

HETEROCYCLES, Vol. 73, 2007, pp. 237 - 240. © The Japan Institute of Heterocyclic Chemistry
Received, 29th June, 2007, Accepted, 30th August, 2007, Published online, 31st August, 2007. COM-07-S(U)43

A NOVEL APPROACH TO 5,5'-DIISOPROPYL-3,3'-BI-2H-CYCLOHEPTA[b]FURAN-2-ONE[†]

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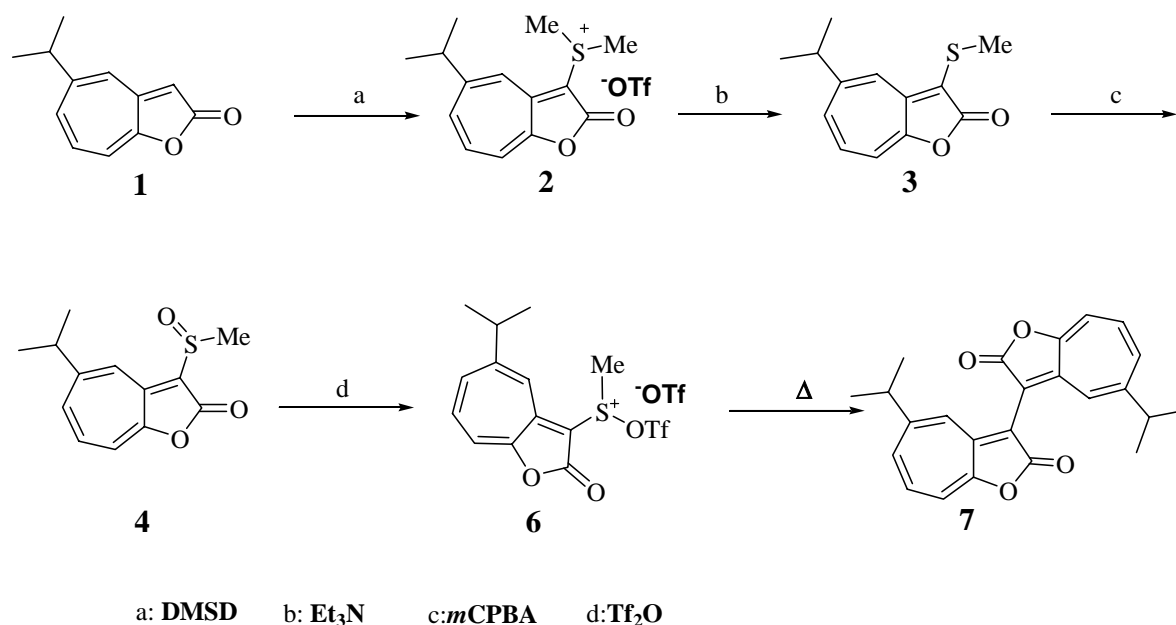
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Abstract— 5-Isopropyl-2H-cyclohepta[b]furan-2-one (**1**) reacted with DMSD to give dimethyl(5-isopropyl-2-oxo-2H-cyclohepta[b]furan-3-yl)sulfonium trifluoromethanesulfonate (**2**), which was treated with Et₃N to give 5-isopropyl-3-methylthio-2H-cyclohepta[b]furan-2-one (**3**). Sulfide **3** was oxidized with *m*CPBA to give sulfoxide **4** and sulfone **5**. The salt **6** which comes from the treatment of **4** with Tf₂O converted to an unexpected product, 5,5'-diisopropyl-3,3'-bi-2H-cyclohepta[b]furan-2-one (**7**), thermally.

2H-Cyclohepta[b]furan-2-ones¹ were known as one of the heteroazulenes. Although there are several reports of electrophilic substitution in azulenes,² reports³ of electrophilic substitution of 2H-cyclohepta[b]furan-2-ones are a very few. 2H-Cyclohepta[b]furan-2-ones were used as precursors of azulenes from long time ago.⁴ Recently, they became to be used as tools for extended π -electronic conjugated systems. New stabilized carbocations and redox systems have been synthesized.³ On account of the synthesis

[†] Dedicate to late Professor Dr. Ivar Ugi.

of new extended π -electronic conjugated systems using 2-oxo-2*H*-cyclohepta[*b*]furan-3-yl group, further research for the reactivity of 2*H*-cyclohepta[*b*]furan-2-one and its derivatives is very important. Previously we reported 2*H*-cyclohepta[*b*]furan-2-one reacted with trifluoromethanesulfonylpyridinium trifluoromethanesulfonate, electrophilically to give 3-dihydropyridinyl-2*H*-cyclohepta[*b*]furan-2-one and subsequent treatment with sodium hydroxide in ethanol gave 3-(4-pyridinyl)-2*H*-cyclohepta[*b*]furan-2-one in excellent yields.⁵ There is not a sulfur derivative of 2*H*-cyclohepta[*b*]furan-2-one as far as I know. Now we will report here another electrophilic substitution reaction of 5-isopropyl-2*H*-cyclohepta[*b*]furan-2-one⁶ (1) with dimethyl(trifluoromethanesulfonyloxy)sulfonium trifluoromethanesulfonate, “dimethyl sulfide ditriflate” (DMSD) which can act as a highly reactive S-electrophile⁷ and conversion to 5,5'-diisopropyl-3,3'-bi-2*H*-cyclohepta[*b*]furan-2-one from this product.



Compound 1 reacted with DMSD which was prepared *in situ* by the reaction of DMSO with Tf₂O to give crude dimethyl(5-isopropyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)sulfonium trifluoromethanesulfonate (2). Purification of 2 is very difficult owing to oil. Crude 2⁹ reacted with triethylamine to give 5-isopropyl-3-methylthio-2*H*-cyclohepta[*b*]furan-2-one (3)¹⁰ as orange oil in 96% yield from 1. Compound 3 was oxidized with *m*CPBA to give sulfoxide 4¹¹ (yellow cryst., mp 88.5-90°C) and sulfone 5¹² (yellow cryst., mp 111-112°C) in 35% and 58% yields, respectively. A solution of Tf₂O in CH₂Cl₂ was added to a solution of 4 in CH₂Cl₂ at 0°C to give a solution of (5-isopropyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)-methyl(trifluoromethanesulfonyloxy)sulfonium trifluoromethanesulfonate (6). After stirring for 30 min at room temperature, the solvent was removed by evaporation to give 5,5'-diisopropyl-3,3'-bi-2*H*-cyclohepta[*b*]furan-2-one (7)¹³ as reddish brown plate crystals (mp 218-219°C, crystallized from 2-propanol) in 68% yield from 4. When compound 1 was added to the solution of 6,

expected product, bis(5-isopropyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)methylsulfonium trifluoromethanesulfonate could not be observed until now. We could get only homocoupling product **7**. It suggests that C3-S bond of sulfonium ion **6** easily cleavages homolytically to give 5-isopropyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-yl radical, followed by dimerization.

Comparing with chemical shifts of seven-member ring protons without at 4-position in compounds **1-7** (see **REFERENCE & NOTES** 8-13), magnitude of low field shifts increases in following order, **1**<**3**<**7**<**4**<**5**<**2**. Sulfur groups work as electron-withdrawing groups in this order. Further optimization of each steps and the research for their reactivity of these products are going on.

In conclusion, although some problems of yields and reaction control still remain, the following dimerizing procedure for compound **1**, electrophilic substitution of **1** with DMSD, demethylation of **2** with Et₃N, oxidation of **3**, activation of **4** with Tf₂O, and radical homocoupling, is accomplished. This process will become a convenient protocol for dimerization 2*H*-cyclohepta[*b*]furan-2-ones without a substituent at 3-position.

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8. **1**; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (bs, 1H, H-4), 6.89 (dd, *J*=9.2 11.2 Hz, 1H, H-7), 6.79 (d, *J*=9.2 Hz, 1H, H-8), 6.69 (d, *J*=11.2 Hz, 1H, H-6), 5.62 (d, *J*=1.2 Hz, 1H, H-3), 2.73 (sept, *J*=6.8 Hz, 1H, -CH(CH₃)₂), 1.17 (d, *J*=6.8 Hz, 6H, -CH(CH₃)₂).
9. **2**; ¹H NMR (400 MHz, CDCl₃) δ 8.13 (d, *J*=1.2 Hz, 1H, H-4), 7.71 (t, *J*=9.6 Hz, 1H, H-7), 7.66 (dd, *J*=9.6, 1.2 Hz, 1H, H-8), 7.57 (dt, *J*=9.6, 1.2 Hz, 1H, H-6), 3.35 (s, 6H, -S⁺(CH₃)₂), 3.25 (sept, *J*=6.8 Hz, 1H, -CH(CH₃)₂), 1.39 (d, *J*=6.8 Hz, 6H, -CH(CH₃)₂).
10. **3**; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J*=1.2Hz, 1H, H-4), 6.99 (dd, *J*=11.2, 9.2 Hz, 1H, H-7), 6.87 (d, *J*=9.2 Hz, 1H, H-8), 6.79 (dd, *J*=11.2, 1.2 Hz, 1H, H-6), 2.89 (sept, *J*=6.8 Hz, 1H, -CH(CH₃)₂), 2.41 (s, 3H, -SCH₃), 1.29 (d, *J*=6.8 Hz, 6H, -CH(CH₃)₂).
11. **4**; ¹H NMR (400 MHz, CDCl₃) δ 8.18 (s, 1H, H-4), 7.37 (dd, *J*=11.2, 9.2 Hz, 1H, H-7), 7.30 (dd, *J*=9.2, 1.2 Hz, 1H, H-8), 7.20 (d, *J*=11.2 Hz, 1H, H-6), 3.16 (s, 3H, -SOCH₃), 3.02 (sept, *J*=6.8 Hz, 1H, -CH(CH₃)₂), 1.32 (d, *J*=6.8 Hz, 6H, -CH(CH₃)₂).
12. **5**; ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, *J*=1.2 Hz, 1H, H-4), 7.65 (d, *J*=10.8, 9.6 Hz, 1H, H-7), 7.58 (dd, *J*=9.6, 1.2 Hz 1H, H-8), 7.47 (dt, *J*=10.8, 1.2 Hz, 1H, H-6), 3.30 (s, 3H, -SO₂CH₃), 3.12 (sept, *J*=6.5 Hz, 1H, -CH(CH₃)₂), 1.36 (d, *J*=6.5 Hz, 6H, -CH(CH₃)₂).
13. **7**; ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, *J*=1.2 Hz, 2H, H-4, 4'), 7.05 (dd, *J*=10.4, 9.2 Hz, 2H, H-7, 7'), 7.01 (dd, *J*=9.2, 1.2 Hz, 2H, H-8, 8'), 6.88 (dt, *J*=10.4, 1.2 Hz, 2H, H-6, 6'), 2.85 (sept, *J*=6.8 Hz, 2H, -CH(CH₃)₂), 1.26 (d, *J*=6.8 Hz, 12H, -CH(CH₃)₂).