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Conformational Control and Photoenolization of Pyridine-3-carboxaldehydes in the Solid State: Stabilization of Photoenols via Hydrogen Bonding and Electronic Control

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We have investigated the solid-state photobehavior of a broad set of pyridine-3-carboxaldehydes **1**−**5**. The introduction of a heteroatom into mesitaldehydes as in aldehydes **1** raises the question of conformational preference in the solid state. The preferred conformations have been unequivocally established from X-ray crystal structure analyses of two of the aldehydes, **1c** and **2c**; it is shown that intramolecular hydrogen bonding could be utilized to achieve conformational control. In contrast to mesitaldehydes, which undergo efficient photocyclization to benzocyclobutenols in the solid state, the heteroatom analogues **1b** and **1c** exhibit a perceptible color change (from colorless to pale yellow for **1b** and yellow-orange for **1c**) upon UV irradiation; the color attributed to (*E*)-enols is persistent for several hours. Continued irradiation leads to an intractable polymeric material. The AM1 calculations, which have been reliably applied to the thermal cyclization of xylylenols to benzocyclobutenols, reveal that the (*E*)-enols of **1** are more stable than those of the mesitaldehydes relative to their corresponding benzocyclobutenols. The stabilization is interpreted as arising from the possibility of engaging the heteroatom in resonance delocalization. That the contribution from such a role of the nitrogen atom is so pronounced is elegantly demonstrated by forming the fluoroborate salts; **1a-HBF$_4$** and **1b-HBF$_4$** readily exhibit highly red-shifted absorption upon exposure to UV radiation as a result of stabilization of the photoenols. Notably, such a remarkable stabilization via *electronic control* of the photoenols is unprecedented. All of the 2-methoxy- and 2-chloro-substituted aldehydes **2**−**5** exhibit photochromism. Ab initio calculations show that the methoxy group in aldehydes **2** and **3** stabilizes the (*E*)-enols via O−H···O *hydrogen bonding* as compared to those of **1** by 5−6 kcal/mol relative to their corresponding benzocyclobutenols. Thus, the presence of methoxy and halo groups at position 2 serves not only to direct the formyl oxygen toward the methyl group for H-abstraction but also to stabilize the (*E*)-enols.

Introduction

The solution- and solid-state photochemistry of *o*-alkyl aromatic ketones has been thoroughly examined;[1−6] the synthetically useful benzocyclobutenols are invariably isolated as photoproducts from both media. In contrast, the solution-state photochemistry of *o*-alkyl aromatic aldehydes is marked by the formation of several photoproducts. For example, the simple *o*-methylbenzaldehyde, a representative case, has been found to afford as many as seven photoproducts depending on the conditions of irradiation.[7,8] The solid-state photochemistry, on the other hand, has been explored very little.[9,10] Our recent systematic investigations on crystalline mesitaldehydes have shown that photochemical formation of benzocyclobutenols from *o*-alkyl aromatic aldehydes proceeds via thermal conrotatory closure of the intermediate *o*-xylylenols/photoenols (Scheme 1).[11] Accordingly, the colored *o*-xylylenols from *o*-anisaldehydes, capable of intramo-

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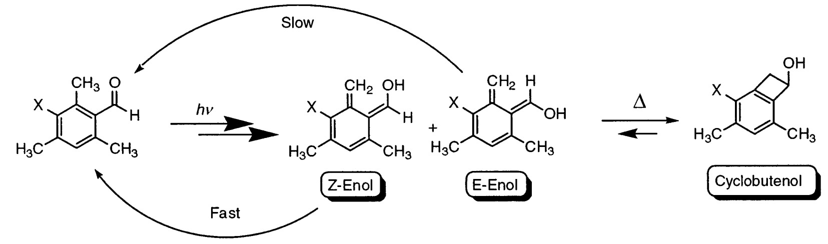
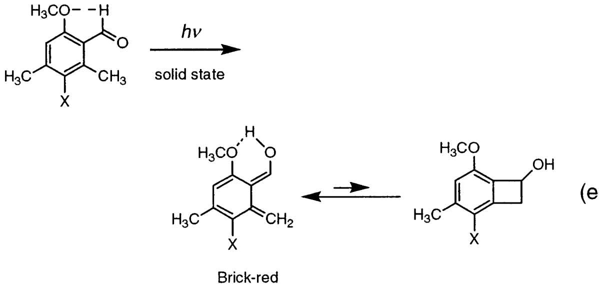
SCHEME 1

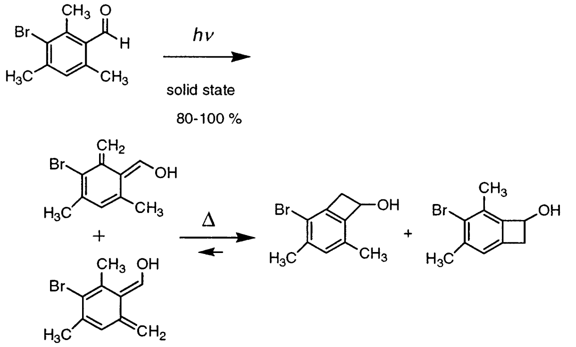


lecular stabilization via hydrogen bonding, lend themselves to the observation of photochromism (eq 1).[12]

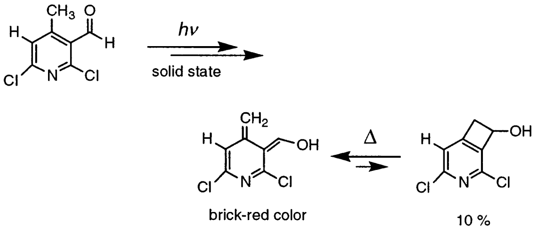


(eq 1)

On the other hand, the photoenols formed from halogen-substituted mesitaldehydes,[11] lacking any stabilizing influences, undergo efficient cyclization to synthetically useful benzocyclobutenols[13−18] (eq 2).

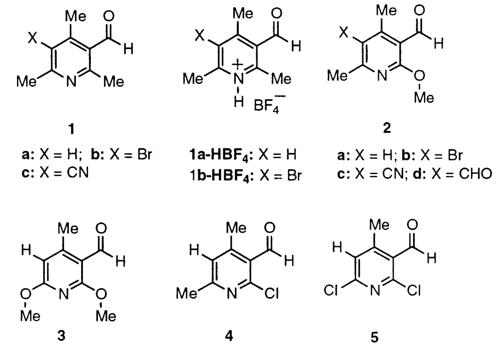


(eq 2)



(eq 3)

CHART 1



Intriguingly, the heteroaromatic analogue, namely, pyridine-3-carboxaldehyde **5** (Chart 1), is found to exhibit photochromism (photoenolization, eq 3).[19] This contrasting photobehavior observed with the heteroatom analogue prompted us to undertake the present investigations. Thus, we designed pyridine-3-carboxaldehydes **1**−**4** as substrates that may readily undergo photochemical γ-hydrogen abstraction to (i) understand the influence of ring heteroatom on the overall photochemical outcome, (ii) unequivocally establish the solid-state *conformational control* via intramolecular C−H···O and C−H···X interactions, and (iii) examine the role of substituents on the absorption properties of the photoenols. Herein, we report a comprehensive account of our results that demonstrates the phenomenon of photochromism based on stabilization of the photodienols (formed after γ-H abstraction) via hydrogen bonding and electronic factors; incidentally, the photochromism[20] based on γ-H abstraction of ketones was pursued vigorously three decades ago and met with limited success.[21,22]

Results

Syntheses of Pyridine-3-carboxaldehydes 1−5. 3-Bromo- and 3,5-dibromo-2,4,6-trimethylpyridine were synthesized by bromination of collidine with NBS in a $CF_3COOH-H_2SO_4$ mixture using a recently reported procedure[23] (Scheme 2). These were readily converted into 3-cyano-2,4,6-trimethylpyridine, 5-bromo-3-cyano-2,4,6-trimethylpyridine, and 3,5-dicyano-2,4,6-trimethylpyridine using CuCN in DMF.[24] Reduction of these cyanopyridines with DIBAL led to isolation of the alde-

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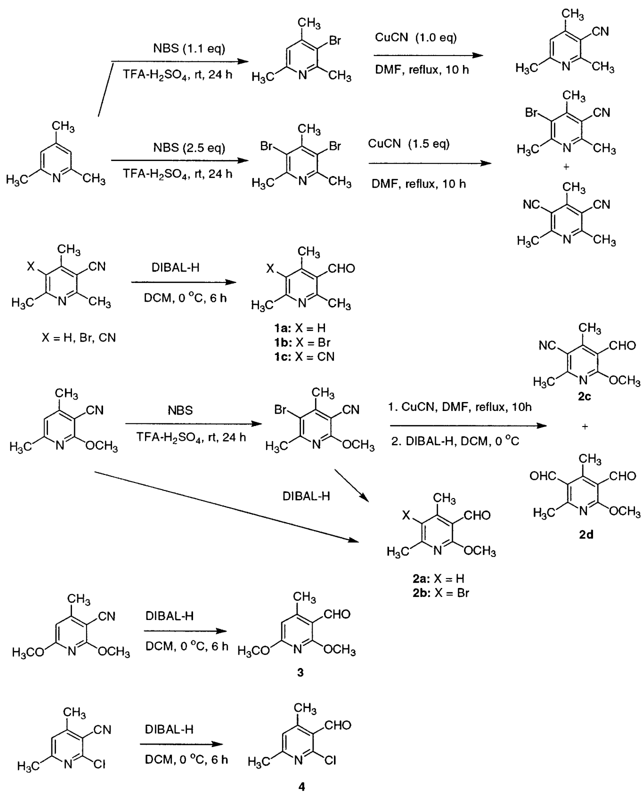
SCHEME 2



hydes **1a**, **1b**, and **1c**, respectively (Scheme 2). Pyridinium salts **1a-HBF$_4$** and **1b-HBF$_4$** were prepared by treating CH_2Cl_2 solutions of **1a** and **1b** with appropriate amounts of fluoroboric acid and isolated by treating the resulting material with a large excess of diethyl ether. Aldehydes **2** were synthesized starting from 2-methoxy-3-cyano-4,6-dimethylpyridine in an analogous manner. Aldehydes **3** and **4** were prepared by DIBAL reduction of the commercially available 2,6-dimethoxy-3-cyano-4-methylpyridine and 2-chloro-3-cyano-4,6-dimethylpyridine, respectively. The synthesis and photochemistry of the aldehyde **5** have been reported previously.[19]

Conformational Preferences of Aldehydes 1−5 in the Solid State. The formyl group of aldehydes **1**−**5** may, in principle, orient itself in either of the two possible ways, i.e., the formyl oxygen oriented toward or away from the ring heteroatom. The crystal structure database analyses[25] of *o*-halo-substituted aldehydes have shown that the formyl hydrogens can participate in intramolecular C−H···X interaction such that the formyl oxygen is oriented away from the halogen atom.[26,27] Thus, in the case of aldehydes **4** and **5**, the conformational preferences are a priori predictable. Indeed, such a preference due to the intramolecular C−H···X interaction was suggested from ab initio calculations and confirmed unequivocally from X-ray crystal structure analysis of one of the aldehydes, i.e., **5**.[19] Similarly, our photochemical results

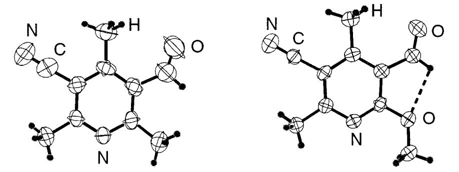


FIGURE 1. Molecular structures of aldehydes **1c** (left) and **2c** (right) from X-ray crystal structure analysis.

on *o*-anisaldehydes have offered evidence for intramolecular C−H···O hydrogen bonding between the formyl hydrogen and the methoxy oxygen such that the formyl oxygen is oriented away from the *o*-methoxy group.[12] Thus, in all of the *o*-methoxy-substituted aldehydes **2** and **3**, the formyl oxygen would be expected to orient itself away from the methoxy group.

However, for aldehydes **1**, lacking any of the aforementioned conformation-orienting interactions, the preferences cannot be predicted. To unequivocally establish the orientational preferences of the carbonyl group, X-ray crystallographic analyses were carried out for aldehydes **1c** and **2c** as representative cases. In Figure 1 are shown the perspective views of their molecular structures. In both aldehydes **1c** and **2c**, the formyl oxygen orients itself toward the methyl group at position 4. Evidently, the orientation of the formyl oxygen in **2c** is influenced by the C−H···O hydrogen bond involving the methoxy oxygen and the formyl hydrogen atom (Figure 1);[28] the distance and angular parameters, viz., $d_{H\cdots O}$ and $\theta_{C-H\cdots O}$, for this interaction are 2.35 Å and 102.4°, respectively. While similar considerations must apply for all aldehydes **2** and **3**, we presume that the orientational preference found in **1c** will prevail for **1b**, **1a-HBF$_4$**, and **1b-HBF$_4$**.

Theoretical Studies of (*Z*)- and (*E*)-Enols. For a comparison of the relative stabilities of (*Z*)- and (*E*)-enols[29] and also to assess the contribution of intramolecular O−H···O hydrogen bonding to the stabilization of the latter, ab initio calculations were carried out at the Hatree-Fock (HF) level using the 6-31G** basis set.[30] The geometry in all cases was fully optimized, with no symmetry restrictions. Frequency calculations were also carried out to ensure the energy minimum in each case. The differences in the energies of (*Z*)- and (*E*)-enols are given in Table 1. As can be seen, the (*Z*)-enols are more stable than the (*E*)-isomers for all aldehydes **1**. In contrast, the (*E*)-enols are more stable than the (*Z*)-isomers for all of the methoxy-substituted aldehydes **2** and **3**. This difference in behavior can be attributed to

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(28) Sum of the van der Waals radii of H and O is 2.7 Å. The dipole−dipole and steric repulsions in the alternative conformation may also be responsible for the observed conformational preference.

(29) Strictly speaking, the ring heteroatom as well as the methoxy or chloro substituents in the dienols call for a reversal of the *E* and *Z* designations that are applicable to the photoenols arising from simple *o*-methyl benzaldehydes. However, for the sake of uniformity, we have ignored the priority for the heteroatom and opted to designate all the dienols in conformity with the designations used for photoenols of benzaldehyde.

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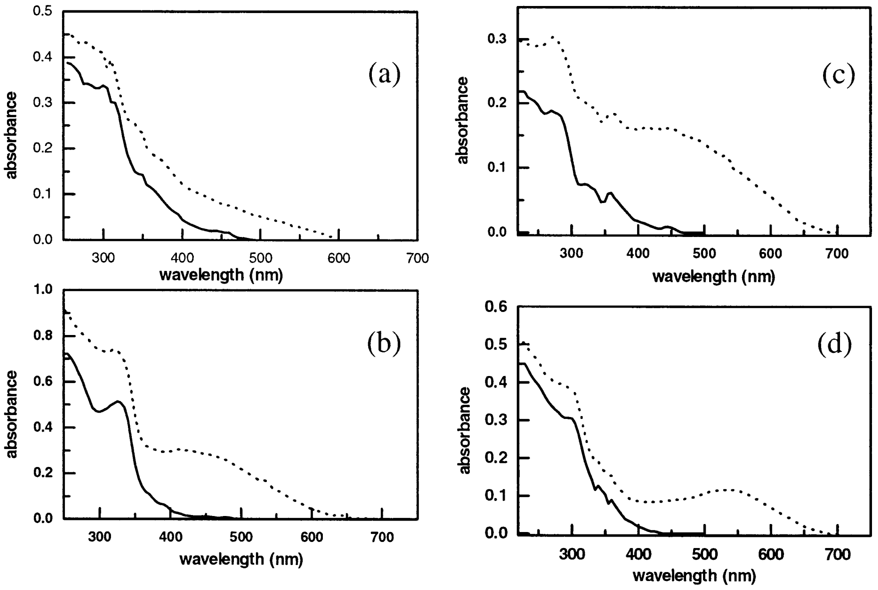


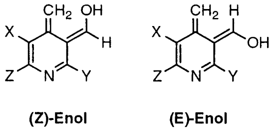
FIGURE 2. Absorption spectra of **1b** (a), **2b** (b), **1a-HBF₄** (c), and **1b-HBF₄** (d) before (solid line) and after (dotted line) exposure to UV radiation.

TABLE 1. Results of ab Initio and Semiempirical Calculations for Aldehydes 1−3

			ΔH (E_{enol} − CB)[a] (kcal/mol)	
entry	aldehyde	ΔE_{enols}[b] (kcal/mol)	AM1	ab initio
1	**1a**	−1.37	−01.82	11.83
2	**1b**	−0.71	−01.92	13.39
3	**1c**	−1.45	−01.04	11.31
4	**2a**	3.85	−07.83	1.57
5	**2b**	4.24	−11.31	2.91
6	**2c**	3.48	−07.17	0.85
7	**2d**	4.70	−13.26	4.52
8	**3**	3.82	−16.59	6.90

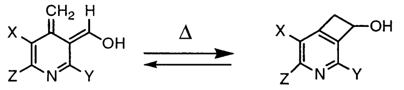
[a] AM1-calculated heats of reaction for the conversion of (*E*)-enol to the corresponding cyclobutenol. [b] Difference in the energies of (*Z*)- and (*E*)-enols ($E_Z - E_E$), as obtained from ab initio calculations.

the stabilization through O−H···O hydrogen bonding in the (*E*)-enols of **2** and **3** and its absence in the (*E*)-enols of **1** (vide infra). Thus, with the assumption that (*Z*)-enols of **1** and **2** are energetically similar (since they lack stabilization through intramolecular hydrogen bonding), one may conclude readily that the (*E*)-enols of **2** are more stable than those of **1** by ca. 5 kcal/mol, i.e., $\Delta E_{Z-E}(\mathbf{2}) - \Delta E_{Z-E}(\mathbf{1}) \approx 5$ kcal/mol.



(Z)-Enol (E)-Enol

Enthalpies of Reaction for (*E*)-Enol to Cyclobutenol Conversion. To assess the relative stabilities of the cyclobutenols and the (*E*)-enols, we computed the enthalpies of reaction (eq 4) for aldehydes **1**−**3** using the semiempirical AM1 method (QCMP 137, MOPAC6/PC),[31] and the results are included in Table 1. A perusal of the AM1 results in Table 1 reveals that the (*E*)-enols are more stable than the cyclobutenols in all cases. The calculations also show that the difference in the energies is ca. 1−2 kcal/mol for all aldehydes **1**, while it is ca. 7−17 kcal/mol in the case of aldehydes **2** and **3**. This difference in the enthalpies of reaction in going from aldehydes **1** to **2** and **3** simply reflects the stabilization of the (*E*)-enols via intramolecular O−H···O hydrogen bonding.



(eq 4)

For comparison, we also performed ab initio calculations for aldehydes **1** and **2**. As can be seen from the values in Table 1, the (*E*)-enols are predicted to be less stable than the cyclobutenols. This is not surprising, as the AM1 calculations depend on parameters chosen judiciously from thermodynamic and spectroscopic data. It turns out that the AM1 method does give qualitatively correct results for the reaction under consideration.[32] Nonetheless, it is gratifying to note that the ab initio calculations do show that the energies of reaction in the case of aldehydes **2** and **3** are far less positive than those for aldehydes **1**.

Solid-State Photobehavior and UV−Visible Absorption Spectra of the Photoenols. With the exception of aldehydes **1a** and **2a**, which are liquids, all other aldehydes **1**−**5** exhibit a striking color change upon exposure to UV−vis radiation. The aldehyde **1b** changes from colorless to a pale yellow color, while **1c** turns yellow-orange. All aldehydes **2** and **3** turn bright orange-red, while **4** and **5** exhibit a brick-red color. In all cases, the attendant color changes are persistent for several hours. Particularly noteworthy is the change in the absorption properties on varying the substitutents. Figure 2 shows the changes in UV−vis absorption, on

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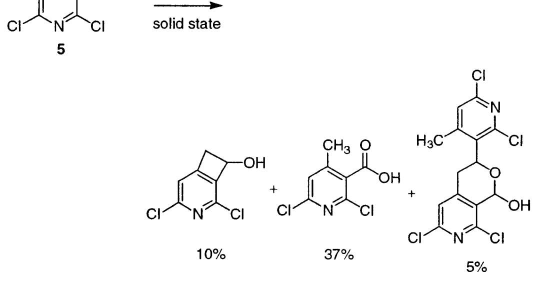
(31) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(32) Coll, G.; Costa, A.; Deya, P. M.; Flexas, F.; Rotger, C.; Saa, J. M. *J. Org. Chem.* **1992**, *57*, 6222.

exposure to UV radiation, of aldehydes **1b** and **2b** (spectra a and b, respectively) as representative cases. The observed color changes are readily attributed to (*E*)-enols[12,33,34] formed by hydrogen abstraction from the *o*-methyl group by the formyl oxygen. The intermediate (*E*)-enols responsible for the observed color revert to the starting aldehydes on heating (ca. 60−70 °C) or on standing at room temperature for several hours (ca. 1−2 days).[35]

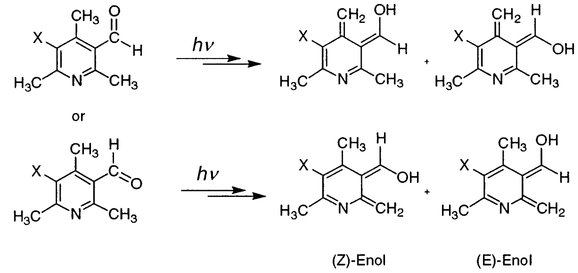
The advantage of the heteroatom in the ring is illustrated by the fact that the liquid aldehyde **1a** could be converted into a crystalline salt (**1a-HBF$_4$**) by treatment with fluoroboric acid. The crystalline **1a-HBF$_4$** and **1b-HBF$_4$** also exhibited remarkable photochromism in that the salts turned brick-red upon exposure to UV radiation (spectra c and d, respectively, in Figure 2). While the color persisted for several minutes under N_2, the reversion was expedited by absorption of trace amounts of moisture by the hygroscopic salts. It is worth noting that the salt formation brings about a dramatic bathochromic shift in the absorption (compare spectra a and d for the photoenols from **1b** and **1b-HBF$_4$**, respectively).

We have subjected aldehydes **1b** and **1c**, as representative cases, to photolysis in a Luzchem photoreactor fitted with 350 nm lamps for 10−15 h. The ^{1}H NMR (400 MHz) analyses of the solid irradiated mixtures indicated no evidence for the formation of cyclobutenols. The TLC analysis indicated a complex pattern, in addition to a highly polar material that eluted only in a highly polar solvent. An intractable polymeric material was obtained in both cases. A thorough analysis of the photoproducts has been carried out for aldehyde **5**;[19] in a preparative photolysis, the cyclobutenol was isolated in 10% yield, and other bimolecular and oxidation products were obtained in 42% yield, with the remainder being an *intractable* polymeric material (eq 5). The solid-state reactions, in general, proceed with minimum displacement of atomic positions.[36] Strict control of the lattice on the reaction coordinate is expected to lead specifically to one of several photoproducts. The bimolecular product in eq 5 suggests that the formation of persistent photoenols leads to creation of defects/disruptions in the crystal lattice. Presumably, the disruptions arising from the buildup of (*E*)-enols on continued irradiation increase the proximity between the neighboring molecules in the crystal lattice to permit bi- and/or polymolecular reactions that are typical of olefins to take place. The formation of intractable polymeric material should be explicable by these considerations.



(eq 5)

SCHEME 3



Discussion

The presence of a nitrogen atom in pyridine-3-carboxaldehydes **1** raises the question of conformational preference of the formyl oxygen in the solid state. The photoirradiation of **1** is expected to lead regiospecifically to two of the four possible photoenols (Scheme 3), as the reactions in the crystalline medium proceed with a minimum displacement of atomic positions;[36,37] of course, the conformation in which the aldehydes crystallize will determine which of the two regioisomeric photoenols will be formed. The X-ray crystal structure analysis of one of the aldehydes, i.e., **1c** (Figure 1), reveals that the carbonyl group orients itself toward the methyl group at position 4. We assume that similar considerations apply to **1b**, **1a-HBF$_4$**, and **1b-HBF$_4$** as well. In the case of aldehydes **2** and **3**, the orientation of the carbonyl group toward the methyl group is preferred due to an intramolecular C−H···O hydrogen bond involving the methoxy oxygen and the formyl hydrogen. As mentioned earlier, a similar preference in *o*-anisaldehydes was suggested from our photochemical results on *o*-anisaldehydes.[12] In the present instance, we have confirmed such a preference from X-ray crystal structure analysis of one of the aldehydes, **2c** (Figure 1). Insofar as aldehydes **4** and **5** are concerned, a scenario analogous to that for aldehydes **2** and **3** has been shown to operate.[19] The X-ray analyses of *o*-halo aromatic aldehydes have shown that the C−H···X interaction between the halogen and formyl hydrogen leads to the carbonyl group being directed away from the halogen atom.[25] X-ray crystal structure analysis of **5** has confirmed this preference.[19]

With this knowledge on the orientation of the formyl oxygen in the solid state of aldehydes **1**−**5**, we shall now consider the observed results of photoexcitation. The primary event of photochemical excitation of aldehydes **1**−**5** is the methyl hydrogen abstraction by the n,π^*-triplet excited carbonyl group. From their extensive studies on photochemical γ-hydrogen abstraction of ketones in the solid state, Scheffer and co-workers have set forth certain geometrical parameters, viz., d, Δ_o, τ_o and

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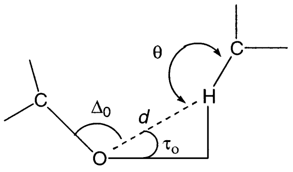
[34] Zwicker, E. F.; Grossweiner, L. I.; Yang, N. C. *J. Am. Chem. Soc.* **1963**, *85*, 2671.

[35] We have carried out the photoinduced-coloration and bleaching cycles 5−10 times and observed no significant decomposition of the aldehydes, as monitored by ^{1}H NMR spectroscopy. The long lifetimes of the colored photoenols precluded fatigue resistance to be established for a larger number of cycles. Given the fact that the continued irradiation leads to an intractable polymeric material, the aldehdyes are unlikely to sustain a large number of coloration−bleaching cycles.

[36] Cohen, M. D. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 386.

[37] Ramamurthy, V.; Weiss, R. G.; Hammond, G. S. *Adv. Photochem.* **1993**, *18*, 67.



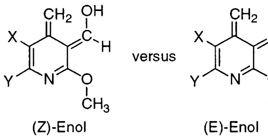
	1c	2c
d (Å)	2.67	2.53
θ (^{0})	97.8	100.2
Δ_o (^{0})	89.3	94.1
τ_o (^{0})	27.7	25.8

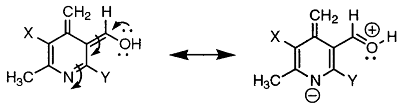
FIGURE 3. Scheffer's geometrical parameters that describe the feasibility of γ-hydrogen abstraction.

θ, which quantitatively describe the feasibility of H-abstraction (Figure 3).[38] The abstraction is said to be at its best when the distance parameter $d \leq 2.7$ Å (sum of van der Waals radii of H and O) and the angular parameters θ, Δ_o, and τ_o are 180, 90−120, and 0°, respectively; experimentally, the latter are seldom realized. The most crucial distance parameter d is less than 2.7 Å for both aldehydes **1c** and **2c** (Figure 3). Further, the angular parameters for both **1c** and **2c** compare well with (and, in fact, are better than) the experimentally observed averages ($d = 2.63 \pm 0.06$ Å, $\theta = 114 \pm 1°$, $\Delta_o = 81 \pm 4°$, and $\tau_o = 58 \pm 3°$) determined for a broad set of phenyl alkyl ketones that undergo γ-hydrogen abstraction.[38] Thus, γ-hydrogen abstraction by the triplet excited carbonyl can occur in both cases in a topochemical fashion to form triplet biradicals that collapse to the colored photoenols (Scheme 1).

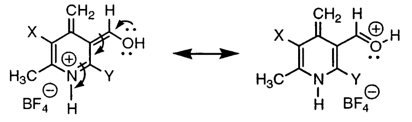
Theoretical studies have shown that the triplet excited biradical formed after hydrogen abstraction is twisted[39] and hence may form either the (*Z*)- or the (*E*)-enol. It is now generally accepted that the (*Z*)-enols are very short-lived and easily revert to the precursor aldehydes.[40] Thus, the possibility of (*Z*)-enols being responsible for the observed color change in all of the aldehydes **1**−**5** may be ruled out. On the other hand, the (*E*)-enols would be longer-lived, as the reverse hydrogen transfer would be difficult. Ab initio calculations suggest that the (*E*)-enols of **2** and **3** are more stable than the (*Z*)-isomers by ca. 3−5 kcal/mol, while the opposite is revealed for aldehydes **1**.[41] Clearly, intramolecular O−H···O hydrogen bonding plays a significant role in stabilizing the (*E*)-enols. The color due to (*E*)-enols is quite persistent for all of the crystalline aldehydes **1**−**5**, and this permitted their characterization through UV−vis absorption spectroscopy. It is worth reiterating that aldehyde **1b** turns pale yellow and **2b** bright red.

A striking contrast between the pyridine-3-carboxaldehydes and the mesitaldehydes[11] is that the (*E*)-enols of the latter convert to the benzocyclobutenols, while the pyridine analogues live sufficiently long to permit reactions typical of olefins resulting in highly intractable polymeric material on continued irradiation. To understand this shift in reactivity of the intermediate (*E*)-enols in going from mesitaldehydes to their heteroatom analogues, we performed semiempirical AM1 calculations to determine the heats of conversion for thermal cyclization of (*E*)-enols to benzocyclobutenols.[32] A comparison of the AM1 results for mesitaldehydes and the heteroaromatic pyridine-3-carboxaldehydes **1** reveals the effect of introducing a heteroatom into the ring (Scheme 4); the (*E*)-enols of pyridine-3-carboxaldehydes **1** are found to be more stable than those of the mesitaldehydes relative to the corresponding cyclobutenols. Whether or not these gas-phase results apply to the condensed-phase results described herein is debatable. The fact that the (*E*)-enols are readily observed in **1** and not in mesitaldehydes suggests that the energy differences similar to those predicted from theoretical calculations must apply in the solid state also. What is it that causes the (*E*)-enols of pyridine carboxaldehydes **1** to be comparatively more stable than those of the mesitaldehydes relative to their corresponding cyclobutenols? Quite conceivably, the heteroatom contributes to additional stabilization of the (*E*)-enols through resonance delocalization as shown in eq 6. Such a resonance contribution suggests that any factor that stabilizes the excess charge on nitrogen may be expected not only to enhance the stability of the intermediate dienol but also to shift its absorption bathochromically. The fact that such an expectation is nicely met is elegantly demonstrated by the photobehavior of HBF_4 salts of **1a** and **1b**. While **1b** exhibits a pale yellow color, its tetrafluoroborate salt turns a brick-red color with a highly red-shifted absorption, thereby attesting to the fact that the resonance delocalization of the kind shown in eqs 6 and 7 contributes to the stability of the photoenols relative to their corresponding cyclobutenols.





(eq 6)



(eq 7)

The results given in Table 1 show that the (*E*)-enols are more stable than their corresponding benzocyclobutenols. The energy difference is as much as 7−17 kcal/mol for the (*E*)-enols of aldehydes **2** and **3**, which underscores the importance of O−H···O hydrogen bonding in addition to the electronic effect of nitrogen in the ring discussed above in preventing cyclization. An analogous scenario involving C−H···X interactions must prevail in the case of the (*E*)-enols of aldehydes **4** and **5**; otherwise, the photochromism would not be observed.

All of the crystalline aldehydes **1**−**5** exhibit photochromism and yield intractable material on continued irradiation. In contrast, 2-methoxy-3-acetylpyridines are reported to undergo photocyclization to the cyclobutenols

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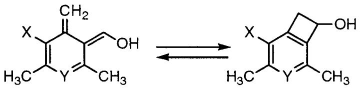
[38] Ihmels, H.; Scheffer, J. R. *Tetrahedron* **1999**, *55*, 885.

[39] Wagner, P. J.; Sobczak, M.; Park, B.-S. *J. Am. Chem. Soc.* **1998**, *120*, 2488.

[40] Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chim. Acta* **1977**, *60*, 2595.

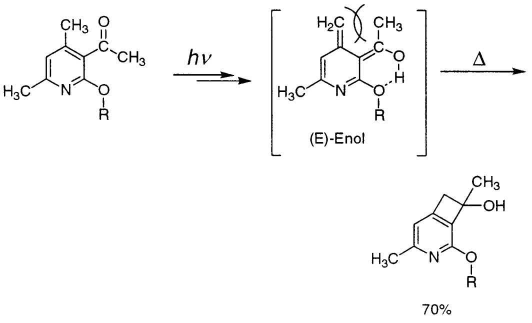
[41] Although the (*Z*)-enols of aldehydes **1** are more stable than those of **2** and **3**, their existence is limited by a competitive and facile 1,5-reverse hydrogen transfer that regenerates the precursor aldehydes. This process is difficult for (*E*)-enols and thus increases their lifetime despite the higher energy. Therefore, the observed color on exposure of aldehydes **1** to UV irradiation should be attributed to (*E*)-enols.

SCHEME 4



	ΔH (kcal/mol)
Y = C; X = H	1.99[11]
Y = N; X = H	-1.82
Y = C; X = Br	3.79[11]
Y = N; X = Br	-1.92
Y = C; X = CN	2.79[11]
Y = N; X = CN	-1.04

(eq 8).[42] The photoenols in this case would be analogous to the ones formed from aldehydes **2** and **3** and thus could be expected to be stabilized by intramolecular hydrogen bonding. The observed efficient cyclization suggests that severe steric encumbrance between the methyl and the hydrogens of the dienolic moiety should be sufficiently high to cause cyclization to thermodynamically more stable cyclobutenols. This appears to be one of the reasons as to why photochromism is observed more often in aldehydes than in ketones in the solid state;[43] invariably, cyclobutenols are the products of photolysis of ketones.



(eq 8)

The phenomenon of photochromism via γ-hydrogen abstraction in *o*-alkyl aromatic carbonyl compounds was extensively explored by Ullman and co-workers three decades ago with the objective of ultimately developing photochromic materials.[21,22] Employing an approach that involved stabilization of photoenols through intramolecular hydrogen bonding, they demonstrated photochromism of certain chromone derivatives in *benzene solutions* at 25 °C. However, a systematic study of possible photochromic materials based on γ-hydrogen abstraction has since been lacking, except for three reports on fortuitous observation of photochromism in the solid state. Our recent[11,12,19] and present investigations demonstrate how hydrogen bonding and electronic stabilization offered by the nitrogen atom may be exploited to observe photochromism more easily in *o*-alkyl aromatic aldehydes than with ketones.

Summary and Conclusions

We have investigated the solid-state photobehavior of a broad set of pyridine-3-carboxaldehydes **1**–**5**. The introduction of a heteroatom into mesitaldehydes as in aldehydes **1** raises the question of conformational preference in the solid state. The preferred conformations have been unequivocally established from X-ray crystal structure analyses of two of the aldehydes; it is shown that intramolecular hydrogen bonding could be utilized to achieve conformational control. In contrast to mesitaldehydes, which undergo efficient photocyclization to benzocyclobutenols in the solid state, heteroatom analogues **1b** and **1c** exhibit a perceptible color change (to pale yellow for **1b** and yellow-orange for **1c**) upon UV irradiation; the color attributed to (*E*)-enols is persistent for several hours. Continued irradiation leads to a highly polymeric material. The AM1 calculations, which have been reliably applied to the thermal cyclization of xylylenols to benzocyclobutenols, reveal that the (*E*)-enols of **1** are more stable than those of the mesitaldehydes relative to their corresponding benzocyclobutenols. The stabilization is interpreted as arising from the possibility of engaging the heteroatom in resonance delocalization. That the contribution from such a role of the nitrogen is so pronounced is elegantly demonstrated by forming the fluoroborate salts; **1a-HBF$_4$** and **1b-HBF$_4$** readily exhibit highly red-shifted absorption upon exposure to UV radiation as a result of stabilization of the photoenols. Such a remarkable stabilization via *electronic control* of the photoenols is unprecedented. All the 2-methoxy- and 2-chloro-substituted aldehydes **2**–**5** exhibit photochromism. Ab initio calculations show that the methoxy group in aldehydes **2** and **3** stabilizes the (*E*)-enols via O–H···O *hydrogen bonding* as compared to those of **1** by 5–6 kcal/mol relative to their corresponding benzocyclobutenols. Thus, the presence of methoxy and halo groups at position 2 serves not only to direct the formyl oxygen toward the methyl group for H-abstraction but also to stabilize the (*E*)-enols.

Experimental Section

Solid-State Photolysis and UV–Vis Absorption Spectra. The UV–vis absorption spectra for all the aldehydes were recorded by forming a fine layer in a 1.00 mm quartz cuvette by slow evaporation of the solution of aldehydes in an appropriate solvent. The spectra were recorded before and after a brief exposure (ca. 1 min) to UV–vis radiation from a high-pressure mercury lamp.

For examining the photochemistry in the solid state, the gently powdered crystals of **1b** and **1c** were dispersed in a test tube and purged thoroughly with N_2 gas. The samples were irradiated in a photoreactor fitted with 350 nm lamps. The samples were shaken from time to time to ensure uniform exposure to the radiation. After 10–15 h, the samples were analyzed by ^1H NMR spectroscopy (400 MHz), which revealed no evidence for cyclobutenols and other readily discernible photoproducts.[11] In a preparative photolysis employing 100 mg of the compound, only polymeric material could be isolated with no indication whatsoever of the formation of cyclobutenols. The TLC analysis indicated a complex pattern.

X-ray Crystallographic Details of Aldehydes 1c and 2c. The protocol adopted for the X-ray crystal structure determination of aldehydes **1c** and **2c** is described below. The individual parameters and refinement conditions pertaining to each compound are recorded in the table entitled Crystal Data and Structure Refinement (Supporting Information).

Crystals suitable for single-crystal diffraction studies of both compounds were grown from ethyl acetate–hexane mixtures by the slow evaporation method. A good single crystal was

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[42] Sakamoto, M.; Fujihira, M.; Takahashi, M.; Enomoto, K.; Nishimiya, N.; Fujita, T.; Watanabe, S. *J. Chem. Soc., Chem. Commun.* **1993**, 1023.

[43] To the best of our knowledge, only one example of a ketone exhibiting solid-state photochromism is known: see ref 9.

mounted along its largest dimension and used for data collection. The intensity data were collected on a single-crystal diffractometer equipped with a molybdenum-sealed tube (λ = 0.71073 Å) and highly oriented graphite monochromator. The lattice parameters and standard deviations were obtained by a least-squares fit to 40 reflections (10.23° < 2θ < 29.98°). Data were collected by $2\theta-\theta$ scan mode with a variable scan speed ranging from 2.0°/min to a maximum of 60.0°/min. Three reflections were used to monitor the stability and orientation of the crystal and were remeasured after every 97 reflections. Their intensities did not change significantly during the entire data collection period. All other relevant information about the data collection is presented in the tables for each of the two compounds.

The structure was solved in both cases by direct methods using the SHELX-97[44] package and also refined using the same program. All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the ideal positions with fixed isotropic U values and were riding with their respective non-hydrogen atoms. A weighting scheme of the form $w = 1/[\sigma^2(\mathrm{Fo}^2) + (\mathrm{aP})^2 + \mathrm{bP}]$ was used. The difference Fourier map, after the refinement, was essentially featureless in all cases. Final atomic coordinates, bond lengths, bond angles, anisotropic displacement parameters, hydrogen atom coordinates, and torsion angles have been recorded in the tables for both aldehydes.

Semiempirical AM1 Calculations. All calculations were run using the MOPAC 6/PC version 6.12. The ground-state energies were computed using the key words "AM1" and "Precise". When Herbert's test was not satisfied, the initial geometries were changed and the energies recomputed until Peter's and Herbert's tests were satisfied.

Ab Initio Calculations. All ab initio calculations were carried out at the HF/6-31G** level using the GAUSSIAN94[30] suite of programs. The geometries were optimized without any symmetry restrictions.

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Supporting Information Available: Syntheses and characterization data for all aldehydes **1**−**4**, ^{1}H and ^{13}C NMR spectra of **1a-HBF$_4$** and **1b-HBF$_4$**, crystallographic data for **1c** and **2c**, summary output files of AM1 calculations and ab initio calculations for **2a**−**d** as representative examples, and UV−vis absorption spectra for aldehydes **1c**, **2c**, **2d**, **3**, and **4** before and after irradiation. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026621N

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[44] Sheldrick, G. M. *SHELX-97, Program for the solution and refinement of crystal structures*; University of Göttingen: Göttingen, Germany, 1997.