Potentially Aromatic Thiophenium Ylides 3.[+] Cyclization of 2-(2′-Thienyl)benzoylcarbene

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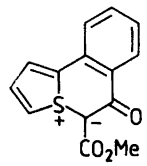
Catalytic decomposition of 2(2′-diazoacetylphenyl)thiophene gives the 4,10*b*-dihydro-inda[1′,2′-1,2]cyclopropa[1,3-*b*]thiophen-6-one (*5*) and the naphtho[1,2-*b*]-thiophen-5-ol (*6*). It is shown that *5* rearranges to *6* under acid catalysis. The mechanisms for the reactions are discussed.



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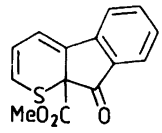

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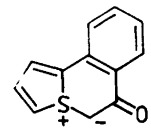

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Cyclic sulfur ylides generated by intra-molecular carbene attack at thiophenic sulfur offer interesting possibilities as novel and potentially aromatic heterocycles. We recently reported our first study in this field on the rhodium(II) acetate catalysed generation and spontaneous rearrangement of the cyclohexa[a]thiophene *1* to the thiopyran *2*[1], and the cyclization of phenyl-2,2′bithienyl-3-yl-carbene.[2]

Here we would like to focus attention on the possibility of producing the ylide without the ester group, e.g. *3*.

Results and Discussion

The necessary carbene precursor of *3* was made by decomposition of 2-(2′-diazoacetylphenyl)-thiophene (*4*), the synthesis of which is outlined in Fig. 1. A dry Gomberg reaction of 2-bromoaniline in thiophene in the presence of isoamyl nitrite afforded 2-(2′-bromophenyl)thiophene in good yield.[3] A Grignard reaction and carboxylation with dry ice gave the corresponding acid which was converted to the acid chloride using thionyl chloride. The conversion to the diazo ketone *4* was achieved in quantitative yield by reaction with diazomethane.

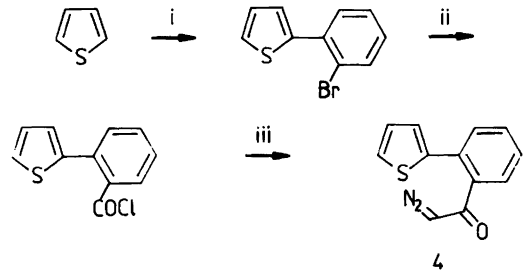

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Fig. 1. Synthesis of 2-(2′-diazoacetylphenyl)thiophene *4*. Reaction conditions: i. *o*-Bromoaniline, isoamyl nitrite, thiophene. ii. Mg, diethyl ether; CO_2, H^+; $SOCl_2$. iii. CH_2N_2, diethyl ether.

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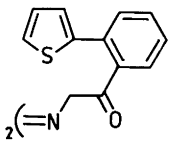
[+]Part 2. See Ref. 2.

When a small amount of rhodium(II) acetate was added to a benzene solution of *4* at room temperature, a rapid evolution of nitrogen took place and within 15 min all the starting material had reacted. An oily product was isolated in 74 % yield by flash chromatography and was identified after extensive use of high field NMR as 4,10*b*-dihydro-inda[1′,2′-1,2]cyclopropa[1,3-*b*]-thiophen-6-one (*5*). The high field part of the ^1H spectrum was first order and selective decoupling permitted assignment of the protons and the coupling constants.[4] The aromatic part was a four spin system and selective decoupling allowed a relative assignment of the protons. Selective irradiation at proton frequencies and observation of NOE effects in the broad band decoupled ^{13}C spectra allowed the heterocorrelations to be made. By using 2-indanone as a model substance for the aromatic part, it was possible to assign all the chemical shifts. Two minor products were also isolated, the fully aromatic naphtho[1,2-*b*]thiophen-5-ol (*6*) (23 %) and the azo compound *7* (2 %). The assignment of the tertiary carbons of the thiophene part of *6* was easy due to the greater coupling constant of the α-carbon. In the ^1H spectrum the resonances at δ 7.60 are slightly broader than those at δ 7.48, indicating that the former have a long range coupling to H4. The benzenoid part of both the ^1H and the ^{13}C spectra was assigned using 1-naphthol as a model substance.



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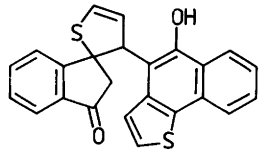
The formation of *5* is consistent with a carbene attack on the thiophenic 2,3-bond. A similar reaction has been realized inter-molecularly by a photolytic reaction between diazo acetic acid and thiophene.[5] On the other hand *5* may have been formed from the desired ylide *3* by a mechanism proposed by Porter, as outlined in Fig. 2.[6]

Here the carbene from *4* cyclizes to sulfur to give *3*. This ylide rearranges through a [1,5]-sigmatropic reaction and produces the zwitterion *8*. In the last step *8* cyclizes to give *5*. The reason why we did not detect the ylide *3* is probably due to its lack of stability – it contains only one electron-withdrawing substituent.

However, all of *6* produced in the reaction cannot come from *5*, the rearrangement of *5* under similar reaction conditions being far too slow. This opens the possibility of a C–H insertion reaction as the primary mechanism for the formation of *6*.Further investigation is in progress to elucidate the mechanism.

When a benzene solution of *5* was treated with catalytic amounts of *p*-toluenesulfonic acid at room temperature, a rearrangement to *6* took place. This reaction is probably the result of protonation of the carbonyl oxygen followed by a ring-opening of the cyclopropane giving the carbenium ion *9* as an intermediate. Ion *9* then rearranges to the more stable carbenium *10* by a Wagner-Meerwein shift and aromatisation gives *6* (Fig. 3).

The driving force for this reaction is considerable: release of ring strain and aromatization of two rings. The formation of *6* was accompanied by a compound which turned out to be the dimer *11*, the structure of which was elucidated by high-field NMR.



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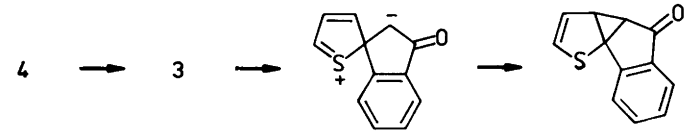

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Fig. 2. Rearrangement of the ylide *3*.

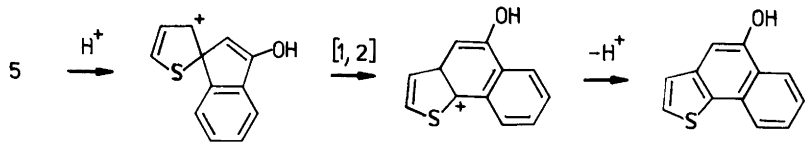
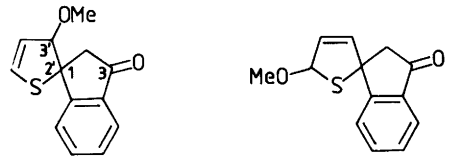


Fig. 3. Acid catalyzed ring-opening of *5*.

As *11* is probably the result of a conserted nucleophilic ring-opening of the cyclopropane *5* by the ambident nucleophile *6*, it was of interest to verify this by conducting the ring-opening in a nucleophilic solvent. If *6* was present when the catalyst was added, the ring-opening was over in min and the reaction produced more of *11* than without *6*. Therefore a methanolic solution of *5* was treated with small amounts of hydrochloric acid. A conversion to a 60:40 mixture of the two spiro compounds *12* and *13* resulted. These could be separated by flash chromatography,[6] but they were later shown to be interconvertible in chloroform with an equilibrium composition of 50:50. The structure of the two isomers was established by high field NMR experiments (NOE) and for *13* differential NOE shows that 3'-H and 2-H together with 7-H and OMe are in the vicinity of each other. This together with the coupling system locks the methoxy group in the 5'-position. The chemical shifts and coupling constants for the AB and ABX parts of the spectra are calculated.

We propose the following reactions for the formation of *12* and *13* (Fig. 4):



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Whether this is a concerted process (a) or a two-step reaction (b) is not clear at the moment, but the fact that both *12* and *13* form and that they equilibrate in chloroform solution points to an ionic mechanism (b) as the main pathway, with the excess of *12* resulting from path (a).

A thermal decomposition of *4* in diglyme at 120 °C gives *6* as the only volatile product. This product may arise from a thermal rearrangement of a primary formed cyclopropane *5*. However, the rate of the reaction from *5* to *6* under similar

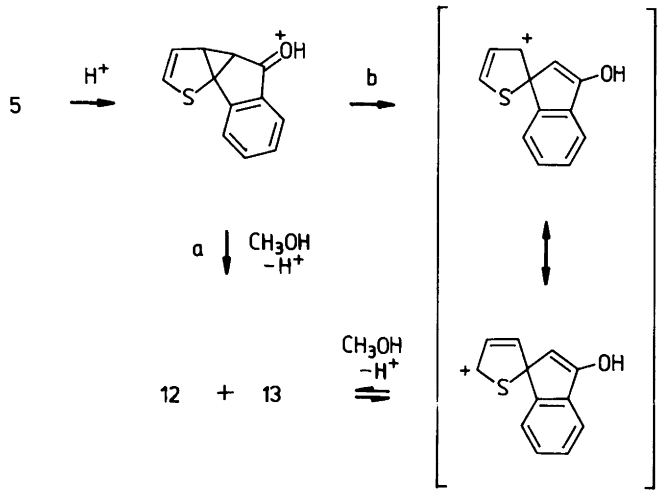

Fig. 4. Nucleophilic ring-opening of *5*.

conditions is 3 times slower. These observations are best accounted for by a C–H insertion reaction as the primary mechanism for the thermal reaction leading to *6*.

We also tried a photochemical decomposition of *4*. Interestingly enough, *6* was produced. But we did not follow this line because the yield was low and all the other products appeared to be polymeric.

We are currently investigating the ring opening reaction of the cyclopropathiophene as well as the properties of the interesting spiro-dihydrothiophenes *12* and *13*.

Experimental

The NMR spectra were recorded on Varian A 60, XL 300 and VM 400 and Bruker CX P200 instruments. The IR spectra were recorded with a Perkin-Elmer 281. The MS spectra were obtained with VG Micromass 7070 F. GLC analyses were carried out with a Hewlett-Packard 5700 A. HPLC analyses were performed with a Perkin-Elmer series 2 liquid chromatograph with a LC 75 detector and with 5 μm LC-18 Supelcosil column. Column chromatography was carried out using Merck no. 9385 Silica 60. The melting points were obtained with a Reichert Thermopan melting point microscope and are uncorrected.

2-(2'-Bromophenyl)thiophene. Isoamyl nitrite (40 g, 0.35 mol) was added to a solution of 2-bromoaniline (40 g, 0.23 mol) in thiophene (500 ml) at 60 °C under nitrogen. The reaction mixture was stirred for 30 min and then treated with a 3 % aqueous solution of sodium bicarbonate, 0.5 M hydrochloric acid and finally with water. The organic layers were dried ($MgSO_4$) and the solvent evaporated to give an oily residue which was distilled. Yield 37 g (67 %), b.p. 98–102 °C/1.3 Pa. ^{1}H NMR (60 MHz, $CDCl_3$): δ 7.3 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 240 (100), 238 (97), 159 (15), 158 (10), 115 (89), 114 (13).

2-(2'-Carboxyphenyl)thiophene. 2-(2'-Bromophenyl)thiophene (20 g, 0.084 mol) in tetrahydrofuran (50 ml) was added to magnesium (2.2 g, 0.092 mol) covered with tetrahydrofuran (25 ml) at 80 °C under nitrogen. The reaction mixture was stirred for 45 min and then quenched in solid carbon dioxide covered with dry diethyl ether. After hydrolysis with 6 M hydrochloric acid, the aqueous phase was taken up in diethyl ether, the ether phase was extracted with 1 M sodium hydroxide and this alkaline aqueous phase was acidified with hydrochloric acid and finally extracted with diethyl ether. After drying ($MgSO_4$) and filtration, the diethyl ether was evaporated to give an oily residue which was crystallized from light petroleum/ethyl acetate. Yield 14.6 g (86 %), m.p. 94.0–95.5 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 7.3 (7H, m), 10.6 (1H, s). MS [IP 70 eV; *m/z* (% rel. int.)]: 205 (11), 204 (100), 187 (21), 171 (37), 115 (29).

2-(2'-Chloroformylphenyl)thiophene. To 2-(2'-carboxyphenyl)-thiophene (10 g, 0.049 mol) was added thionyl chloride (12 g, 0.10 mol). The mixture was stirred for 4 h at room temperature and then the excess thionyl chloride was evaporated and the residue distilled. Yield 8.5 g (77 %), b.p. 111–116 °C/1.3 Pa. ^{1}H NMR (60 MHz, $CDCl_3$): δ 7.4 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 220 (3), 187 (46), 186 (100), 158 (37), 115 (19), 114 (16), 113 (11), 79 (11), 63 (11).

2-(2'-Diazoacetylphenyl)thiophene (4). Diazomethane (Diazald) (3.0 g, 0.070 mol in dry diethyl ether (140 ml) was added to 2-(2'-chloroformylphenyl)thiophene (4.5 g, 0.020 mol) in dry diethyl ether (20 ml) in an ice bath. The reaction mixture was allowed to stand overnight and was the evaporated. The product was recrystallized from ethanol. Yield 4.5 g (98 %), m.p. 98–99 °C. IR (KBr): 2100 cm^{-1} (s). MS [IP 70 eV; *m/z* (% rel. int.)]: 200 (14), 173 (10), 172 (51), 171 (100), 145 (14), 139 (10), 128 (10), 127 (16), 126 (12), 115 (10). ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.1 (1H, s), 7.0 (2H, m), 7.3 (5H, m).

Naphtho[1,2-b]thiophen-5-ol (6). 2-(2'-Diazoacetylphenyl)thiophene (3) (0.25 g, 0.0011 mol) was dissolved in diglyme (50 ml) and kept at 120 °C for 4 h. The solvent was then evaporated and the product sublimed at 100 °C/1.3 Pa. Yield 0.11 g (50 %), m.p. 135–136 °C. MS [IP 70 eV; *m/z* (% rel. int.)]: 201 (16), 200 (100), 172 (22), 171 (66), 127 (10), 100 (10), 86 (8), 85.5 (10, 171/2), 85 (10); m^+ 200 → 172 obs. 148.3, calc. 147.9. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39 (OH, s), 6.94 (H4, s), 7.42 (H7,8, m), 7.48 (H2, d, *J* 5.4 Hz), 7.60 (H3, d, *J* 5.4 Hz), 7.72 (H9, dd, *J* 6.8 and 2.4 Hz), 8.05 (H6, dd, *J* 6.3 and 2.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 105.44 (C4), 121.20 (C3),

123.48 (C6), 124.19 (C7), 124.77 (C2), 125.05 (C5a), 126.07 (C8), 127.06 (C9), 130.15 (C9b), 132.23 (C9a), 139.60 (C3a), 149.03 (C5); *J* (C4, H4) 157.1 Hz, *J* (C4, H2) 5.1 Hz, *J* (C3, H3) 169.3 Hz, *J* (C3, H3) 169.3 Hz, *J* (C3, H1) 4.1 Hz, *J* (C6, H6) 157.7 Hz, *J* (C6, H8) 7.6 Hz, *J* (C7, H7) 160.7 Hz, *J* (C7, H9) 8.6 Hz, *J* (C2, H2) 185.9 Hz, *J* (C2, H3) 6.6 Hz, *J* (C8, H8) 160.2 Hz, *J* (C8, C6) 8.0 Hz, *J* (C9, H9) 160 Hz, *J* (C9, H7) 8 Hz, *J* (C9a, H8) 7.1 Hz, *J* (C9a, H6) 7.1 Hz.

Catalytic decomposition of the diazoketone 4. To 2-(2′-diazoacetylphenyl)thiophene (0.20 g, 0.00088 mol) in benzene (50 ml) was added rhodium(II) acetate (2 mg) at room temperature. After stirring for 20 min, the solution was filtered and the solvent evaporated. The residue was immediately taken up in diethyl ether/hexane and flash chromatographed according to Still[6] with diethyl ether/hexane (60:40) as eluent. This gave 0.13 g (74 %) of an oil which was identified as *4,10b-dihydro-inda-[1′,2′-1,2]cyclopropa[1,3-b]thiophen-6-one* (5). MS [IP 15 eV; *m/z* (% rel. int.)]: 201 (20), 172 (33), 171 (100), 127 (15), 85 (15), 58 (71), 57 (20), 55 (15). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.85 (H2, d, *J* 2.0 Hz), 3.40 (H4, dd, *J* 2.6 and 2.0 Hz), 5.88 (H5, dd, *J* 5.9 and 2.6 Hz), 6.35 (H2, d, *J* 5.9 Hz), 7.36 (H8, m, *J* 7.3, 7.0 and 1.6 Hz), 7.54 (H9, H10, m. 7.65 (H7, d, *J* 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.42 (C5), 47.45 (C10b), 62.78 (C4), 123.67 (C10), 124.23 (C3, C7), 128.06 (C8), 130.08 (C2), 133.54 (C6b), 134.11 (C9), 148.56 (C10a), 200.05 (C6); *J* (C5, H5) 180.6 Hz, *J* (C4, H4) 176.1 Hz, *J* (C4, H5*) 10.5 Hz, *J* (C4, H3*) 8.3 Hz, *J* (C10, H10) 163.8 Hz, *J* (C10, H8) 8.0 Hz, *J* (C8, H8) 164.3 Hz, *J* (C8, H10) 5.4 Hz, *J* (C2, H2) 181.5 Hz, *J* (C2, H3) 7.5 Hz, *J* (C2, H4) 7.5 Hz, *J* (C9, H9) 162.7 Hz, *J* (C9, H7) 6.9 Hz, *J* (C9, H8) 2.8 Hz. Two other products were also separated: 23% of *6* and *2% of 2–thenyl(2-yl-benzoyl)azomethane* (7). MS [IP 70 eV; *m/z* (% rel. int.)]: 430 (3), 382 (16), 380 (16), 366 (21), 237 (19), 221 (19), 201 (24), 200 (91), 188 (16), 187 (100), 173 (22), 172 (18), 171 (59), 147 (16), 139 (16), 127 (15), 125 (15), 115 (63), 113 (15), 111 (29). ^{1}H NMR (200 MHz, Acetone-d_6): δ 4.33 (CH_2, CH_2', s), 7.07 (H4, H4′, dd, *J* 3.6 and 1.6 Hz), 7.16 (H3, H3′, dd, *J* 5.1 and 3.6 Hz), 7.55 (8H, m), 7.62 (H2, H2′, dd, *J* 5.1 and 1.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 47.07 (CH_2), 126.36, 126.82, 127.17 (2x), 127.37, 129.38, 130.32, 131.49(q), 136.79(q), 139.74(q), 197.38 (C=0).

Acid catalyzed decomposition of 5. To a solution of *5* (0.07 g, 0.00035 mol) in benzene (20 ml) was added *p*-toluene sulfonic acid (1 mg) at room temperature. After 3 h the solvent was evaporated and the two products were separated on a silica column with 60 % diethyl ether in hexane. This gave as main product 0.04 g (57 %) of *6* and 0.02 g (29 %) of *4-{spiro[(2′,3′-dihydrothiophen)2′,1-(3-indanon)3′-yl}naphtho[1,2-b]thiophen-5-ol* (11), m.p. 101–105°C. MS [IP 70 eV; *m/z* (% rel. int.)]: 401 (10), 400 (37), 368 (11), 367 (18), 238 (25), 237 (100), 224 (27), 200 (11), 171 (11). ^{1}H NMR (200 MHz, Acetone-d_6): δ 3.25 (H2, d, *J* 19.3 Hz), 3.60 (H2, d, *J* 19.3 Hz), 6.13 (H4′, dd, *J* 6.0 and 2.4 Hz), 6.18 (H5′, dd, *J* 6.0 and 1.9 Hz), 7.06 (H3′, dd, *J* 2.4 and 1.9 Hz), 7.58 (5H, m), 7.73 (H2, d, *J* 5.4 Hz), 7.83 (1H, m), 7.97 (H3, d, *J* 5.4 Hz), 8.09 (1H, m), 8.37 (1H, m), 8.39 (OH, s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.32 (CH_2), 55.52 (CH), 65.84 (spiro), 111.12, 122.14, 122.14, 123.11, 123.25, 120.37, 124.68(q), 125.55 (2x), 125.97, 126.39(q), 127.51, 129.11, 130.67(q), 131.47, 134.88(q), 135.99, 136.31(q), 136.80, 150.04(q), 157.75(q), 202.08 (C=0).

Nucleophilic ring opening of 5. To a solution of *5* (0.13 g, 0.00065 mol) in methanol (20 ml) was added hydrochloric acid (0.1 ml, 0.5 M in methanol). After 20 min the solvent was evaporated and the residue was taken up in diethyl ether and applied on a silica column and eluated with 70 % diethyl ether in hexane. This gave as main product 0.05 g (34 %) of a clear oil identified as *spiro[3-indanon-1,2′-(3′-methoxy-2′,5′-dihydrothiophene)]* (12). MS [IP 70 eV; *m/z* (% rel. int.)]: 233 (14), 232 (100), 201 (21), 200 (10), 187 (20), 173 (14), 128 (18). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.18 (H2, d, *J* 19.4 Hz), 3.33 (H2, d, *J* 19.4 Hz), 3.37 (Me, s), 5.96 (H5′, dd, *J* 6.0 and −0.6 Hz), 5.98 (H4′, dd, *J* 2.5 and −0.6 Hz), 6.37 (H3′, dd, *J* 6.0 and 2.5 Hz), 7.45 (2H, m), 7.67 (2H, m). ^{13}C NMR (50 MHz, $CDCl_3$): δ 53.32 (C2), 54.48 (1″), 64.10 (C1), 95.76 (C3′), 123.12 (C4), 126.11 (C7), 128.83 (C5), 129.01 (C5′), 135.56 (C6), 135.76 (C3a), 140.38 (C4′), 156.93 (C7a), 202.72 (C3); *J* (C2, H2), 135.6 Hz, *J* (C1″, H1″) 146.2 Hz, *J* (C1″, H4′) 5.2 Hz, *J* (C3′, H3′) 167 Hz, *J* (C4, H4) 164.9 Hz, *J* (C4,

H6) 7.7 Hz, *J* (C7, H7) 163.0 Hz, *J* (C7, H5) 7.7 Hz, *J* (C5, H5) 162.2 Hz, *J* (C5, H7) 7.8 Hz, *J* (C5′, H5′) 168.2 Hz, *J* (C5′, H4′) 3 Hz, *J* (C6, H6) 161.0 Hz, *J* (C6, H4), 7.1 Hz, *J* (C4′, H4′) 166.1 Hz, *J* (C4′, H5′) 4 Hz.

The second product 0.03 g (20 %) was identified as *spiro[3-indanon-1,2′-(5′-methoxy-2′,5′-dihydrothiophene)]* (13), m.p. 97–99 °C. MS [IP 70 eV; *m/z* (% rel. int.)]: 232 (14), 232 (100), 201 (18), 200 (12), 187 (20), 173 (13), 171 (11), 128 (17). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.20 (H2, d, *J* 19.8 Hz), 3.16 (H2, d, *J* 19.8 Hz), 5.91 (H3′, dd, *J* 5.9 and 0.7 Hz), 6.01 (H4′, dd, *J* 5.9 and 2.5 Hz), 6.09 (H5′, dd, *J* 2.5 and 0.7 Hz) 7.42 (1H, m), 7.67 (3H, m). ^{13}C NMR (50 MHz, $CDCl_3$): δ 51.01 (C2), 57.21 (C1″), 63.34 (C1), 96.10 (C5′), 122.74 (C4), 126.99 (C7), 128.68 (C3′)*, 128.74 (C5)*, 134.61 (C3a), 135.88 (C6), 140.62 (C4′), 157.88 (C7a), 202.86 (C3), *J* (C2, H2) 134.0 Hz, *J* (C1″, H1″) 142.4 Hz, *J* (C1″, H4′) 4.9 Hz, *J* (C5′, H5′) 163 Hz, *J* (C5′, H4′) 6 Hz, *J* (C4, H4) 166.9 Hz, *J* (C7, H7) 164.2 Hz, *J* (C7, H5) 7.6 Hz, *J* (C6, H6) 162.1 Hz, *J* (C6, H4) 7.1 Hz, *J* (C4′, H4′) 168.6 Hz.

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