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Photochemistry of Hantzsch 1,4-dihydropyridines and pyridines

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Abstract

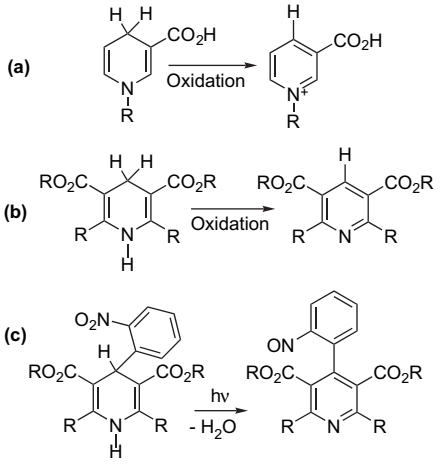
The photochemistry of some Hantzsch 4-phenyl-1,4-dihydropyridines bearing a substituent on the phenyl ring (the three isomeric chloro derivatives and the 4′-nitro derivative) has been studied. All of these compounds underwent inefficient aromatization to the corresponding pyridines (quantum yield $<10^{-4}$ at 366 nm, $<10^{-2}$ at 254 nm). This process is scarcely affected by molecular oxygen and is initiated by proton transfer (from C_4–H), probably to the solvent, from the excited singlet. In turn, the thus formed pyridines were photoreactive with comparable or higher efficiency. Thus, the 4-(3′-chlorophenyl) and 4-(4′-chlorophenyl) Hantzsch pyridines underwent positional rearrangement to form two isomers each. The reaction occurs via Dewar benzene–prismane path. In the case of the minor isomer a further 1,3-shift take place at the Dewar benzene level. The 4-(2′-chlorophenyl) derivative underwent C–Cl bond homolysis, which led to cyclization of the phenyl group onto one of the ester groups forming a pyrane ring.

Keywords: Photochemistry; Hantzsch 1,4-dihydropyridines; Aromatization; Pyridines

1. Introduction

The dihydropyridine–pyridium redox reactions have, as it is well known, a primary role in metabolism with NAD^+ and $NADP^+$ coenzymes (see Scheme 1a). The easily prepared Hantzsch esters (1,4-dihydropyridine-3,5-dicarboxylates)[1,22] come close to these characteristics and are used as antioxidants in a variety of applications (see Scheme 1b).[2]

It may be interesting to evaluate whether a photochemical path may affect this reaction, particularly since these dihydropyridines absorb strongly in the UVA range. However, the photoreactivity has been studied only for some 4-phenyl-1,4-dihydropyridine-3,5-dicarboxylates that are used as cardiac drugs,[3] for which photolability is a serious problem. As a matter of fact, the photochemistry of these compounds has been investigated in depth for the highly photolabile 4-(2′-nitrophenyl) derivatives, such as nifedipine and nisoldipine,[4] which give the corresponding 4-(2′-nitrosophenyl)pyridines (Scheme 1c) both in solution and in the solid state. Minor products that have been detected (e.g., the corresponding nitro and azoxy derivatives) clearly result from further thermal reactions of the nitroso derivative.[4,5] The mechanism of this photoprocess has been clarified through extensive investigations by a variety



Scheme 1. Dihydropyridine–pyridine (or pyridinium ion) reactions and photochemistry of a nitrophenyldihydropyridine.

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of techniques, and is not characteristic of the dihydropyridine per se, but rather is an example of the well known intramolecular hydrogen abstraction by *o*-nitrobenzyl derivatives.[6]

In contrast, only sparse work has been carried out on other Hantzsch dihydropyridines. Among cardiac drugs, it has been found that some 4-phenyl derivatives bearing a nitro group in position 3′, such as nitrendipine and nicardipine, undergo a photochemical oxidation to the 4-(3′-nitrophenyl)pyridines, although the process is much less efficient.[7] It appeared desirable that more phenyldihydropyridines were studied, in order to obtain more knowledge on the photochemistry of such derivatives, in particular for compounds not containing a nitro group, in order to ascertain whether this substituent had a determining effect on the photochemistry.

If the reaction involved aromatization, it was relevant to understand the photochemistry also of the corresponding pyridines, since the photoreactions of the two derivatives may occur competitively. Here again the literature is not extensive, and while the photochemistry of simple pyiridine derivatives is known[8] that of heavily substituted derivatives such as Hantzsch pyridines has been little investigated.[9]

2. Results

Pursuing our interest in the photochemistry of Hantzsch dihydropyridines,[4b,7] we decided to extend the examination to further derivatives, in particular to the three isomeric 4-(chlorophenyl) derivatives **1**–**3** (that are also models of cardiac drugs). Furthermore, the photodegradation of the 4-(4′-nitrophenyl) derivative **4** was tested, in order to complete the series of the previously investigated 2′- and 3′-isomers[4,7] and to allow the comparison between homogeneous 4-(chlorophenyl) and 4-(nitrophenyl) families of Hantzsch dihydropyridines. Additionally, we also explored the photoreactions of the corresponding pyridines.

The absorption spectra of dihydropyridines **1**–**3** were almost identical, with a long-wavelength band around 355 nm (ε=7000 $M^{-1}\,cm^{-1}$) tailing beyond 400 nm, and a further band at 235 nm (ε=23,000 $M^{-1}\,cm^{-1}$). The absorption in the UVA is due to a $\pi\pi^*$, internal charge transfer transition. Compound **4** showed in addition a further band at 282 nm (ε=11,250 $M^{-1}\,cm^{-1}$), due to the nitrophenyl group (Fig. 1).

Irradiations were carried out both in MeOH or in MeCN, at 254 and at 366 nm. The result was similar in every case, with a decrease of both absorption maxima and an increase of new band at 275–280 nm. Isosbestic points were conserved up to >70% conversion, indicating that either a single product or a mixture with constant composition was generated. The quantum yield of decomposition was measured on 2.5×10^{-4} M solutions and the results are reported in Table 1.

Product studies were carried out on 5×10^{-3} M solutions. In the case of **1**, two main products were isolated and identified as the corresponding pyridine derivative (**5**, about 60% of the starting compound, identified by comparison with the thermal oxidized derivative prepared by using HNO_3)[10a] and a different phenylpyridine of structure **6**, where a molecule of HCl had been lost and a further lactone ring had been formed. The

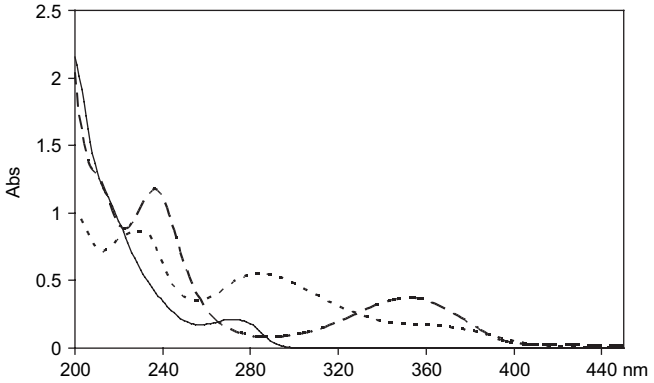


Figure 1. Absorption spectrum of dihydropyridine **1** (- - -), of the corresponding pyridine **5** (—) and of the compound **4** (…), 5×10^{-5} M in acetonitrile.

latter compound was identical to a sample prepared by a path known in the literature.[10b] The proportion of such product increased with conversion, indicating that it resulted from a secondary photoreaction of **5**. This was confirmed by independent irradiation of a solution of **5** under the same conditions (see Scheme 2, Table 2).

Compound **2** gave three products, again with a conversion dependent yield. The primary photoproduct was pyridine **7** (30%), which in turn was converted to the two further products. These were in a constant ratio (ca. 2:1), although growing with time with respect to **7** and were obtained in the same ratio also by separate irradiation of **7**. Chromatography gave a mixture of such products and spectroscopic investigations gave sufficient elements for recognizing them as isomers of **7**. In particular, NMR experiments fully supported their identification as rearranged chlorophenylpyridines and allowed the determination of the structure, mainly on the basis of NOE effects and HMBC correlation (see Section 5).

The most abundant isomer (13%) has the methyl group in positions 2 and 3 and the aryl group was not vicinal. Long range correlations between some of the pyridine carbons and the methyl or phenyl hydrogens allowed assignment of structure **8** (see Section 5 for details). The minor isomer (7%) had the methyl groups in 3 and 4, with no NOE with the aryl group and HMBC correlations indicating that the two C–COOMe groups flanked the methyl groups, thus allowing to recognize formula **9**.

Compound **3** followed a closely similar path, with formation of pyridine **10** as the primary product and a mixture of two further pyridines **11** and **12** arising through secondary irradiation (as tested by separated experiments on **10**). NMR spectra revealed that **11** and **12** differed from **8** and **9** only for the position of the chloro atom in the phenyl ring. As for the nitrophenyl derivative **4**, this was aromatized to pyridine **13**, which underwent no further change on the timescale used.

The reaction quantum yields of the dihydropyridines **1**–**4** were measured in low conversion experiments in MeCN and MeOH, by irradiation both at 360 and at 254 nm (corresponding to the two main bands in the absorption spectrum), both in air equilibrated and in argon equilibrated solutions. In no cases did the presence of air change the observed values by >20%.

Table 1
Quantum yield of reaction for the photolysis of isomeric chloro- and nitro-substituted 4-phenyl-1,4-dihydropyridines in argon equilibrated solutions (2.5×10^{-4} M)

Conditions	Compound					
	2′-Cl	3′-Cl	4′-Cl	2′-NO_2[a]	3′-NO_2[b]	4′-NO_2
MeCN, 254 nm	4.5×10^{-3}	1.2×10^{-3}	7.4×10^{-4}	0.24	3×10^{-3}	6×10^{-3}
MeOH, 254 nm	3.3×10^{-3}	7.9×10^{-4}	1.2×10^{-3}	0.23	1.3×10^{-2}	2.8×10^{-2}
MeCN, 366 nm	5.3×10^{-5}	2.5×10^{-5}	3.2×10^{-5}	0.27	6×10^{-4}	8×10^{-4}
MeOH, 366 nm	7.1×10^{-5}	4.8×10^{-5}	4.7×10^{-5}	0.35	4×10^{-3}	7×10^{-3}

[a] From Ref. 4b.
[b] From Ref. 7.

Thus, only the data under argon are reported in Table 1, where the data for the 2′- and 3′-nitro analogues are also gathered for the sake of comparison.

The photoreactions could conveniently be followed by UV spectroscopy, since the absorption spectra of the pyridines **5**, **7**, **10**, and **13** were considerably blue-shifted with respect to the starting dihydropyridines. The spectra were characterized by a band (ε ca. 4000 $M^{-1}\,cm^{-1}$) at ca. 280 nm (see Fig. 1), which was rather similar to that of simple pyridines.

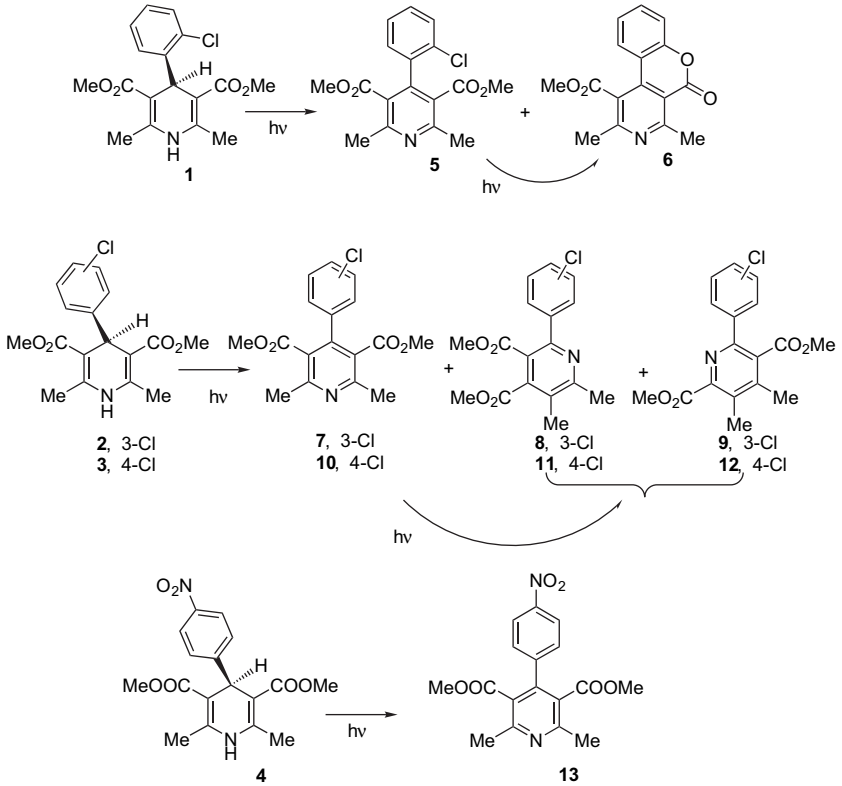
3. Discussion

3.1. Photochemistry of the dihydropyridines

A look at the efficiency of the photoreactions of the 4-(chlorophenyl)- and the 4-(nitrophenyl)dihydropyridines shown in Table 2 singles out the case of the 4-(2′-nitrophenyl) derivative. This gives the corresponding nitrosophenylpyridine, i.e., an intramolecular redox process, with remarkable efficiency.[4]

In all of the other cases, net oxidation of the dihydro derivatives (general formula **14**, see Scheme 3) to give the corresponding nitrophenyl or chlorophenyl pyridine takes place, but the reaction is sluggish. Thus, the quantum yield of reaction is in the order of 10^{-5} by irradiation in the long-wavelength band and reaches 1×10^{-3} at shorter λ_{irr}. We find no difference in the quantum yield in Ar saturated or air equilibrated solutions, and confirmed the indifference to the presence of oxygen by experiments carried out after thorough degassing of the solution by four freeze–degassing–thaw cycles to 1×10^{-6} Torr. Apparently, oxygen has no role in the aromatization of Hantzsch dihydropyridines by direct irradiation. The occurring of aromatization by photosensitized oxygenation has been reported for some compounds of this type,[11] but that appears to be a different reaction.

That the rather weak C_4–H bond undergoes homolysis or heterolysis in the excited state is reasonable in view of the stabilization of the resulting pyridinyl radical (**17**) and of the aromatic pyridinium cation (**18**) as well as of the structure of the



Scheme 2. Photoproducts from dihydropyridines **1**–**4**.

Table 2
Products from the irradiation of 4-(chlorophenyl)-1,4-dihydropyridines **1**–**3**

Starting compound	Products (% yield)
1, 2′-ClC_6H_4–	**5** (60%), **6** (15%)
2, 3′-ClC_6H_4–	**7** (30%), **8** (13%), **9** (7%)
3, 4′-ClC_6H_4–	**10** (50%), **11** (10%), **12** (5%)

excited state. In fact, the strong absorptivity of the $S_0 \rightarrow S_1$ transition supports the internal electron transfer character of the corresponding excited state. As a result, this has some zwitterionic character,[12] with a partial positive charge on the enamine moiety (**14*** ≡ **15**, see Scheme 3). Analogy can be drawn with the known chemistry of the 1,4-dihydropyridine radical cation, for which a heterolytic multi-step mechanism initiated by transfer of a proton from position 4 followed by one-electron loss has received computational support.[13] This suggests that in the present case ionization and deprotonation is a viable process.[14]

This fits with the increased efficiency observed at shorter λ_{irr}, since in that case the excited state is formed with a surplus vibrational energy that facilitates the cleavage. A further indication is given by the fact that the 2′-chlorophenyl derivative is somewhat more reactive than its isomers, although, differently from the case of the nitro analogues, no intramolecular H transfer path is available here. Reasonably, the increase is rather related to the larger stabilization gain in 2′-substituted derivatives when loss of the hydrogen in 4 relieves crowding at that position.

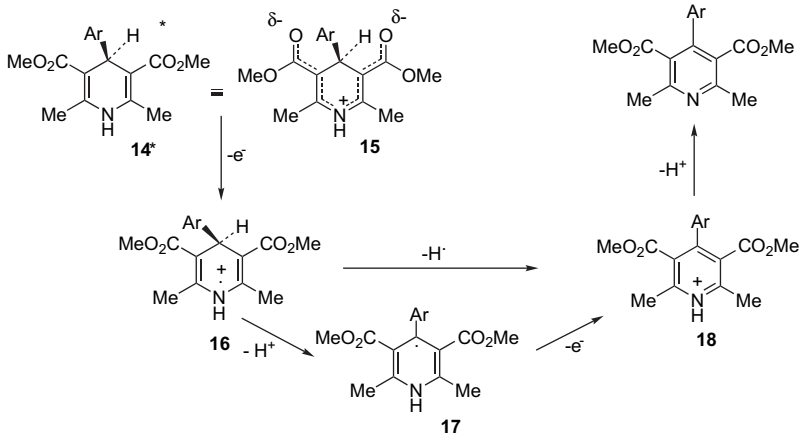
Furthermore, a nitro group in 3′ or 4′ (when this is in 2′ a different mechanism comes in, as mentioned above) enhances the yield of aromatization because the nitrophenyl group participates to the delocalization of the negative charge, thus increasing the zwitterionic character of the excited state, and again facilitates ionization and deprotonation.

As for the multiplicity of the excited state involved, the lack of oxygen effect supports that the reactive state is short-lived. This is reasonably the singlet, since photophysical studies indicated that dihydropyridines of this type undergo negligible ISC.[7,15] Thus, the aromatization of dihydropyridines is obtained upon direct irradiation, although with a low yield, and involves hydrogen transfer, probably to the solvent. In fact, the product distribution was the same with 2.5×10^{-4} and 5×10^{-3} M dihydropyridine starting concentration, and there is no indication of a base (dihydropyridine) induced deprotonation, not expected also in view of the short excited state lifetime. Taking into account the intensive absorbance of these compounds in the near UV, this phenomenon may occur also with ambient light and may be important in the photodegradation (and phototoxicity) of drugs of dihydropyridine structure.

3.2. Photochemistry of the pyridines

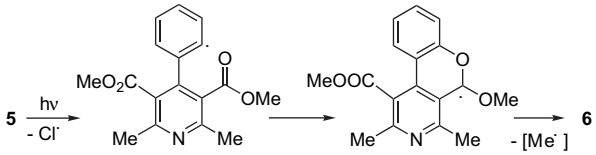
At any rate, the rearomatization path remains inefficient and secondary photoreactions of the pyridines become competitive with the primary process. The UV spectrum of these derivatives is characterized by an intense absorption around 280 nm as the long-wavelength band. Apart from a red shift of some 15 nm, this band is quite similar to that of parent pyridine. In the case of simple pyridines it has been discussed whether this means that the lowest singlet state of pyridine is ππ* or there is a hidden, weak transition and the first singlet excited state is nπ*. Actually different calculation methods give different results.[7] With the present compounds there is no indication of hydrogen abstraction that may indicate the role of the latter state, probably because this is shifted to higher energy by electron-withdrawing ester groups, and the three isomeric 4-chlorophenyl derivatives undergo two different reactions, one in the case of **5** and one in the case of **7** and **10**.

The conversion of **5** to **6** is related to the photodechlorination observed with chlorobiphenyls and reasonably implies homolytic cleavage of the C–Cl bond. The fact that this process has been detected only with the 2′-chlorophenyl derivative **5** suggests however that some specific interaction is involved in this case. Actually, the C–Cl bond projects over the ring π orbitals, a fact that may facilitate the cleavage due to the formation of a chloro atom–benzene π complex that involves a significant stabilization.[16] Easy intramolecular attack onto the ester function finally leads to formation of the observed lactone (Scheme 4). A far analogy for this process may be



Scheme 3. Suggested mechanism for the photochemistry of dihydropyridines (general formula **14**).

indicated in the photodechlorination and cyclization of some 2′-chlorobenzylpyridinium salts.[17] Alternatively, it may be that cyclization by attack of the ester oxygen atom precedes HCl loss, as has been established in the photoreaction of amides and esters of 2,6-dichlorocynnamic acid to give 5-chlorocoumarin.[18]



Scheme 4. Photochemical reaction of pyridine **5**.

As mentioned, cleavage of the chlorine is observed only when this is in position 2′. With the 3′- and 4′-chlorophenyl derivatives, the process occurring is the positional rearrangement of the pyridine substituents. To our knowledge, a single investigation has been carried out on the photochemistry of Hantzsch type pyridines,[9] where the product structure has been assigned primarily on the basis of proton exchange experiments in methyl groups in position 2 or 4. More generally, the rearrangement in pyridines implies the intermediacy of benzvalene(s) or Dewar benzene(s) and depends on the structure of the compound irradiated and on conditions, which affect the multiplicity and the electronic configuration of the reacting excited states. In the present case, the characteristic pattern of photorearrangement observed in the gas phase with methylpyridines (i.e., one atom inserts between the two next neighbors) and attributed to azaprefulvene intermediates is not observed.[8]

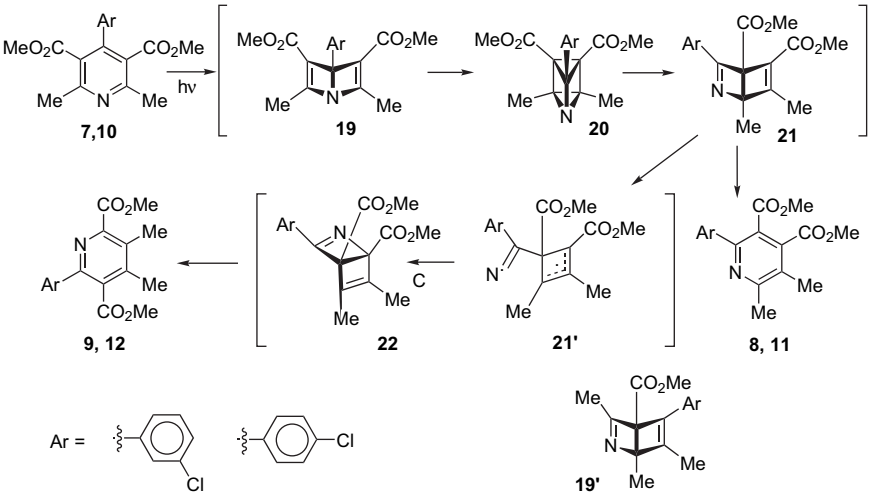
Examination of the accessible paths shows that the main products from the two pyridines, that is, **8** and **11**, are those expected from 1,4-ring closure to give Dewar benzene **19** and intramolecular cycloaddition to prismane **20**, followed by the alternative ring opening to the other Dewar benzene **21**, which finally reopens to the observed products. The prismane path in fact well accounts for the positional rearrangements in methyl- and dimethylpyridines.[8]

As for the minor products **9** and **12**, their proportion with respect to **8** and **11** was found to be constant at different degrees of conversion, consistently with the fact that these arise through a single photochemical act with competition between the two paths, rather than via two subsequent, independent, photochemical reactions. Their structure did not correspond to that expected from the alternative Dewar benzene (**19′**)–prismane path, nor to any benzvalene path, but could be rationalized as involving a 1,3-shift of the nitrogen atom in Dewar benzene **21** to give isomeric **22** via diradical **21′** (Scheme 5). A similar mechanism has been previously postulated for the rearrangement of methyl 2-pyridinylacetate to methyl anthranylate.[19] Notice also that a cyclobutenecarboxylate has been found to add photochemically to nitriles forming an aza Dewar benzene and a pyridine from it.[20]

Finally, with the 4-(4′-nitrophenyl)pyridine **13** there is no photocleavable group as in the 2′-chlorophenyl analogue, and the above photorearrangement does not take place, or at least not with reasonable efficiency. It is possible that with the nitro group ISC both from the initial excited singlet to the triplet state (that may have a nπ* character) and from the triplet back to the ground state are faster, as it happens for many nitroaromatics.[21] This would shorten the lifetime of both excited states and leave little room for chemical reaction, since there is no intramolecular H transfer path available.

4. Conclusions

In conclusion, aromatization is a general, although quite inefficient, process in the photochemistry of Hantzsch 1,4-dihydropyridines. The efficiency depends on the strength of the C_4–H bond and is increased when a substituent at C_4 further weakens that bond by sterical hindering or electronic effect. The generally low efficiency of the photoreaction is due to the short lifetime of the singlet excited state (the triplet has



Scheme 5. Photorearrangement of pyridines **7** and **10**.

no role because of the inefficient ISC). Structural modifications that enhance the lifetime of the singlet may increase the efficiency of the cleavage. This would make an interesting photoactivated hydrogen donating system, which would be valuable because of the strong absorption in the UVA of these molecules. The process appears to be little affected by the phenyl group in 4 and likewise by susbtituents on that group. An exception occurs when a different (intramolecular) reaction comes in, as with the 4-(2′-nitrophenyl) derivative that reacts several orders of magnitude faster. As for the corresponding phenylpyridines, these undergo photorearrangement of the benzene ring via Dewar benzene (preferred 1,4-bonding) at a rate comparable to—or larger than—that of aromatization, unless a fragmentable group in 2′ makes photocleavage of that group the faster alternative.

5. Experimental

5.1. General

Compounds **1**, **2**, **3**, and **6** were prepared according to a published procedure[22] and compound **5** was of commercial origin (Aldrich, Steiheim, Germany). Absorption spectra were registered on 5×10^{-5} M solutions in spectrophotometric cuvettes (1 cm optical path) on the range of 200–450 nm on a Jasco V-550 UV–vis Spectrophotometer, using Spectra Manager as software UV, with scan rate 1 nm s^{-1}.

5.2. Photochemistry

Small-scale experiments were carried out on 3 mL samples of 2.5×10^{-4} M solutions of the dihydropyridines in MeCN or MeOH in quartz tubes after argon flushing when appropriate. These were irradiated by means of two or four external lamps, either 15 W low-pressure mercury arcs (254 nm) or 15 W phosphor-coated lamps (center of emission 366 nm; midheight width 35 nm). The course of the reaction was monitored by TLC (cyclohexane/ethyl acetate 7:3) and by HPLC (Jasco) by using a Supelco Discovery HS C-18 25 cm×4.6 mm, 5 μm column and eluting with acetonitrile/water mixture (50:50, flow 1.3 mL/min, λ_{an}=250 nm for compound **1**, **2**, and **3**; 55:45, flow 0.8 mL/min, λ_{an}=250 nm for compound **5**; 70:30, flow 0.5 mL/min, λ_{an}=250 nm for compounds **6**). Retention times were t_R 11.3 min (compound **1**), t_R 13.4 min (compound **2**), t_R 14.2 min (compound **3**), t_R 13.0 min (compound **5**), t_R 9.7 min (compound **6**).

Preparative experiments were carried out on 300 mL portions of 5×10^{-3} M solutions of the dihydropyridines in an immersion well apparatus after argon flushing. These were internally irradiated by means of one 125 W medium pressure mercury arc through Pyrex until a total conversion was reached (TLC and HPLC).

Evaporation of the solvent and chromatography afforded the photoproducts, characterized by examination of their properties, in particular HPLC, IR, and NMR. Phenylpyridines **5**, **6**, **7**, **10**, **13** were identical to samples prepared by literature procedures.

5.2.1. Photochemistry of dimethyl 4-(3′-chlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridindicarboxylate (2)

Irradiation of this compound for 20 h and separation of raw photolysate as indicated above gave product **7** as well as a mixed fraction containing compounds **8** and **9** as a glassy solid. Anal. Calcd for $C_{17}H_{16}ClNO_4$: C, 61.18; H, 4.89; N, 4.20. Found: C, 61.0; H, 4.9; N, 4.0.

Dimethyl 3-(3′-chlorophenyl)-5,6-dimethyl-2,4-pyridindicarboxylate (**8**), ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 2.65 (s, 3H), 3.67 (s, 3H), 3.95 (s, 3H), 7.3 (m, 3H), 7.6 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.2 (CH_3), 23.0 (CH_3), 52.0 (CH_3), 52.3 (CH_3), 122.6 (C, C-3), 126.0 (CH), 126.7 (C, C-5), 128.1 (CH), 128.2 (CH), 128.9 (CH), 133.8 (C), 140.5 (C), 140.8 (C, C-4), 152.7 (C, C-2), 159.8 (C, C-6), 166.9 (C), 167.4 (C).

Dimethyl 6-(3′-chlorophenyl)-3,4-dimethyl-2,5-pyridindicarboxylate (**9**), ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 2.47 (s, 3H), 3.73 (s, 3H), 4.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 14.7 (CH_3), 16.5 (CH_3), 52.1 (CH_3), 52.3 (CH_3), 125.9 (CH), 126.7 (C, C-6), 128.1 (CH), 128.4 (CH), 129.1 (CH), 130.4 (C, C-3), 133.9 (C), 140.2 (C), 145.2 (C, C-4), 149.0 (C, C-2), 151.7 (C, C-6), 166.4 (C), 168.2 (C).

5.2.2. Photochemistry of dimethyl 4-(4′-chlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridindicarboxylate (3)

Irradiation of this compound for 20 h and separation of raw photolysate as indicated above gave product **10** as well as a mixed fraction containing compounds **11** and **12** as a glassy solid. Anal. Calcd for $C_{17}H_{16}ClNO_4$: C, 61.18; H, 4.89; N, 4.20. Found: C, 59.8; H, 4.9; N, 3.9.

Dimethyl 3-(4′-chlorophenyl)-5,6-dimethyl-2,4-pyridindicarboxylate (**11**), ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3H), 2.64 (s, 3H), 3.67 (s, 3H), 3.95 (s, 3H), 7.41 (d, J=7 Hz, 2H), 7.49 (d, J=7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.6 (CH_3), 23.4 (CH_3), 52.5 (CH_3), 52.7 (CH_3), 122.9 (C, C-3), 126.9 (C, C-5), 128.4 (CH), 129.6 (CH), 134.8 (C), 137.9 (C), 140.9 (C, C-4), 153.3 (C, C-2), 160.2 (C-6), 167.4 (C), 167.9 (C).

Dimethyl 6-(4′-chlorophenyl)-3,4-dimethyl-2,5-pyridindicarboxylate (**12**), ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 2.46 (s, 3H), 3.72 (s, 3H), 3.99 (s, 3H), 7.41 (d, J=7 Hz, 2H), 7.52 (d, J=7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.1 (CH_3), 15.9 (CH_3), 52.5 (CH_3), 52.7 (CH_3), 126.8 (C, C-5), 128.5 (CH), 129.6 (CH), 130.5 (C, C-3), 134.9 (C), 137.5 (C), 145.7 (C, C-4), 149.3 (C, C-2), 152.1 (C, C-6), 167.3 (C), 168.1.

5.2.3. Structure assignment

The 4′-chlorophenyl derivatives were chosen for the detailed assignment, because of the simplified aromatic pattern, but closely analoguous results were obtained with the 3′ substituted compounds. The work was based on NOESY and HMBC experiments for determining the reciprocal position of methyl groups and for the assignment of quaternary carbons.

In the 2D-NOESY experiment no NOE correlation was observed between aromatic hydrogens and any of the methyl groups in either isomer.

As for HMBC, three experiments were carried out ($J_{(CH)long\ range}$=10.5, and 2 Hz). With both isomers, two quaternary carbons (126.9 and 160.2 for **11**, 130.6 and 145.7 for **12**) were correlated with both methyl signals; with **11** the carboxyl at δ 167.9 correlated with the methyl group at 2.35. The methyl groups were vicinal, but none of them was vicinal to the phenyl. In **11** long range correlations between a C (153.3) and aromatic hydrogens and between C (140.9) and the methyl (2.3) were observed. Taking into account that the more deshielded carbons are those α to the pyridine nitrogen, this supports the above assignment of C-6 and C-2. Similarly, in **12** the more deshielded carbon is C-6 (152.1) that shows a long range correlation with aromatic hydrogens.

5.3. Quantum yields

The quantum yields of the reaction were measured in quartz tubes on 3 mL samples of 2.5×10^{-4} M solutions of the dihydropyridines in MeCN or MeOH after argon flushing when appropriate, irradiated by means of 12 phosphor-coated lamps (15 W, center of emission 366 nm; midheight width 35 nm) or 4 low-pressure mercury arcs (15 W, 254 nm), until a 10–25% conversion was reached (HPLC). The light flux was measured by ferrioxalate actinometry.[23]

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References and notes

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