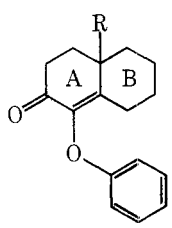
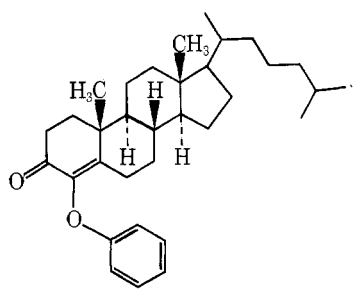
Heteroatom Directed Photoarylation. Stereochemistry of Aryloxyenone Photocyclization

Summary: Aryloxyenones **1a, 1b,** and **2** undergo high yield photocyclization–rearrangement to dihydrofurans **3, 8,** and **6,** with a *cis*-decalone ring fusion, via the relatively strain-free carbonyl ylide intermediate **7a.**

Sir: A structural feature common to the morphine, hasubanan, and aspidosperma alkaloids is the presence of an aryl nucleus at a ring junction carbon atom. A highly desirable tactic for synthesis of these alkaloids is the direct bonding of an aryl nucleus to a carbon atom already located at a ring junction. However, few pertinent synthetic methods presently exist, and with these, regiochemical and stereochemical problems can be anticipated. In this regard, photocyclization of aryl vinyl ethers seemed to possess considerable synthetic potential,[1] and our interest in the total synthesis of medicinally important alkaloids provided stimulus for investigation of the photochemistry of fused-ring aryloxyenones, e.g., **1a, 1b,** and **2.**[2]



1a, R = CH_3
b, R = $CO_2CH_2CH_3$



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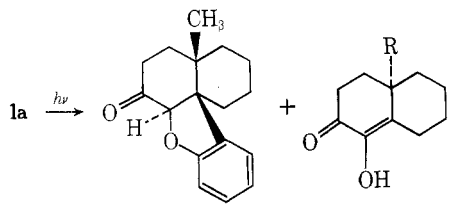
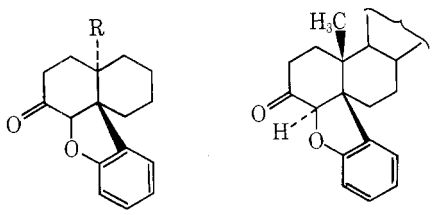
Herein, we report the remarkable stereochemical control possible with aryl vinyl heteroatom photocyclization (heteroatom directed photoarylation)[3] and discuss factors responsible for observed stereoselectivity.

Pyrex-filtered irradiation of **1a** in degassed benzene solution saturated with *p*-toluenesulfonic acid gave two major photoproducts: dihydrofuran **3** (90% isolated yield) and diketone **4** (R = CH_3, 4–5%). VPC analysis indicated that three unidentified products also were present; however, none exceeded 1% of the total reaction components. Significantly, only dihydrofuran **3** possessing a *cis*-decalone ring system was isolated and none of the isomeric dihydrofuran **5** (R = CH_3) with a *trans*-decalone ring system could be detected; examination of NMR spectra of **1a** photoreactions indicated that formation of **5** could have been detected at a 1% level. Thus, the stereoselectivity of photocyclization of **1a** must be of the order of 90:1.

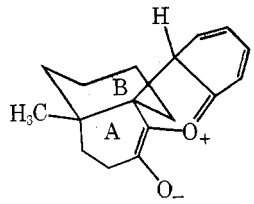


3 **4**

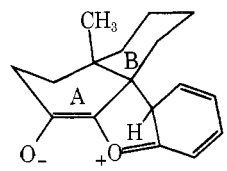


5 **6**

We feel that the origin of this remarkable stereoselectivity may be a result of relative ring strain in carbonyl ylides **7a** and **7b,** which are hypothetical intermediates in the conversions



7a

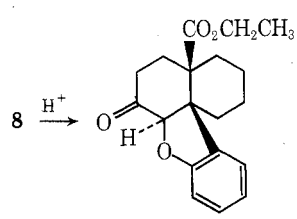


7b

1a → **3** and **1a** → **5,** respectively.[1] Conrotatory photocyclization[4] of **1a** via an orientation resulting from approach of the aryl nucleus toward the β face of the enone system would give **7a,** while conrotatory cyclization from an approach toward the α face would give **7b.** Clearly, existence of a planar π-electron system in **7** imposes a great deal of ring strain in configuration **7b,** but relatively little in **7a;** on the basis of unfavorable ring strain in **7b,** photocyclization of **1a** would be expected to preferentially lead to carbonyl ylide intermediate **7a,** the precursor of isolated *cis*-decalone **3.**

Having established a reasonable hypothesis for stereoselective control in photocyclization of **1a,** we sought to test the generality of control by structural modifications of **1a,** e.g., **1b** (steric alteration) and **2** (ring strain alteration).

Approach of the aryl nucleus toward the β face of the enone system during cyclization of **1a** results in little steric interaction with the angular methyl group. Replacement of the methyl group with an exceedingly bulky carbethoxy group (i.e., **1b**) might be expected to hinder β-face approach and result in a loss of the stereoselectivity encountered with **1a.** However, when **1b** was irradiated in benzene solution saturated with *p*-toluenesulfonic acid, no *trans*-fused decalone (i.e., **5,** R = $CO_2CH_2CH_3$) could be detected; *cis*-fused decalone **8** (40% yield), *cis*-fused decalone **9** (3%), and diketone **4** (R =



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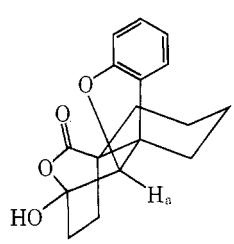

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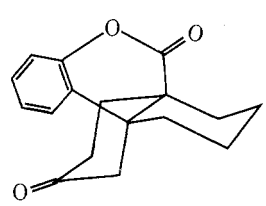

11

$CO_2CH_2CH_3$, 14%) were produced, together with a good deal of polymer.[5] Interestingly, polymer formation was eliminated in benzene–methanol–acetic acid solution (equal volumes of each solvent component);[1] formation of **8** (29%) and **9** (35%) and extensive ether cleavage (35%) was noted. Formation of *cis*-fused decalone **8** (67% yield), with no evidence for formation of **9** or **4** (R = $CO_2CH_2CH_3$), occurred when irradiation (366 nm) of **1b** was performed in benzene solution in the presence of the triplet sensitizer benzophenone.

Assignment of stereochemistry in **3, 6,** and **9** is based on NMR spectral data and chemical reactivity. Thus, in the NMR spectra of **3, 6,** and **9,** H_a appears as a sharp singlet at 4.43, 4.50, and 4.43 ppm, respectively. In that for **8,** H_a appears at 5.10 ppm and experiences W coupling (J_{ab} = 1.5 Hz). While **8** and **9** are not thermally interconvertible below 140 °C (refluxing xylene solution), **8** undergoes transformation into **9** in refluxing benzene solution saturated with *p*-toluenesulfonic acid (half-life ~5 h) or refluxing benzene–acetic acid solution (equal volumes of each solvent component, half-life ~14 h). Treatment of either **8** or **9** with 1 N potassium hydroxide in methanol followed by acidification gave a single lactol **10** (mp 232–233 °C).[5] NMR absorption for H_a in **10** appears as a sharp singlet at 4.25 ppm. Finally, **8** and **9** give lactone **11** (ir 5.69 and 5.80 μ) on treatment with zinc dust in refluxing propionic acid solution.[1]

In contrast to conversions **1** → **7a,** in which ring B may assume a chair conformation, conrotatory photocyclization of **2,** to give a cis-AB ring fusion, must result in a carbonyl ylide possessing a ring-B boat conformation. On the other hand, cyclization of **2,** to give a trans-AB ring fusion, would maintain the ring-B chair conformation present in **2.**[6] A carbonyl ylide derived from **2,** with a trans-AB ring fusion, would be expected to have approximately the same ring strain as hypothetical **7b,** while a carbonyl ylide with a cis-AB ring fusion should be somewhat more strained than **7a.** If the additional ring strain imposed on **7a** is significant, then photocyclization of **2** might be expected to be less stereoselective than that of **1a.** In fact, photolysis of **2** did not produce a dihydrofuran with a trans-AB ring fusion, but rather gave cis-fused **6** in high yield along with a small amount of ether cleavage.

Thus, our studies with **1b** indicate that, while replacement of the methyl group in **1a** with the bulky carbethoxy group does seem to make photocyclization less facile (note extensive ether cleavage in **1b**), this steric alteration does not lead to a detectable inversion in stereoselectivity of carbonyl ylide formation. Furthermore, the constraints imposed by the steroid framework in **2,** which would seem to operate in discord with formation of a cis-AB ring fusion, also do not alter stereoselectivity of carbonyl ylide formation. In general then, photocyclization–rearrangement of 1-aryloxy-$\Delta^{1(9)}$-octalone-2 systems should produce a dihydrofuran possessing a *cis*-decalone ring fusion. Application of the principles discussed here to the synthesis of complex organic molecules along with a detailed investigation of excited singlet and triplet state reactivity in aryloxyenones is currently being investigated.

Acknowledgment. This work was supported by the National Institutes of Health (Grant No. GM 21159-01). We thank Professor Albert Eschenmoser for a stimulating and helpful discussion during the early stages of this work. Assistance in the synthesis of **1b** and **2** by undergraduate research participants B. Gail Kurr and Cathy Stein is gratefully acknowledged.

References and Notes

(1) A. G. Schultz and R. D. Lucci, *J. Org. Chem.*, **40,** 1371 (1975).
(2) Aryloxyenones **1a** (mp 71–73 °C) and **2** (mp 122–123 °C) were prepared from phenol and the corresponding epoxy ketone by a method previously reported,[1] while preparation of **1b** (mp 62–64 °C) followed an annelation approach from ethyl 2-cyclohexanonecarboxylate and 1-phenoxy-3-buten-2-one, the details of which will be described elsewhere.
(3) The methodological term heteroatom directed photoarylation is intended to characterize photochemically initiated electrocyclic reactions, which, by influence of an appropriate heteroatom, result in bond formation between two atoms at least one of which initially resides in an aromatic nucleus. In the present case, formation of a *carbon-carbon* bond is "directed" by an oxygen atom to give a dihydrobenzofuran. It should be noted that a variety of previously studied photoreactions may be considered to belong to this general reaction classification. To cite a few, the elegant investigation of "non-oxidative photocyclization" of *N*-aryl enamines [O. L. Chapman, G. L. Elan, A. Bloom, and J. Clardy, *J. Am. Chem. Soc.*, **93,** 2918 (1971)] and the photocyclization of benzoic acid anilides [B. S. Thyagarajan, N. Kharasch, H. B. Lewis, and W. Wolf, *Chem. Commun.*, 615 (1967)], acrylic acid anilides [P. G. Cleveland and O. L. Chapman, *ibid.*, 1064 (1967)], and biaryl isocyanates [J. S. Swenton, T. J. Ikeler, and G. LeRoy Smyser, *J. Org. Chem.*, **38,** 1157 (1973)] are well-known examples.
(4) A. G. Schultz and M. B. DeTar, *J. Am. Chem. Soc.*, **96,** 296 (1974).
(5) The acid- or base-catalyzed conversion of **8** to **9** must occur as a result of enolization at the carbon bearing H_a. We assume that tautomerization will occur to give the stable *cis*-dihydrofuran ring fusion in **9** as shown; see ref 1. Remaining stereochemical assignment in **8** must await further structural studies.
(6) Crystallographic studies with progesterone [H. Campsteyn, L. Dupont, and O. Dideberg, *Acta Crystallogr.*, **B28,** 3032 (1972)], testosterone [G. Precigouz et al., *Cryst. Struct. Commun.*, **2,** 435 (1973)], and 26-hydroxycholestenone *p*-bromobenzoate [E. Caspi et al., *J. Am. Chem. Soc.*, **93,** 6283 (1974)] demonstrate that ring B in all of these compounds assumes a chair conformation.
(7) Postdoctoral research associate 1973–1975.

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1,4,5,8-Tetrathiatetralin, a Tetrathiafulvalene Isomer

Summary: 1,4,5,8-Tetrathiatetralin (**2**) has been obtained by a four-step synthesis from carbon disulfide. Compound **2,** unlike the isomeric tetrathiafulvalene (**1**), is not readily oxidized to a cation radical.

Sir: Tetrathiafulvalene (**1**) and its selenium analogs have been the subject of great interest, since they are valuable π donors in the preparation of charge-transfer salts having metallic properties.[1] The hitherto unknown 1,4,5,8-tetrathiatetralin (**2**)[2] is an isomer of **1** which differs structurally from the latter only in the arrangement of the two ethyne bridges. We now report the first synthesis of **2** and some physical and electrochemical properties of this substance.

Electrochemical reduction of carbon disulfide to the dianion **3,**[3] followed by alkylation with 1,2-dibromoethane, gave (18%) trithiocarbonate **4** as golden plates, mp 121.5–122.5 °C. Hydrolysis of **4** by hot ethanolic potassium hydroxide, followed by alkylation with 1,2-dibromoethane, gave (70%) the tetrahydro derivative **5** of **2** as white needles, mp 154–156 °C. Compound **5** was dehydrogenated by refluxing overnight with DDQ in xylene to give, after silica chromatography, the dihydro derivative **6** of **2** (45%) as pale yellow needles, mp 80–81 °C, as well as **2** itself (37%) in the form of lemon yellow needles: mp 125–126 °C; $\lambda_{max}^{cyclohexane}$ 235 nm (ϵ 8000), 248 (sh, 6100), 270 (sh, 5000).

Although **2** may be viewed as a potentially aromatic 14-π-electron system, its NMR spectrum ($CDCl_3$) shows a singlet at δ 6.46 ppm, a position very close to that (6.55) of the olefinic protons of its dihydro derivative **6.** This observation suggests that **2,** like the parent monocyclic analog *p*-dithiin,[4] lacks aromatic stabilization and thus, may possess a nonplanar conformation.

Moreover, in sharp contrast to **1, 2** is not readily oxidized by tetracyanoquinodimethane to give a radical ion charge-transfer salt. A quantitative measure of this difference in