3-[1-(4-Chlorophenyl)-2-oxo-3,3-diphenyl-2,3-dihydro-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl]-1,1-diphenylprop-1-en-2-yl-diphenylacetate (3b).** To a solution of [2-(benzylsulfanyl)-6-methylpyridinium-1-yl](4-chlorophenyl)imide (**1b**) (1 mmol) in dichloromethane (11 mL) was added 0.582 g (3 mmol) diphenylketene and was stirred at room temperature for 7 days. The obtained precipitate was filtered off, washed with diethyl ether, and crystallized from acetonitrile. This compound was white crystals (0.09 g, 15%); mp 183−185 °C; IR (KBr) $\nu_{max}$: 3444, 3058, 3028, 2922, 1754, 1732, 1515, 1450, 1119, 697 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.97 (2H, s, $C\alpha\underline{H}_2$), 5.34 (1H, s, $C\gamma\underline{H}$), 6.94 (1H, d, *J* = 8.0 Hz, H6), 7.00 (4H, m, $H2^{IV}$ + $H6^{IV}$ + $H2^{V}$ + $H6^{V}$), 7.01 (1H, d, *J* = 8.0 Hz, H7), 7.20 (2H, m, $H4^{II}$ + $H4^{III}$), 7.21 (4H, m, $H3^{IV}$ + $H5^{IV}$ + $H3^{V}$ + $H5^{V}$), 7.29 (2H, m, $H4^{IV}$ + $H4^{V}$), 7.32 ($H3^{II}$ + $H5^{II}$ + $H3^{III}$ + $H5^{III}$), 7.37 (2H, m, $H2^{I}$ + $H6^{I}$), 7.46 ($H2^{II}$ + $H6^{II}$ + $H2^{III}$ + $H6^{III}$), 7.49 (2H, m, $H3^{I}$ + $H5^{I}$); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 51.5 (C$\alpha$), 61.7 (C3), 63.0 (C$\gamma$), 116.3 (C7), 123.4 (C6), 127.1 ($C4^{II}$ + $C4^{III}$), 127.5 ($C4^{IV}$ + $C4^{V}$), 127.6 ($C2^{I}$ + $C6^{I}$), 128.5 ($C3^{II}$ + $C5^{II}$ + $C3^{III}$ + $C5^{III}$), 128.6 ($C3^{IV}$ + $C5^{IV}$ + $C3^{V}$ + $C5^{V}$), 128.7 ($C2^{II}$ + $C6^{II}$ + $C2^{III}$ + $C6^{III}$), 129.1 ($C2^{IV}$ + $C6^{IV}$ + $C2^{V}$ + $C6^{V}$), 130.0 ($C3^{I}$ + $C5^{I}$), 132.2 ($C1^{I}$), 134.0 ($C4^{I}$), 136.7 (C7a), 137.9 ($C1^{IV}$ + $C1^{V}$), 140.1 ($C1^{II}$ + $C1^{III}$), 149.4 (C5), 152.5(C3a), 174.8 (C2), 205.3 (C$\beta$). Anal. Calcd for $C_{54}H_{39}ClN_2O_3$: C, 81.14; H, 4.92; N, 3.50. Found: C, 81.18; H, 4.95; N, 3.57.

## ■ ASSOCIATED CONTENT

### Supporting Information

Copy of $^1H$ and $^{13}C$ NMR spectra of all new compounds as well as a copy of 2D spectra of **2c**, X-ray crystallographic data as well as (CIF) for compound **2a**, and Cartesian coordinates and total energies of all computed species. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data for the crystal structure of **2a** A = Br have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1023943.

## ■ AUTHOR INFORMATION

### Corresponding Author

*Phone: +36-1-3826918. Fax: +36-1-3826297. E-mail: hajos.gyorgy@ttk.mta.hu (G.H.).

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

T.A.R. was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

## ■ REFERENCES

(1) Palkó, R.; Egyed, O.; Riedl, Zs.; Rokob, T. A.; Hajós, Gy. *J. Org. Chem.* **2011**, *76*, 9362.
(2) Riedl, Zs.; Kövér, P.; Soós, T.; Hajós, Gy.; Egyed, O.; Fábián, L.; Messmer, A. *J. Org. Chem.* **2003**, *68*, 5652.
(3) Palkó, R.; Egyed, O.; Bombicz, P.; Riedl, Zs.; Hajós, Gy. *Tetrahedron* **2008**, *64*, 10378.
(4) Staudinger, H. *Chem. Ber.* **1911**, *44*, 1622.
(5) Taylor, E. C.; McKillop, A.; Hawks, G. H. *Org. Synth.* **1972**, *52*, 36.
(6) Kimbrough, R. D. *J. Org. Chem.* **1964**, *29*, 1242.
(7) Ried, W.; Dietrich, R. *Liebigs Ann. Chem.* **1963**, *666*, 113.
(8) Bast, K.; Behrens, M.; Durst, T.; Grashey, R.; Huisgen, R.; Shiffer, R.; Temme, R. *Eur. J. Org. Chem.* **1998**, 379.
(9) Kobayashi, S.; Semba, T.; Takahashi, T.; Yoshida, S.; Dai, K.; Otani, T.; Saito, T. *Tetrahedron* **2009**, *65*, 920.
(10) Sakamoto, M.; Nakai, T.; Yanagishawa, H.; Kawasaki, T. *Heterocycles* **2009**, *77*, 409.
(11) Palkó, R.; Riedl, Zs.; Egyed, O.; Fábián, L.; Hajós, Gy. *J. Org. Chem.* **2006**, *71*, 7805.
(12) Some recently published diaza-Cope rearrangements are: (a) Kim, H.; Chin, J. *Org. Lett.* **2009**, *11*, 5258. (b) Kwon, S. H.; Lee, S. M.; Byun, S. M.; Chin, J.; Kim, B. M. *Org. Lett.* **2012**, *14*, 3664.
(13) Pachecho, J. C. O.; Opatz, T. *J. Org. Chem.* **2014**, *79*, 5182.
(14) Bertina, B.; Rouvier, E.; Cambon, A. *J. Fluorine Chem.* **1994**, *66*, 287.
(15) Weissflog, E. *Phosphorus Sulfur Relat. Elem.* **1981**, *12*, 89.
(16) Ono, N.; Miyake, H.; Saito, T.; Kaji, A. *Synthesis* **1980**, *11*, 952.
(17) Patney, H. K. *Org. Prep. Proced. Int.* **1994**, *26*, 377.
(18) Tanaka, K.; Kaori, A. *Org. Lett.* **2005**, *7*, 1537.
(19) Evans, A. R.; Martin, R.; Taylor, G. A.; Yap, C. H. M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1635.
(20) Abou-Gharbia, M. A.; Jouillé, M. M. *J. Org. Chem.* **1979**, *44*, 2961.
(21) Li, J.-Q.; Liao, R.-Z.; Ding, W.-J.; Cheng, Y. *J. Org. Chem.* **2007**, *72*, 6266.
(22) Giera, H.; Huisgen, R.; Polborn, K. *Eur. J. Org. Chem.* **2005**, 3781.
(23) Cheng, Y.; Ma, Y.-G.; Wang, X.-R.; Mo, J.-M. *J. Org. Chem.* **2009**, *74*, 850.
(24) Nubbemeyer, U. *Synthesis* **2003**, 961.
(25) Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939.
(26) Majumdar, K. C.; Bhattacharyya, T.; Chattopadhyay, B.; Sinha, B. *Synthesis* **2009**, 2117.
(27) Graulich, N. *Wiley Interdiscip. Rev.: Comput. Mol. Sci.* **2011**, *1*, 172.
(28) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *2*, 364.
(29) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724.
(30) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.
(31) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.
(32) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.
(33) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378.
(34) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.
(35) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.
(36) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. *J. Comput. Chem.* **1983**, *4*, 294.
(37) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265.
(38) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision A.02; Gaussian, Inc.: Wallingford, CT, 2009.
(39) de Marothy, S. *XYZ Viewer 0.97*; Stockholm University: Stockholm, Sweden, 2010.
(40) *CrystalClear SM 1.4.0*; Rigaku/MSC Inc.: The Woodlands, TX, 2008.
(41) Higashi, T. *NUMABS*, rev. 2002; Rigaku/MSC Inc.: The Woodlands, TX, 1998.
(42) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112−122.
(43) Spek, A. L. *Acta Crystallogr.* **2009**, *D65*, 148.
(44) Macrae, C. F.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Shields, G. P.; Taylor, R.; Towler, M.; van de Streek, J. *J. Appl. Crystallogr.* **2006**, *39*, 453.