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ENANTIOSELECTIVE PHOTODECONJUGATION OF CONJUGATED LACTONES INDUCED BY SMALL AMOUNTS OF A CHIRAL INDUCTOR

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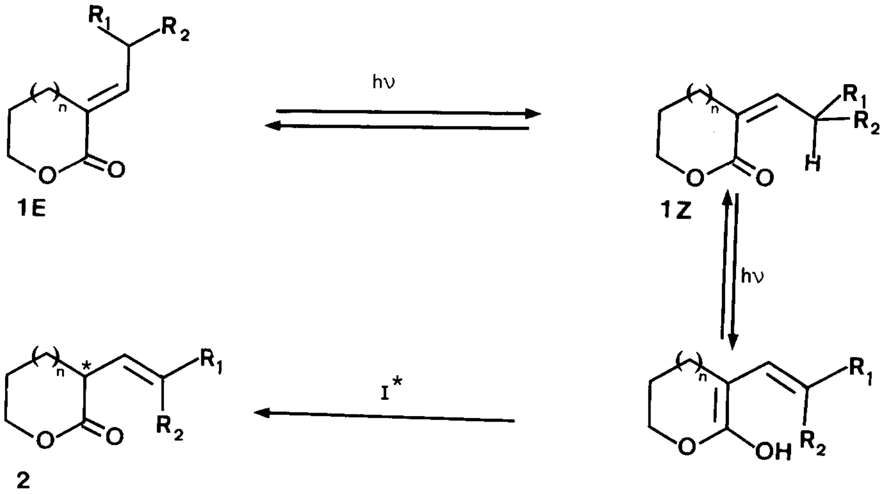
Abstract : In the presence of small amounts of (-) ephedrine, photodeconjugation of conjugated lactones is enantioselective. The enantiomeric excess which depends on the structure of the starting material and on the temperature of the reaction medium can be up to 25%.

Conjugated enones and esters bearing at least one γ-hydrogen atom produce a very unstable photoenol when irradiated with UV light (1). Depending on the reaction conditions, the photoenol can lead to the corresponding photodeconjugated product (2) or to the starting material. Despite the interest in photoenolization, only a few synthetic applications have been proposed for this reaction. However, condensation of dienophiles on the photoenol derived from conjugated enones have received a particular attention (3).

Recently, we described that the photodeconjugation of α-alkylidene butyro and valero lactones could be quantitative in methanol as solvent (4). During the reaction, a new asymmetric centre is created. The protonation of the photoenol has also been shown to be facilitated by bases such as amines, and even compounds believed to be photostable were thus deconjugated (5). The protonation of enolates in the presence of chiral acidic reagents can be enantioselective (6) ; unfortunatly, strong bases are needed for the preparation of the enolates and the application of this method remains limited. The photochemical production of enols should allow a similar asymmetric induction under very mild conditions. Furthermore,the concentration of the enolic intermediate being low, it might be possible to induce the enantioselective protonation in the presence of catalytic amounts of a chiral reagent.

With this aim, we studied the deconjugation of α-alkylidene lactones 1a-1d in an aprotic solvent in the presence of a chiral agent having an alcoholic function able to protonate and an amino group to assist the reaction (table).

Irradiation of a dilute solution of α-ethylidene valerolactone 1a, at 254 nm and at room temperature in the presence of (-) ephedrine (0.1 equivalent) led to rapid deconjugation



	n	R^1	R^2	Conditions$^{a)}$	Yield %	$|\alpha|^{20}_{D}$ (C, solvent)	Config.	e.e. %
1a	1	H	H	pentane-ether (90-10); 25°C	(b)	+1.56°± 0.25 (1.28, ether)	R	2.2 ± 0.1
				pentane-CH_2Cl_2 (95-5); -78°C	(b)	+ 18° ± 0.6 (3.2, ether)	R	26.7 ± 0.9
1b	0	H	H	pentane-CH_2Cl_2 (95-5); -78°C	(b)	-2.5° ± 0.2 (1.4, CH_2Cl_2)	R	(c)
1c	0	Me	H	CH_2Cl_2, -78°C	80	-7.7° ± 0.1 (0.9, MeOH)	R	10 ± 0.2
1d	0	Me	Me	CH_2Cl_2, 25°C	64	-5.2° ± 0.4 (1.6, CH_2Cl_2)	R	5 ± 0.4
				CH_2Cl_2, -78°C	85	-27.7°± 0.4 (4.8, CH_2Cl_2)	R	25.1 ± 0.4

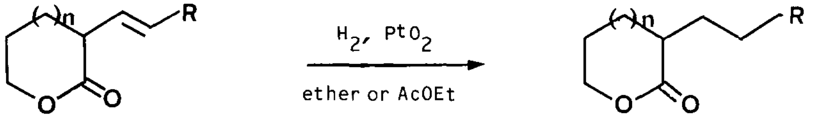
(a) Irradiation were carried out at $\lambda = 254$ nm ; molar concentrations were 10^{-2} for lactones and 10^{-3} for (-) ephedrine

(b) Yield almost quantitative from the N.M.R. spectrum of the crude reaction mixture. Reconjugation occured very easily

(c) Not determined.

of the starting material. After elimination of ephedrine on T.L.C., the deconjugated lactone 2a was shown to possess a small optical activity $|\alpha|_D = -1.56°$ ± 0.25, c = 1.28 in ether). As expected, the diastereotopic discrimination increased when the temperature was lowered and as shown in the table the specific rotation of 2a was far higher when irradiation was performed at -78°C. A similar enantioselective photodeconjugation was observed for 1b-1d.

To determine the configuration of the new asymmetric center in the major enantiomer and the optical yield of the deconjugation, 2a and 2c were hydrogenated in the presence of PtO_2 at room temperature and atmospheric pressure(7).

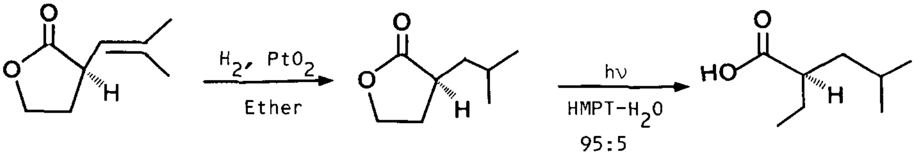


2a,c

3a,c

From the reported value for pure 3a-(R) $|\alpha|_D = -56°$ (8) the (S) configuration was attributed to our sample of 3a and we deduced the (R) configuration for the corresponding sample of 2a ; an enantiomeric excess of 26.7 ± 0.9% was established.

For the unknown lactones 2d and 3d the following correlation was used in order to minimize the epimerization of the asymmetric center. The photochemical reduction carried out



2d

4d

in a neutral medium (9) should not affect the configuration of C_2 of 4d. The specific rotation or pure 4d (S) $|\alpha|_D = 13.44°$ (10) indicated the configuration of the asymmetric centers was (R) for 2d and 4d, (S) for 3d and that the enantiomeric excess can reach 25.1 ± 0.4%.

In conclusion, we have shown that the photodeconjugation of alkylidenelactones in the presence of catalytic amounts of (-) ephedrine led to the photodeconjugated lactones of 3 -(R) configuration for the major enantiomer. Extension of this new process of asymmetric induction is currently under active investigation.

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