Preparation of 8*H*-Furo[3,4-*d*]dibenz[*b*,*f*]azepine. A Novel Heterocyclic Ring system [1]

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The synthesis of 8*H*-furo[3,4-*d*]dibenz[*b*,*f*]azepine **8** from 5*H*-dibenz[*b*,*f*]azepine **1a** is described. The preparation of **8** represents the synthesis of a new heterocyclic system.

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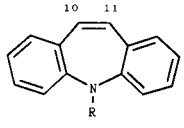
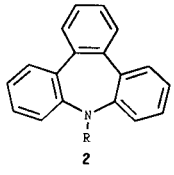
5*H*-Dibenz[*b*,*f*]azepines **1** have been of considerable interest over the years [2], particularly their role as drugs [3]. We have previously reported the reaction of the parent compound **1a** with silver(I) [4] and *t*-butyl hypochlorite [5] and noted the propensity of **1a** to undergo ring contraction at the 10, 11 position to form acridine and acridine derivatives. Others have also noted this ring contraction of **1a** [6].

Since the double bond in the 10, 11 position of **1a** appears to be quite reactive, we decided to investigate the potential of this bond as a participant in the Diels-Alder reaction. We viewed the Diels-Alder adducts of **1** as a possible route to the tribenz[*b*,*d*,*f*]azepine (**2**) ring system. Our



1a R = H
1b R = $COCH_3$

interest in **2** stems from the fact that the double bond at the "10, 11" position would be incorporated in a ring and thus **2** should not be plagued by the ring contraction which occurs in **1a**. Although the 10, 11 position of dibenz[*b*,*f*]azepines is capable of [2 + 2] cycloaddition (dimerization) [7] and [3 + 2] intramolecular cycloaddition [8], we are unaware of any reports concerning the [2 + 4] cycloaddition.



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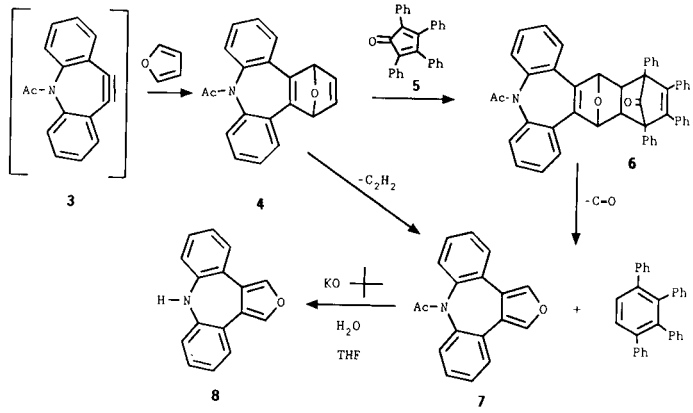
Reaction of **1a** or **1b** with numerous dienes including cyclopentadiene, furan, tetraphenylcyclopentadienone, tetrachlorothiophenedioxide, α,α'-dibromo-*o*-xylene/zinc, 1,3-diphenylisobenzofuran, isobenzofuran, butadiene sulfone and 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene failed and unreacted **1a** or **1b** was recovered. Failure of **1a** and **1b** to react as a dienophile may result from the high electron density of double bond at the 10, 11 position due to the electron releasing nitrogen. The inertness of **1a** as a dienophile is in agreement with the low reactivity of the related system, *Z*-1,2-diphenylethene [9].

Although **1a** and **1b** do not participate as dienophiles in the Diels-Alder reaction, Boykin [10] reported that the alkyne analog **3** (an unstable intermediate) of **1b** reacts with furan to produce the 3,6-epoxy-3,6-dihydrotribenzazepine **4**. With minor modifications, we repeated Boykin's synthesis of **4** from **1a**.

We observed during the melting point determination of **4**, that decomposition takes place with bubbling at 236°. It was also noted that upon subjecting **4** to gc/ms with the gc column temperature at 225°, a single peak with a parent ion at 301 and a fragmentation pattern consistent with **4** is obtained. However, with the column temperature at 250°, a second peak results with a parent ion at 275 and a fragmentation pattern consistent with 8-acetyl-8*H*-furo-[3,4-*d*]dibenz[*b*,*f*]azepine (**7**). The melting point behavior and the gc/ms at 250° are consistent with the loss of acetylene from **4** to produce **7**. This information served as our first indication that **4** was a good candidate for retro-Diels Alder reactions and that the 8*H*-furo[3,4-*d*]dibenz-[*b*,*f*]azepine system (as in **7** and **8**) was stable.

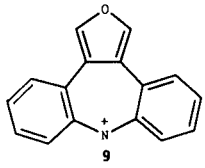
We first attempted to produce **7** by direct thermolysis of **4** above 236°. Analysis of this reaction by gc/ms (under the same conditions where **6** and **7** are observed) produced no peaks. We suspect **7** may be unstable under these conditions and form non-volatile higher molecular weight compounds.

We then proceeded to react **4** with tetraphenylcyclopentadienone (**5**) in refluxing chloroform to form the



Diels-Alder adduct 10-acetyl-4,4a,5,10,15,15a-hexahydro-1,2,3,4-tetraphenyl-5,15-epoxy-1,4-methano-1*H*-dibenzo-[*b*,*f*]naphth[2,3-*d*]azepin-17-one (**6**). Refluxing **6** in *o*-xylene produces **7** and 1,2,3,4-tetraphenylbenzene, presumably by loss of carbon monoxide and a subsequent retro-Diels-Alder reaction. Alternatively, (our present method of choice) **7** can be produced directly by refluxing **4** and **5** in *o*-xylene. Hydrolysis of **7** using potassium *t*-butoxide in water/THF as developed by Gassman [11] gave 8*H*-furo-[3,4-*d*]dibenz[*b*,*f*]azepine (**8**).

Compound **8** is a stable crystalline material with a mp of 120°. Synthesis of the aromatic nitrenium ion **9** from **8** is currently under investigation. We are also exploring the potential of the furan ring of **7** and **8** as the diene participant in Diels-Alder reactions.



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EXPERIMENTAL

5*H*-Dibenz[*b*,*f*]azepine (**1a**) and tetraphenylcyclopentadienone **5** were purchased from Aldrich Chemical Company, Milwaukee, Wisconsin and were used without further purification. The gc/mc were obtained on a Hewlett Packard Model 5995C equipped with a 25 meter fused silica capillary column OV101. Nmr spectra were obtained on a Varian T-60 or a Varian Gemini 200. Infrared spectra were obtained on a Perkin-Elmer 1310. Melting points were obtained on a Mel-Temp apparatus and are uncorrected. Compound **4** was prepared as previously reported [6].

Synthesis of 8-Acetyl-8*H*-furo[3,4-*d*]dibenz[*b*,*f*]azepine (**7**) from the Reaction of Compounds **4** and **5**.

Compound **4** (1.50 g, 5.0 mmoles) and tetraphenylcyclopentadienone **5** (1.88 g, 4.9 mmoles) were refluxed in *o*-xylene (30 ml) for 22 hours. The *o*-xylene was removed *in vacuo*. The residue was stirred in methanol (15 ml) for 1.5 hours. 1,2,3,4-Tetraphenylbenzene was removed by filtration and evaporation of the methanol from the filtrate left the crude **7**. Compound **7** was used in the next step without further purification.

Compound **7** had ^{1}H-nmr (60 MHz deuteriochloroform): 1.9 (s, 3H), 7.2-7.6 (m, 8H), 7.8 (s, 2H, furan); ms: m/z (relative intensity) 275 (33, M+), 233 (100), 204 (13), 176 (4).

8*H*-Furo[3,4-*d*]dibenz[*b*,*f*]azepine **8**.

The entire crude product **7** from above was refluxed with potassium *t*-butoxide (1.12 g, 9.9 mmoles) and water (0.054 ml, 3.0 mmoles) in tetrahydrofuran (20 ml) for 5 minutes. The THF was evaporated and the residue was extracted with methylene chloride and water. The organic layer was dried over sodium sulfate and the solvent removed *in vacuo*. Recrystallization from hexane produced two crops of orange-yellow needle-like crystals of **8** (0.32 g, 41% from **4**) mp 120°. Chromatography on silica gel of the remaining black residue (elution with carbon tetrachloride) afforded an additional (0.17 g, 22% from **4**).

Compound **8** had ^{1}H-nmr (200 MHz deuteriochloroform): 5.3 (s, broad, 1H, NH), 6.82 (d, 2H), 6.96 (dd, 2H), 7.16 (dd, 2H), 7.38 (d, 2H), 7.59 (s, 2H, furan); ^{13}C-nmr (deuteriochloroform): 120.86, 123.56, 123.86, 125.19, 128.32, 129.03, 139.62, 146.17; ms: m/z (relative intensity) 233 (100, M+), 204 (29), 176 (6).

Anal. Calcd. for $C_{16}H_{11}NO$: C, 82.40; H, 4.76; N, 6.01; O, 6.86. Found: C, 82.29; H, 4.82; N, 5.92; O, 6.99.

10-Acetyl-4,4a,5,10,15,15a-hexahydro-1,2,3,4-tetraphenyl-5,15-epoxy-1,4-methano-1*H*-dibenzo[*b*,*f*]naphth[2,3-*d*]azepin-17-one (**6**).

Compound **4** (0.30 g, 1.0 mmole) and 1,2,3,4-tetraphenylcyclopentadienone **5** (0.38 g, 1.0 mmole) were refluxed in chloroform (20 ml) for 4 hours. The chloroform was evaporated *in vacuo* to dryness. Recrystallization from acetone/chloroform (4:1) produced two crops of **6** (0.47 g, 69%) mp 180°.

Compound **6** had ^{1}H-nmr (200 MHz deuteriochloroform): 1.83 (s, 3H), 3.28 (s, 2H), 5.92 (s, 2H), 6.8-7.1 (m, 10H), 7.2-7.7 (m, 18H); ^{13}C-nmr (deuteriochloroform): 22.31, 48.00, 64.71, 84.39, 125.15, 127.33, 127.99, 128.11, 128,94, 129.83, 130.36, 135.52, 136.45, 139.15, 144.40, 146.86, 171.32 (amide carbonyl), 197.63 (ketone carbonyl); ir (potassium bromide): 1775 (ketone carbonyl); 1678 (amide carbonyl).

Acknowledgements.

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REFERENCES AND NOTES

[1] To the best of our knowledge, the furo[3,4-*d*]-*N*-*H*-azepine was a hitherto unknown class of heterocycles.

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