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Reactive spin state dependent enantiospecific photocyclization of axially chiral α-substituted acrylanilides†

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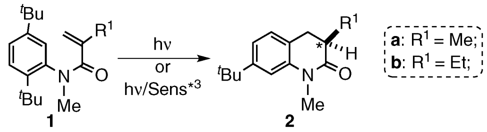
The enantiomeric ratio (e.r.) in the 3,4-dihydroquinolin-2-one photoproduct during 6π-photocyclization of α-substituted axially chiral *ortho-tert*-butyl-acrylanilides depends on the nature of the reactive spin state (singlet or triplet), where the singlet-spin state reactivity gives a racemic mixture and the triplet reactivity gives an e.r. value >95 : 5.

The role of the excited spin state (singlet S_n or triplet T_n) determining the course of light initiated reactions is well documented in the literature.[1–8] There are a number of elegant examples of reactions from S_1 or T_1 leading to different reactivities and/or photoproducts.[4–6,9] Various groups in the last four decades have investigated[10–13] the role of reactive spin states in regioselective and diastereoselective photochemical transformations in solution[14,15] and in organized assemblies.[16,17] An intriguing aspect in this regard involves the spin dependent selectivity in photochemical reactions leading to the same photoproduct with varying enantioselectivities.[10,11] One of the classical reports involves γ-hydrogen abstraction in which the singlet spin-state reactivity gives very high enantiomeric excess and triplet reactivity leads to a racemic mixture of photoproducts.[10,11] Herein we report a reactive spin state (S_1 or T_1) dependent photocyclization of axially chiral α-substituted acrylanilides **1a–b** to 3,4-dihydro-2-quinolin-2-one photoproduct **2**, where the singlet reactivity (*via* direct irradiation) leads to a racemic mixture, while the corresponding triplet reactivity (*via* triplet sensitization) leads to enantiomeric ratios (er values) >95 : 5 in the 3,4-dihydro-2-quinolin-2-one photoproduct **2** at ambient conditions.

We recently reported[18,19] that axially chiral chromophores can be employed to achieve a very high enantiomeric excess in the photoproduct(s) in solution. Constraints that make the reactants axially chiral are based on the well-established concepts of rotamer control *via* restricted bond rotation that have been successfully employed for various chemical transformations.[20–23] During our investigation of axially chiral acrylanilides, we observed efficient photocyclization upon triplet-sensitized irradiations. To examine the role of the reactive spin-state we investigated the enantiospecific 6π-photocyclization of **1a–b** (Scheme 1) under direct and triplet-sensitized irradiations to divulge the critical role of the reactive spin-state (S_1 or T_1) in determining the enantiomeric ratio (er values) in **2**.

Triplet sensitized irradiation of **1a–b** in acetone (serving as both solvent and sensitizer) gave photoproduct **2** with er values >95 : 5 at ambient conditions (Table 1). Optical antipodes of **1** gave the opposite enantiomers in **2** indicating that the system was well behaved. For example, triplet sensitized irradiation of (−)-**1b** and (+)-**1b** in acetone gave er values >95 : 5 of **2b** and *ent*-**2b** respectively (Scheme 1; HPLC insert). Direct irradiation of (−)-**1b** or (+)-**1b** under identical

Table 1 Enantiospecific 6π-photocyclization of **1** under direct and triplet sensitized irradiations[a–e]



Entry	Cmpd[b]	Solvent	Sens.[c]	Mode	T/°C	er **2**[e]
1	(+)**1a**	Acetone	Acetone	Triplet	20	96 : 04 (A)
2		Acetone	Acetone	Triplet	27	90 : 10 (A)
3		TFE	—	Singlet	27	Racemic
4		MeOH	—	Singlet	27	Racemic
5	(−)**1a**	Acetone	Acetone	Triplet	20	97 : 03 (B)
6		Acetone	Acetone	Triplet	27	90 : 10 (B)
7		TFE	—	Singlet	27	Racemic
8		MeOH	—	Singlet	27	Racemic
9	(+)**1b**	Acetone	Acetone	Triplet	20	97 : 03 (A)
10		Acetone	Acetone	Triplet	27	90 : 10 (A)
11		TFE	—	Singlet	27	Racemic
12	(−)**1b**	Acetone	Acetone	Triplet	20	96 : 04 (B)
13		Acetone	Acetone	Triplet	27	90 : 10 (B)
14		TFE	—	Singlet	27	Racemic

[a] Reported values are an average of a minimum of 3 runs with ±5% error. TFE: trifluoroethanol. [b] (+) and (−) represent the signs of their CD signals at 285 nm in methylcyclohexane (MCH). [c] Sensitizer's triplet energies (E_T) for acetone: ∼79 kcal mol^{-1}. [d] Conversion calculated by ^{1}H NMR using α,α′-dichloro-*p*-xylene as internal standard (refer to ESI †). [e] A and B refers to the first and second peak that elutes out on the HPLC chiral stationary phase separation for a given pair of enantiomers.

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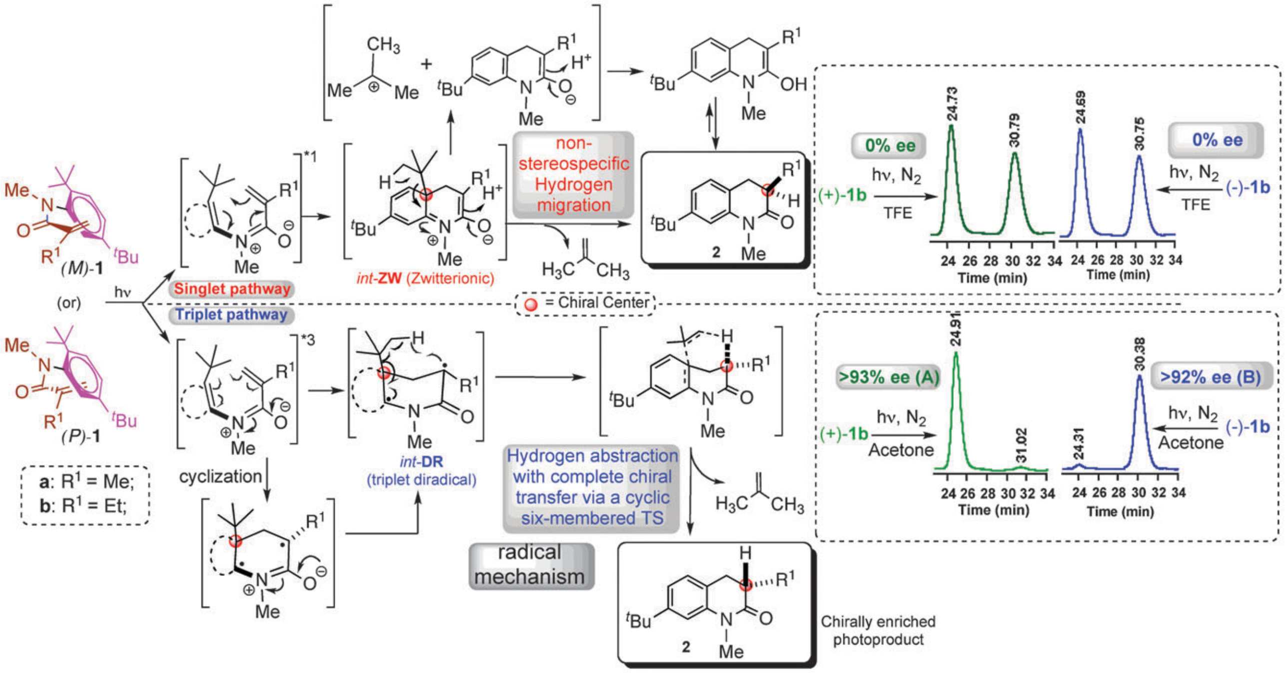

Scheme 1 Photocyclization of axially chiral α-substituted acrylanilides under direct (singlet) and sensitized (triplet) irradiations.

conditions in trifluoroethanol (TFE) gave a racemic mixture of **2**. There was a minimal decrease in the er values from > 95 : 5 to 90 : 10 upon increasing the temperature from 20 °C to 27 °C due to the slow racemization (slow N–C(aryl) bond rotation in the reactant **1a–b** at elevated temperatures). Both **1a–b** showed fluorescence (Fig. 1A) at room temperature in methylcyclohexane (MCH). The emission maxima shifts bathochromically upon changing the solvent from non-polar MCH to polar solvents like ethanol or acetonitrile (ESI †), similar to the fluorescence emission behaviour of other methacrylanilides reported in the literature.[24] Additionally, for **1a–b** we observed phosphorescence (Fig. 1A) at 77 K in MCH glass with a triplet energy (E_T) of ~77.3 kcal mol^{-1} and a lifetime (τ_p) of ~1.58 s (Fig. 1B) (ESI †). Based on the emission studies, it is clear that the lowest excited singlet and triplet state has a ππ* configuration in **1a–b**.

Based on the established paradigm[25] for photochemical reactions *viz*. photocyclization, a zwitterionic intermediate is expected for the photocyclization from the ππ* singlet excited-state $S_1(\pi\pi^*)$ and a diradicaloid intermediate is likely from the corresponding ππ* triplet excited-state $T_1(\pi\pi^*)$.[25] This prompted Ogata and co-workers[24,26] to propose a zwitterionic intermediate originating from the singlet ππ* (S_1 ππ*) excited-state for the 6π-photocyclization of achiral acrylanilide (N–H substituted derivative without the *ortho*-*tert*-butyl group on the phenyl ring). In the case of **1a–b**, we believe that the restricted N–C(aryl) bond rotation not only imparts axial chirality (molecular chirality) to the system but also enables us to access the triplet state (as we observe phosphorescence) at 77 K in MCH glass. While in the case of an achiral N–H acrylanilide (*viz*., *ortho*-*tert*-butyl N–H acrylanilide **1d**) we failed to observe any phosphorescence at 77 K, both achiral and axially chiral *N*-methyl derivatives **1a–c** (axially chiral **1a–b** and achiral **1c**) gave observable phosphorescence at 77 K in MCH glass (ESI †). Thus the presence of the N–Me substituent is crucial to access the triplet-excited manifold. We believe that the enolization of the N–H acrylanilides (as in **1d**; Fig. 1C) to the enol form enables it to cyclize only from the singlet-excited state, as it is oriented optimally for 6π-photocyclization. On the other hand, in the case of the *N*-methyl derivatives (as in **1a–c**; Fig. 1C), the nitrogen lone pair is part of the 6π-backbone leading to photoreactivity from the ππ*

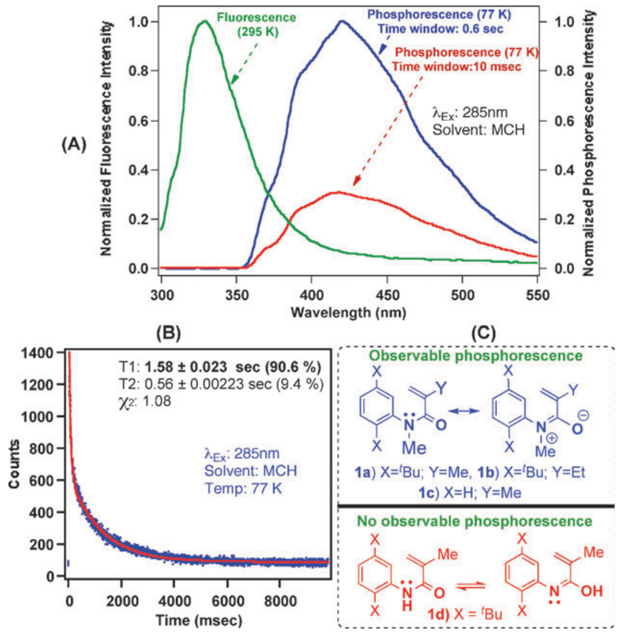

Fig. 1 (A) Fluorescence (green at 298 K) and phosphorescence (red, blue at 77 K) of **1a** in methylcyclohexane (MCH). (B) Phosphorescence decay kinetics at 77 K in MCH glass. (C) Role of *N*-methyl and N–H substitution.

excited state. Based on the phosphorescence, the triplet ππ* state of **1a–b** lies at ~77 kcal mol^{-1}. Hence triplet energy transfer from acetone ($E_T \approx 79$ kcal mol^{-1})[27] is quite likely. The involvement of the triplet spin state *viz.*, T_1(ππ*) in the reaction path way was ascertained by carrying out the reaction under O_2 saturated conditions that resulted in <5% conversion.[28] Thus 6π-photocyclization of **1a–b** could possibly occur from either the singlet (S_1) or the triplet (T_1) spin-state depending on the reaction conditions.[29]

Based on our mechanistic study[28] we showed that the 6π-photocyclization upon direct irradiation in the case of *ortho-tert*-butyl substituted axially chiral acrylanilides occurs at the *ortho* carbon *via* the zwitterionic intermediate "*int*-**ZW**" (Scheme 1; top) followed by a non-stereo-specific hydrogen migration with the eventual loss of the *ortho-tert*-butyl substituent. As the photocyclization occurs from the S_1(ππ*) excited state upon direct irradiation in the case of **1a–b**, the formation of a zwitterionic intermediate (*int*-**ZW**) is expected.[24,26,30,31] Similarly, triplet sensitized irradiation of **1a–b** leads to photocyclization from the T_1(ππ*) excited state resulting in a diradical (triplet diradical) intermediate "*int*-**DR**" (Scheme 1; bottom). This triplet diradical "*int*-**DR**" subsequently abstracts a hydrogen atom from the *ortho-tert*-butyl substituent leading to 3,4-dihydroquinolin-2-one photoproduct **2**. The high enantiomeric ratio (Table 1) in the photoproduct **2** under sensitized irradiation points out a stereospecific hydrogen abstraction *via* a cyclic six membered transition (Scheme 1; bottom) state from the triplet diradical intermediate (*int*-**DR**). Thus the excited spin state S_1(ππ*) or T_1 (ππ*) not only leads to the same photoproduct *via* two different reactive intermediates and/or transition states, but also determines the er values in the photoproduct.

Axially chiral chromophores in conjunction with their corresponding achiral counterparts, offer rich and divergent photoreactivity that helps us to better understand mechanisms of light induced stereospecific transformations. Our current investigation with α-substituted acrylanilides has highlighted the critical role of the reactive spin state in determining the enantiomeric excess through two different photochemical pathways leading to the same photoproduct.

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