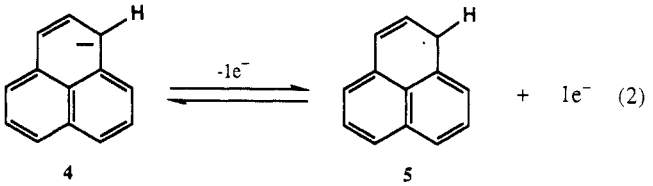
The acidity and redox data necessary to estimate C–H homolytic bond strengths for phenalene (1) and benzanthrene (3), relative to fluorene (2), are shown in Table I.

Consider the acidity data first. Inspection of Table I reveals that DMSO-phase pK_a's for phenalene and benzanthrene are 18.2 and 20.2, respectively.[21] Therefore, for the phenalene framework, replacement of the two vinylic hydrogens in 1 with a fused benzene ring (as in 3) strengthens the indicated bond (in a DMSO-phase heterolytic sense) by 3.4 kcal/mol.[17,22] The data also indicate that, in DMSO, phenalene is 4.9 pK units more acidic than fluorene (2), and, interestingly, only 0.3 pK units more acidic than 1,3-cyclopentadiene (pK_a = 18.0[9]).[17]

The redox data listed in Table I were collected with the aid of second harmonic alternating current voltammetry, a technique that yields "crossing potentials", a parameter similar in interpretation to half-wave potentials for reversible redox couples, for the redox process under consideration.[23] At cyclic voltammetry sweep rates of 0.1 V/s, the oxidation of the phenalenide anion (4 in eq 2), forming the phenalenyl radical (5), is reversible, while the oxidations of the benzanthrenide and fluorenide anions are irreversible. Therefore, on the time scale of the CV experiments, the planar phenalenyl radical is persistent,[24] while the planar benzanthrenyl and fluorenyl radicals are not. It is also of interest to note that, in DMSO solution, the phenalenide anion, compared to the fluorenide anion, is 6.7 kcal/mol *less* basic, yet 12.0 kcal/mol *easier* to oxidize.



4 5

ΔBDE data for phenalene, fluorene, and benzanthrene are also found in Table I. These data reveal that replacement of the two vinylic hydrogens in 1 with a fused benzene ring (as in 3) strengthens the indicated bond (in a DMSO-phase homolytic sense) by ca. 2 kcal/mol, an effect comparable in magnitude to that observed in the gas phase for propene and toluene (C–H BDEs = 86 and 88 kcal/mol, respectively).[25] More significantly, the indicated C–H bond in phenalene is about 18 kcal/mol weaker than the indicated C–H bond in its isomeric analogue, fluorene. Using the 56 kcal/mol constant in eq 1[11] yields an estimate of 64 kcal/mol for the sp^3 C–H bond in phenalene.[26] Previous estimates of the C–H BDE for phenalene have ranged from 48 to 73 kcal/mol.[8] Our value for the C–H BDE for phenalene is within these estimates and is indicative of one of the weakest C–H bonds present in any closed-shell neutral hydrocarbon.[27] The weakness of the sp^3 C–H bond in phenalene seems reasonable in light of the presence of the phenalenyl radical in liquids derived from fossil fuels. However, the small difference in the C–H BDEs for benzanthrene and phenalene does not seem sufficient to fully account for the observed difference in the *kinetic* stabilities of the radicals derived from these species. We are currently examining this issue.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Illinois Department of Energy and Natural Resources, for support of this work.

(17) The pK_a for phenalene was measured vs 9-phenylfluorene and 9-(*p*-tolyl)fluorene.[9] The phenalene pK_a *per hydrogen* is ca 0.5 pK_a units less than the value in Table I, because there are six equivalent sites at which the phenalenide anion can be protonated. The *per hydrogen* pK_a has been inserted into eq 1, and is used when *comparing* acidities of species in Table I. We thank an editor for this suggestion.

(18) A commercially available (Aldrich) sample of fluorene (2) was thrice recrystallized (from ethanol) to a constant melting point.

(19) Arnett et al.[5] obtained a SHACV value of –0.25 V for the fluorenide oxidation in sulfolane/3-methylsulfolane.

(20) The pK_a for benzanthrene was measure vs 9-benzylfluorene and 2-naphthylacetonitrile.[9]

(21) Streitwieser et al.[2] have measured cyclohexylamine-phase pK_a values of 18.5 and 21.4 for 1 and 3.

(22) Replacement of two vinylic hyrogens in cyclopentadiene (pK_a = 18.0) with a fused benzene ring [forming indene (pK_a = 20.1)] results in a similar 2.9 kcal/mol strengthening (in a heterolytic sense) of the appropriate sp^3 C–H bond.[9]

(23) The $E_{1/2}$ value for the reversible CV oxidation of the phenalenide anion is equal to the SHACV crossing potential shown in Table I.

(24) Gerson, F. *Helv. Chim. Acta* **1966**, *49*, 1463–1467.

(25) McMillen, D. F.; Golden, D. M. *Ann. Rev. Phys. Chem.* **1982**, *33*, 493–532.

(26) (a) Kebarle et al.[26b] have estimated that the gas phase sp^3 C–H homolytic BDE for fluorene is 80 ± 5 kcal/mol. The ΔBDE data in Table I therefore suggest that the BDE for phenalene is ca. 62 kcal/mol. (b) McMahon, T. B.; Kebarle, P. *J. Am. Chem. Soc.* **1976**, *98*, 3399–3406.

(27) (a) The gas phase C–H BDE for isotoluene has been determined to be 65±3 kcal/mol.[27b] (b) Bartmess, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 335–337.

Dimethyl Sulfoxide Phase NH Equilibrium Acidities for Urazole and Substituted Urazoles: For Urazole and 1-Substituted Urazoles, Which Proton Is More Acidic?

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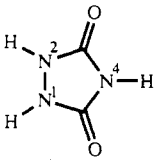
Summary: Determinations of the dimethyl sulfoxide (DMSO) phase pK_a's for urazole (pK_a = 13.1) and various (methylated and phenylated) mono- and disubstituted urazoles indicate that replacement of hydrogen with methyl and/or phenyl acidifies the urazole moiety, indicate that the acidifying effects of these substituents are additive, and suggest that the protons bound to the N-1 and N-4 atoms in urazole are of comparable thermodynamic acidity.

We have undertaken a systematic study of the dimethyl sulfoxide (DMSO) phase pK_a's for urazole[1] (1) and several substituted urazoles. Examination of the structure[2] of 1 reveals two varieties of protons: the protons bonded to



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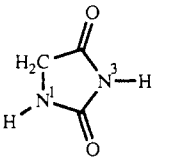

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(1) The IUPAC name for urazole is 1,2,4-triazolidine-3,5-dione.

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Table I. NH Equilibrium Acidity Constants (pK_a's, in Dimethyl Sulfoxide Solution at 25 °C[5]) for Urazole, Substituted Urazoles, and Other Nitrogen Acids

acid	pK_a[6]	indicator acids[7] (no. runs, internal agreement[8])
urazole (1)	13.1	9-$PhSO_2FlH$ (3, 0.02); 9-$EtSO_2FlH$ (3, 0.01)
hydantoin (2)	15.0	9-PhSFlH (4, 0.01); 9-Fl(=O)-2-ClPHZ (2, 0.01)
1-methylurazole (3)	12.2	9-$PhSO_2FlH$ (3, 0.01); 9-$EtSO_2FlH$ (3, 0.01)
1-phenylurazole (4)	9.9	9-CNFlH (3, 0.05); 9-CO_2MeFlH (3, 0.03)
4-methylurazole (5)	12.3	9-$PhSO_2FlH$ (3, 0.02); 9-$EtSO_2FlH$ (3, 0.01)
1,4-dimethylurazole (6)	11.4	9-Fl(=O)-2,4-Cl_2PHZ (3, 0.03); 9-$EtSO_2FlH$ (3, 0.01)
1-phenyl-4-methylurazole (7)	9.0	2-$BrCO_2MeFlH$ (3, 0.06); 9-CNFlH (3, 0.01)
4-phenylurazole (8)	11.0	9-$PhSO_2FlH$ (3, 0.01); 9-CO_2MeFl (2, 0.03)
1-methyl-4-phenylurazole (9)	10.15	9-CO_2MeFlH (3, 0.02); 2-$PhSO_2$-9-(*p*-$tolSO_2$)FlH (1)
1,4-diphenylurazole (10)	7.9	2-$BrCO_2MeFlH$ (3, 0.03); 9-CNFlH (2, 0.01)
1,2-dimethylurazole (11)	12.35	9-Fl(=O)-2,4-Cl_2PHZ (3, 0.01); 9-$EtSO_2FlH$ (3, 0.001)
1-methylhydantoin (12)	14.7	reference 5

N-1 and N-2 atoms (i.e. amide protons), and the proton bonded to N-4 (i.e. the imide proton). While aqueous phase acidity data for selected urazoles have suggested that the amide proton found in 1-phenylurazole is about 100 times more acidic than the imide proton in the same species,[3] we have found few other data for these and related protonated on nitrogen species.[4a,b] In this paper we report DMSO-phase acidity constants for urazole as well as selected substituted urazoles and hydantoins. Comparisons of the acidity constants for these species enable determinations of the relative lability of the amide and imide NH protons for urazole and 1-substituted urazoles, in an acid–base heterolytic sense. Our analyses of DMSO-phase acidity data for urazole and several substituted urazoles suggest that thermodynamic acidities for the amide and imide protons present in 1 are in fact comparable in magnitude.

Inspection of Table I reveals that the DMSO-phase pK_a for urazole (1) is 13.1. The fact that 1 (in DMSO) is ca. 2 pK units more acidic than hydantoin (2, pK_a = 15.0) may be due to the fact that resonance structures for the urazole monoanion incorporate π electrons from all five atoms in the urazole heterocycle, enabling greater delocalization of the negative charge (the ring system in the hydantoin monoanion contains a methylene group). Evidence for the importance of the ring structure in urazole can be inferred from comparisons of urazole acidity data with values for DMSO-phase pK_a's for urea and ammonia. While urazole is ca. 14 pK units more acidic than urea (pK_a = 27.0),[5] urea is also ca. 14 pK units more acidic than ammonia ($pK_a \approx$ 41.0).[9] The lack of any saturation effect for substitution of a second C(O)NH group onto the ammonia substrate is further evidence for an enhanced stabilization of the anion derived from 1, a stabilization due in part to the cyclic nature of 1 and its conjugate base.

Inspection of Table I reveals that replacement of hydrogen with phenyl and/or methyl substituents at N-1 and/or N-4 acidifies the urazole moiety. Acidifying methyl effects of this type, while unusual, are not unprecedented. The data also suggest that the acidifying effects of phenyl and/or methyl substituents at N-1 and N-4 are additive. For example, while 1-phenylurazole and 4-phenylurazole (pK_a's = 9.9 and 11.0, respectively) are 3.2 and 2.1 pK units more acidic than urazole (1, pK_a = 13.1), 1,4-diphenylurazole (pK_a = 7.9) is 5.2 units more acidic than 1. Similar additivities hold for the other disubstitued urazoles present in Table I (i.e. 1,4-dimethylurazole, 1-methyl-4-phenylurazole, and 1-phenyl-4-methylurazole). Since the only NH proton(s) present in **5–10** are amide protons, the aforementioned additivities strongly suggest that the amide protons present in **1**, **3**, and **4** are at least as acidic as the imide N-4 proton in these species. The observed additivities also point to a lack of involvement of protonated-on-oxygen tautomers in the DMSO-phase monoanions derived from **1**, **3–5**, and **8**, since the monoanions derived from **6**, **7**, **9**, and **10** lack the presence of even a single acidic NH proton.

Other comparisons are helpful when evaluating the relative acidities of the amide and imide protons in urazole and 1-substituted urazoles. First, comparison of acidity constants for hydantoin (2, pK_a = 15.0) and 1-methylhydantoin (pK_a = 14.7) reveals that substitution of methyl for hydrogen in the hydantoin framework acidifies the hydantoin imide proton by 0.3 pK units. Second, replacement of one of the hydrogen atoms in urea (pK_a = 27.0) with methyl (as in methylurea, pK_a = 26.85) acidifies the urea moiety, after statistical correction, by 0.45 pK units. Therefore, since the pK_a for 1,2-dimethylurazole (11), a species possessing only the N-4 imide proton, is 12.35, a reasonable prediction for the pK_a of the N-4 imide proton in urazole itself is about 13 (the measured value for urazole is 13.1).

On the other hand, acidity data for 4-methylurazole (pK_a = 12.3) and 1,4-dimethylurazole (pK_a = 11.4), species that contain only amide protons, suggest that replacement of hydrogen on N-1 with a methyl group acidifies the urazole moiety by 0.9 pK units. Therefore, if the amide proton is considered to be the most acidic proton in urazole, then one would expect that 1-methylurazole would be about 0.9 pK units more acidic than urazole. Examination of the data in Table I (pK_a for 1-methylurazole = 12.2) confirms this expectation, since a value of 13.1 has been measured for the pK_a of urazole. The data therefore suggest that the thermodynamic acidities of the amide N-1 and imide

(2) Spectroscopic data [^{1}H NMR (in DMSO-d_6) and IR] are consistent with numerous literature observations suggesting that urazole and substituted urazoles exist in the dioxo form as represented in 1 for urazole.

(3) Gordon, A. A.; Katritzky, A. R.; Popp, F. D. *Tetrahedron Supp. No. 7* 213–217.

(4) (a) Ohashi, S.; Leong, K.; Matyjaszewski, K.; Butler, G. B. *J. Org. Chem.* **1980**, *45*, 3467–3471. Gordon, P. G.; Audrieth, L. F. *J. Org. Chem.* **1955**, *20*, 603–605. (b) The aqueous phase pK_a's for urazole and hydantoin are 5.8 and 9.0, respectively.[4c] (c) Bausch, M. J.; Selmarten, D.; Gostowski, R.; Dobrowolski, P. *J. Phys. Org. Chem.*, submitted for publication.

(5) The acidity data in Table I are not statistically corrected and were collected using the Bordwell–Matthews overlapping indicator method for DMSO-phase acidities. For a recent review on the DMSO-phase acidity scale, see: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(6) The pK_a's in Table I are accurate to ±0.1 pK unit.

(7) Abbreviations for indicator acids in Table I: 9-$PhSO_2FlH$ = 9-(phenylsulfonyl)fluorene; 9-$EtSO_2FlH$ = 9-(ethylsulfonyl)fluorene; 9-CNFlH = 9-cyanofluorene; 9-CO_2MeFlH = 9-(methoxycarbonyl)fluorene; 2-Br-9-CO_2MeFlH = 2-bromo-9-(methoxycarbonyl)fluorene; 2-$PhSO_2$-9-(*p*-$tolSO_2$)FlH = 2-(phenylsulfonyl)-9-(*p*-tolylsulfonyl)fluorene; 9-PhSFlH = 9-(phenylthio)fluorene; 9-Fl(=O)-2-ClPHZ = 9-fluorenone 2-chlorophenylhydrazone; 9-(Fl=O)-2,4-Cl_2PHZ = 9-fluorenone 2,4-dichlorophenylhydrazone; 9-PhXnH = 9-phenylxanthene.

(8) The internal agreement refers to the standard deviation between runs for the measured pK's with a given indicator. Each run (titration) consists of at least three data points.

(9) Bordwell, F. G.; Drucker, G. E.; Fried, H. E. *J. Org. Chem.* **1981**, *46*, 632–635.

N-4 protons in urazole are similar, and that the amide N-1 proton in 1-methylurazole is about 0.5 pK units more acidic than the imide N-4 proton contained in that species. We are less certain of the relative DMSO-phase acidities of the amide and imide protons in 1-phenylurazole. An assumption that the ratio of the acidifying effect of a 4-phenyl substituent (on an amide proton) to the acidifying effect of a 1-phenyl substituent (on an imide proton) will be similar to what was observed in the case of 4-methyl and 1-methyl substituents (where the 4-methyl substituent acidifies the amide proton by 0.8 pK units, while the 1-methyl substituent acidifies the imide proton by ca. 0.4 pK units, a ratio of 2:1) leads to the prediction that the pK_a of the imide proton in 1-phenylurazole is about 12. Comparison of the measured acidity constant for the amide proton in 1-phenylurazole (pK_a = 9.9) with the estimate for the imide NH acidity constant in 1-phenylurazole suggests that the difference in the acidity constants for the two protons in 1-phenylurazole is about 2 orders of magnitude, a difference that agrees nicely with Katritzky's estimates for the relative acidities of these protons in water.[3]

In further attempts to better understand structural features of the monoanions derived from urazoles **1–12**, we are presently engaged in NMR and UV spectroscopic investigations of these species. Also underway are studies of the homolytic strengths of amide and imide N–H bonds in urazole and substituted urazoles, and studies of the acidities and stabilities of the incipient urazolyl radicals. Preliminary results indicate that the N-1–H (amide) bond in urazole is ca. 15 kcal/mol weaker (in a homolytic sense) than the N-4–H (imide) bond in the same species.[10]

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the United States Army Research Office (Contract No. DAAL-03-90-G-0046), and the Southern Illinois University Materials Technology Center for support of this work.

(10) Bausch, M. J.; David, B.; Prasad, V.; Vaughn, A. *J. Phys. Org. Chem.*, submitted for publication.

Stereoselective Oxidative Spiroketalization of a *C*-Arylglucal Derived from Palladium-Catalyzed Coupling. Synthesis of the *C*-Arylglucoside Spiroketal Nucleus of the Papulacandins

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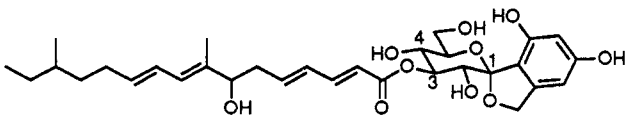
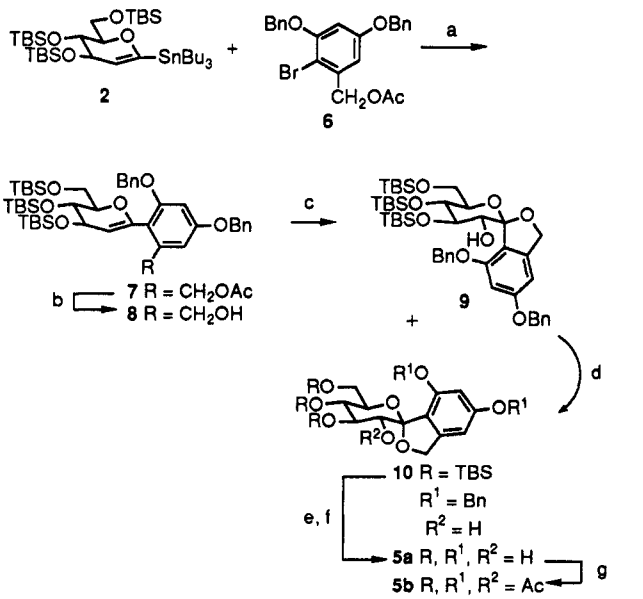
Summary: The synthesis of the *C*-arylglucoside tricyclic spiroketal nucleus of the papulacandins **5b** was achieved utilizing two key steps, namely the palladium-catalyzed coupling of the aryl bromide **6** and the stannyl glucal **2** and stereoselective oxidative spiroketalization of the derived *C*-arylglucal **7**.

There has been a great deal of interest in recent years in the synthesis of *C*-arylglycosides since many of the natural products that contain this novel structural framework exhibit antibiotic or antiviral activity.[1] In 1976, Traxler and co-workers isolated a series of four closely related antifungal antibiotics, named papulacandins A–D, from *Papularia sphaerosperma*.[2] The mechanistic basis for the inhibitory activity of papulacandin B toward the growth of the fungus *Geotrichum lactis* was traced to a penicillin-like ability to inhibit glucan synthesis during the manufacture of the cell wall.[3] Papulacandin D (**1**),[4] the simplest member of the family, illustrates the unique, and synthetically challenging, structural feature common to all



1 Papulacandin D

Scheme I[a]



[a] Reaction conditions: (a) $Pd(Ph_3P)_2Cl_2$ (5 mol %), see text for conditions; (b) LAH, Et_2O, 0 °C; (c) DMDO, CH_2Cl_2; (d) PPTS, $CHCl_3$, room temperature; (e) H_2, P on C (10%), EtOAc, 40 °C; (f) TBAF, THF, room temperature; (g) Ac_2O, py, DMAP, room temperature.

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(3) (a) Baguley, B. C.; Rommele, G.; Gruner, J.; Wehrli, W. *Eur. J. Biochem.* **1979**, *97*, 345. (b) Perez, P.; Varona, R.; Garcia-Acha, I.; Duran, A. *FEBS Lett.* **1981**, *129*, 249. (c) Rommele, G.; Traxler, P.; Wehrli, W. *J. Antibiot.* **1983**, *36*, 1539.

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