Novel photoinduced aromatization of Hantzsch 1,4-dihydropyridines

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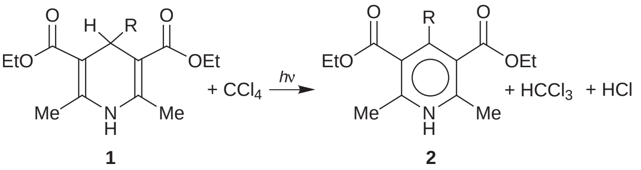
4-Alkyl- and/or aryl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylates (Hantzsch 1,4-dihydropyridines) are quantitatively oxidized to the corresponding pyridine derivatives by irradiation in CCl_4 *via* a photoinduced electron transfer mechanism.

A plethora of reagents has been used for oxidation of 1,4-dihydropyridine (DHP) derivatives,[1] a class of model compounds of NADH and drugs for treatment of cardiovascular diseases.[2] Generally, strong inorganic oxidants, such as nitric acid,[3] ceric ammonium nitrate[4] or ferric or cupric nitrates,[5] must be used to accomplish the oxidation. Recent developments include using nitric oxide,[6] pyridinium chlorochromate[7] and clay-supported cupric nitrate accompanied by ultrasound-promotion[8] to improve the efficiency of the aromatization. However, yields are generally moderate and/or tedious work-up procedures are required. We report herein a very convenient, clean and efficient approach for the oxidation of Hantzsch 1,4-dihydropyridines by direct photolysis of the substrate in CCl_4. To the best of our knowledge, this is the first report on photochemical aromatization of Hantzsch 1,4-dihydropyridines (DHPs).

DHP **1** (1 mmol) was dissolved in 25 ml of CCl_4 or CCl_4–MeCN (9:1 v/v) and irradiated with a 250 W high pressure mercury lamp in a Pyrex bottle under argon atmosphere at ambient temperature. After irradiation the solvent was removed under reduced pressure and the corresponding pyridine derivative **2** was obtained in pure form and almost quantitative yield (Scheme 1). One exception is 4-(2-furyl)-DHP **1g** which gave 85% of **2g** together with 13% of de-furyl product **2a**. The results are summarized in Table 1.

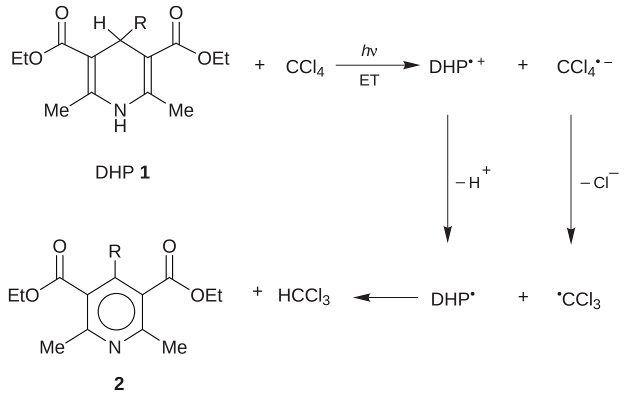
It was found that $CHCl_3$ was generated during the reaction, as evidenced by GC, and the solution became acidic after irradiation. Hence there is no doubt that C–Cl bond cleavage takes place during the photolysis. Similar CCl_4- and/or $HCCl_3$-promoted photo-fragmentation reactions have recently been reported from this laboratory[9,10] and by Whitten and co-workers.[11] Therefore, a photoinduced electron transfer mechanism is proposed, as outlined in Scheme 2.



Scheme 1

Table 1 Aromatization of Hantzsch dihydropyridines **1** by direct photolysis in CCl_4

Substrate	R	*t*/h	Product	Conversion (%)	Yield (%)
1a	H	1	**2a**	~ 100	~ 100
1b	Me	3	**2b**	~ 100	~ 100
1c	Et	3	**2c**	~ 100	~ 100
1d	Ph	3	**2d**	~ 100	~ 100
1e	*p*-$MeOC_6H_4$	3	**2e**	~ 100	~ 100
1f	*p*-ClC_6H_4	3	**2f**	~ 100	~ 100
1g	2-furyl	3	**2g**, **2a**	~ 100	85, 13



Scheme 2

The critical step in this mechanism is the extremely fast dechlorination of the radical anion of CCl_4. It is well known that alkyl and aryl halides are subject to reductive dissociation upon accepting an electron either electrochemically or photochemically.[12] The lifetime of the radical anion of CCl_4 was reported to be extremely short (less than 10 ps).[13] Therefore, C–Cl bond breaking and electron transfer may even take place concertedly which, in turn, effectively circumvents the back electron transfer and makes the reaction very efficient. Maslak and co-workers[14] have termed unimolecular fragmentation of radical ions as mesolytic cleavage and demonstrated the tremendous facilitation of bond cleavages obtainable from the mesolytic processes. The present reaction involves mesolytic cleavages of both radical anions (aniomesolysis) and radical cations (catiomesolysis), hence, it can be considered as a double mesolytic fragmentation reaction. The aniomesolysis helps to prevent back electron transfer, which enhances the quantum yield of the photolysis, and the catiomesolysis facilitates the deprotonation from DHP. These two effects make the reaction very efficient. This strategy may be applicable to the enhancement of the efficiency of other photoinduced electron transfer reactions. In addition, since no additional oxidant is required other than the solvent CCl_4, and no any waste is produced, this reaction can also be considered as a facile green chemical reaction for the synthesis of pyridine derivatives and may be extended to other synthetic reactions

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