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Photochemical Preparation of Highly Functionalized 1-Indanones

Pablo Wessig,* Clemens Glombitza, Gunnar Müller, and Janek Teubner

Institut für Chemie, Humboldt-Universität zu Berlin, D-12489 Berlin, Germany

pablo.wessig@chemie.hu-berlin.de

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A series of *o*-alkylphenyl alkyl ketones **1** were synthesized by different methods. The presence of a leaving group X adjacent to the carbonyl group is the special peculiarity of these ketones. Upon irradiation the keto carbonyl group of these compounds undergoes an n−π* excitation followed by a 1,5-hydrogen migration from the *o*-alkyl substituent to the carbonyl oxygen atom. The thus formed 1,4-diradicals are subject to a very rapid elimination of acid HX, giving 1,5-diradicals. We called this process *spin center shift*. After intersystem crossing these diradicals cyclize to 1-indanones **20** in good yields. Depending on the solvent and on substituents, *o*-alkoxyalkyl ketones **22** or benzo[*c*]furanes **21** are obtained as byproducts. The mechanism of the cyclization was elucidated by quantum chemical calculations and kinetic measurements.

Introduction

Ring closure reactions are of fundamental importance in organic chemistry belonging to the broad occurrence of cyclic structural elements both in natural products and in synthetic drugs. Besides many valuable thermal methods, photochemical ring closure reactions have gained increasing importance in recent years. Among the various photochemical cyclization reactions the Norrish−Yang reaction[1] turned out to be particularly versatile. With this reaction a variety of cyclic structures with different ring sizes could be obtained.[2] Nevertheless, the relatively rigid regioselectivity rules of the classical Norrish−Yang reaction limit its range of application. Recently, we developed a new concept called *spin center shift* that considerably extends the scope of the Norrish−Yang reaction.[3] The basic idea of this concept is the introduction of a suitable leaving group X adjacent to the carbon atom of the photochemical excited carbonyl group (**I**). The presence of this leaving group causes a very rapid elimination of an acid HX at the stage of the primarily formed diradicals **II** and, consequently, a shift of one of the two radical centers by one atom in the diradicals **II** (Scheme 1).

Depending on the structure of the residue R, linking the two radical centers, the products may be derived from mesomer **IVa**, as well as from mesomer **IVb**. By utilization of this approach, we developed novel routes to cyclopropanes[3b,c] (**V**, R = C[sp^3]) and 1,3-oxazine-4-ones[3a] (**VI**, R = CO−NR‴).

Herein we wish to report on a further application of the spin center shift concept, the synthesis of highly functionalized 1-indanones.

The 1-indanone skeleton is regularly found in natural products, e.g., in the cytotoxic pterosines that occurs in Bracken fern.[4]

Results and Discussion

The concept of spin center shift, i.e., the shift of one of two radical centers of a photochemically generated diradical due to acid elimination, may be realized in different ways. Scheme 2 depicts four reactant types which all may be preparatively utilized. Type **VII** is characterized therein that the leaving group X is located at a carbon atom inside the chain, connecting the carbonyl group and the photochemically attacked C−H bond. The diradicals **IX** formed after the elimination of the acid HX from diradicals **VIII** may be formulated as two mesomeric structures (**IXa** and **IXb**), differing from each other in the electron distribution at the enolate radical moiety. The products of carbon centered mesomers **IXa** are carbocyclic compounds **Xa**[3b,c] whereas the oxygen centered mesomers **IXb** provide cyclic enol ethers **Xb**.[3a] In type **XI** the leaving group is bound at a carbon atom outside the chain connecting the carbonyl group and the attacked C−H bond. As with diradicals **IX**, diradicals **XIII** (formed from **XI** in two steps) also exist as two mesomers. The carbon centered mesomers **XIIIa** result from the cyclic ketones **XIVa**, whereas the oxygen

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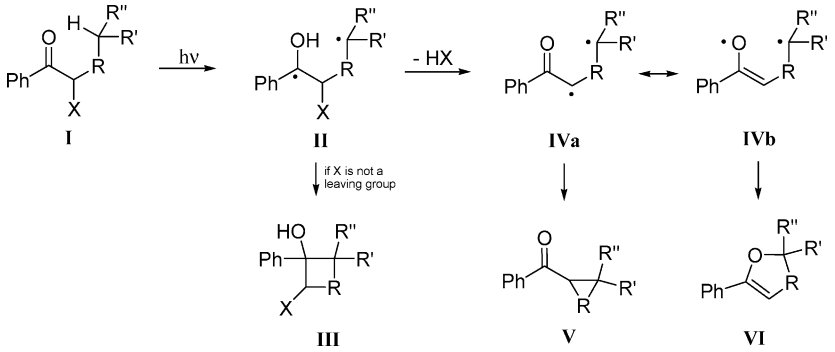
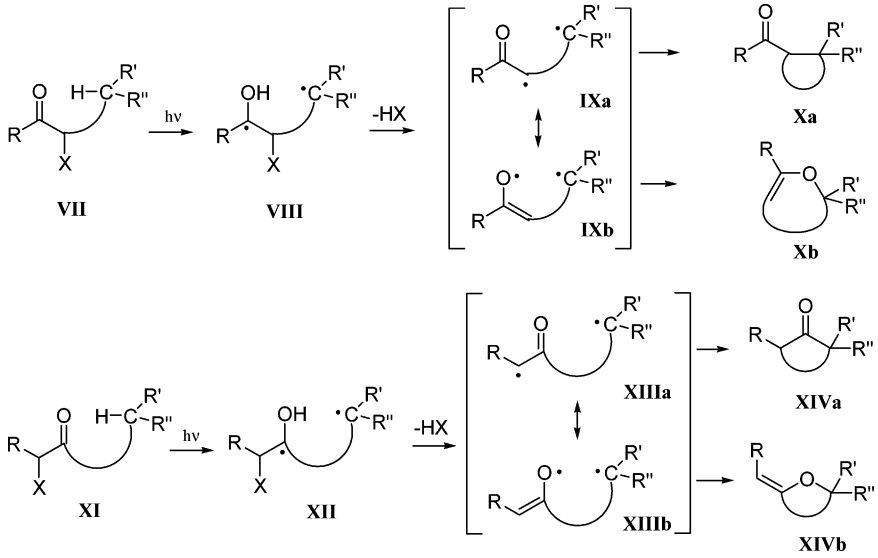
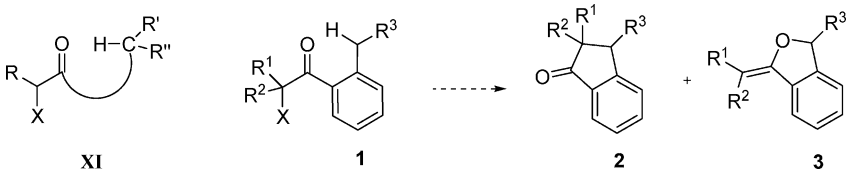
SCHEME 1. The Norrish−Yang Reaction and the Principal of Spin Center Shift



SCHEME 2. Various Types of Reactants for the Spin Center Shift



SCHEME 3. Realization of Type XI



centered mesomer **XIIIb** reacts to form semicyclic enol ethers **XIVb** (Scheme 2).

A concrete realization of type **XI** is found in *o*-alkylaryl alkyl ketones **1**. Upon irradiation ketones **1** should give 1-indanones **2** (which correspond to **XIVa**) or 2-alkylidene dihydrobenzo[*c*]furanes **3** or a mixture of both (Scheme 3).

The photochemical formation of 6-methyl-1-indanone via photochemical transformation, similar to those depicted in Scheme 3, has been previously described.[5−8] The preparation of 1-indanones was not the main intention of these investigations though. Herein we will describe the photochemical behavior of ketones **1** bearing a variety of different substituents R^1−R^3 as well as leaving groups X. Furthermore, we will discuss the mechanism of the reaction by means of quantum chemical calculations and kinetic measurements.

Synthesis of Ketones 1. The systematic investigation of the photochemical behavior of ketones **1** with varying substituents required the development of reliable methods for the synthesis of specifically ortho-disubstituted benzenes. A literature survey revealed that no generally applicable approach exists for this problem. Although some methods for the selective ortho-functionalization of monosubstituted benzenes have been published, we prepared ketones **1** by modification of the residues of commercially available ortho-disubstituted benzene derivatives.

In Scheme 4 the methods used for the preparation of *o*-tolyl ketones **1a**−***l*** (R^3 = H) are summarized. The alkyl- and phenyl-substituted acetophenones **7** were prepared from *o*-methylbenzaldehyde **4** by addition of Grignard reagents and subsequent oxidation of the obtained alco-

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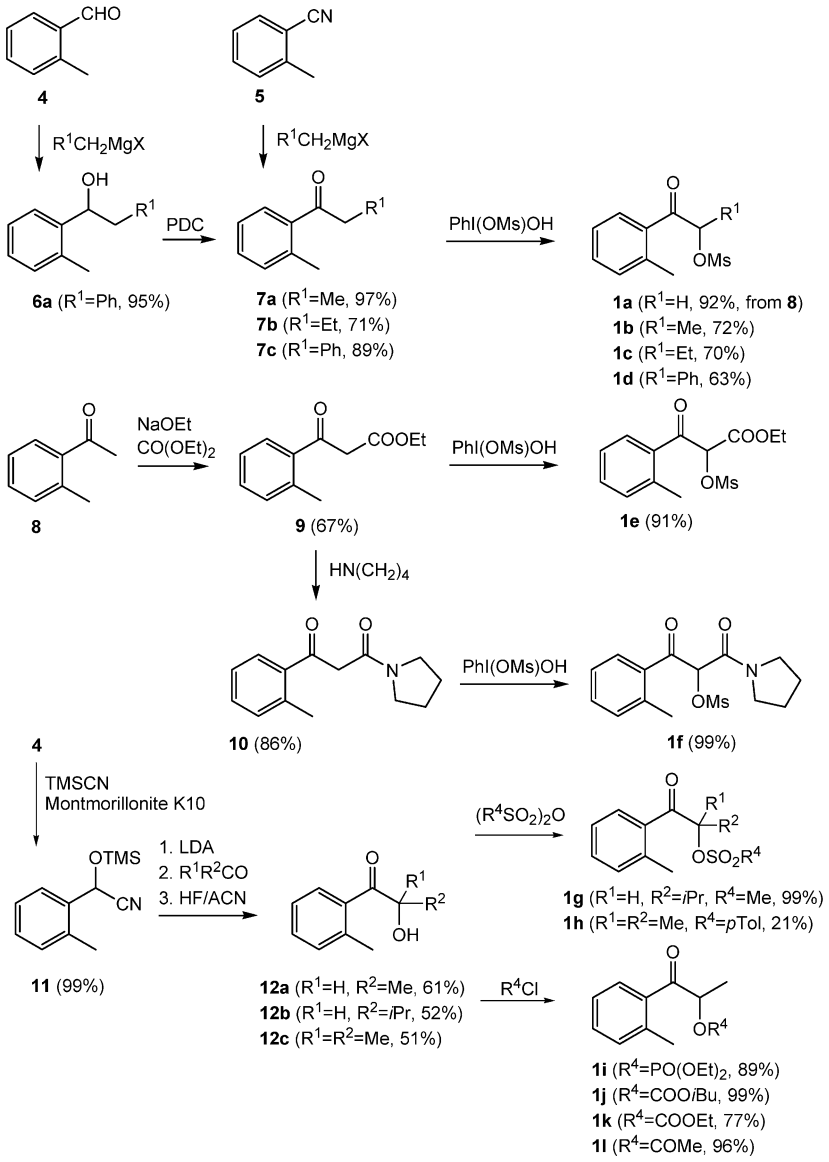
SCHEME 4. Preparation of *o*-Tolyl Ketones 1a−*l*



hols **6** with PDC or directly from *o*-tolunitrile **5**. The one-step introduction of the mesyloxy group succeeded by treating ketones **7** with hydroxymesyloxyiodobenzene (PhI(OMs)OH), an analogue of Koser's reagent, yielding ketones **1a**−**d**.[9] PhI(OMs)OH can easily be prepared from commercially available diacetoxyiodobenzene and methane sulfonic acid in aqueous acetonitrile.

The preparation of *β*-ketoester **1e** and *β*-ketoamide **1f** started with *o*-methylacetophenone **8**, which was first subjected to a Claisen condensation with diethyl carbonate, affording the ester **9**. Treatment of **9** with pyrrolidine gave the amide **10**. Both **9** and **10** were converted to **1e** and **1f** respectively by reaction with PhI(OMs)OH.

The direct introduction of the mesyloxy group with PhI(OMs)OH is not applicable to substrates with branched alkyl substituents. Obviously, the reaction with the hypervalent iodine reagent is relatively sensitive about steric hindrance. The alternative route to ketones **1g**,**h** is based on the reaction between lithiated α-trimethylsilyloxy-*o*-tolylacetonitrile **11** with aldehydes and ketones according to Hünig.[10] The thus obtained hydroxy ketones **12** were converted to **1g**,**h** by means of sulfonyl anhydrides. We were also interested in a variation of the leaving group, concerning an optimization of the photochemical cyclization, and developing new photolabile protective groups. Therefore we prepared the phosphate **1i**, the carbonates **1j**,**k**, and the acetate **1l** by acylation of the hydroxy ketone **12a** with the corresponding acid chlorides (Scheme 4).

Scheme 5 summarizes the synthetic steps to α-mesyloxyacetophenones **1m**−**o**, having different substituents R^3. The synthesis of *o*-ethyl-substituted ketone **1m** commences with *o*-bromoethylbenzene **16**, which was first converted to the corresponding Grignard reagent with Riecke magnesium.[11] It should be noted that the preparation of Grignard reagents from ortho-substituted ha-

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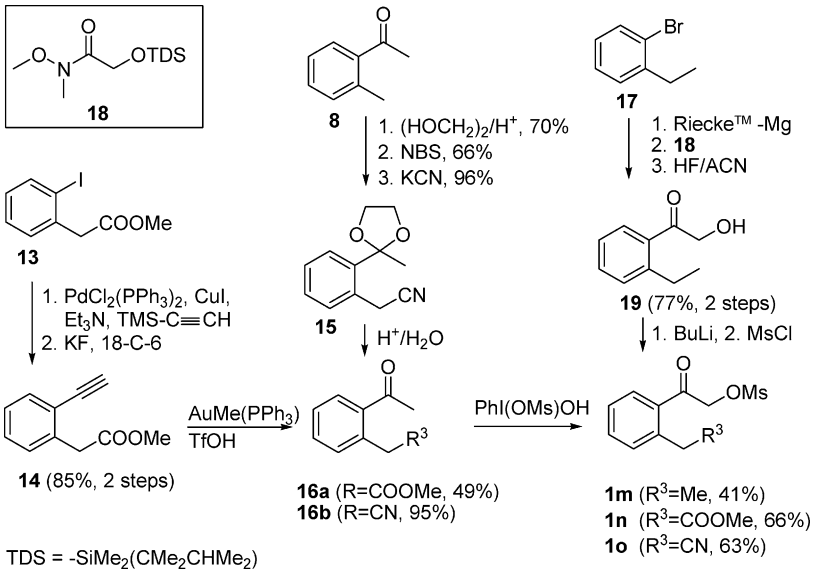
SCHEME 5. Preparation of Ketones 1m−o



lobenzenes with magnesium turnings is often troublesome. These difficulties can be circumvented by using the highly reactive Riecke magnesium. The Grignard reagent obtained from **17** was treated with the Weinreb amide **18**, which was prepared from ethyl glycolate in two steps. Deprotection of the primary hydroxy group gave the hydroxy ketone **19** with an overall yield of 77%. Surprisingly, the mesylation of the hydroxy group in **19** turned out to be difficult. The reaction of **19** with MsCl in pyridine gave the α-chloro ketone instead of the desired mesylate.[12] Replacement of MsCl by Ms_2O afforded **1m**, but in low yields even in the presence of DMAP. A satisfactory yield was achieved by deprotonation of the hydroxy group with BuLi followed by treatment with MsCl.

The synthesis of methyl ester **1n** started with a Sonogashira[14] coupling of methyl *o*-iodophenylacetate **13**[13] with trimethylsilylacetylene and subsequent desilylation. The arylacetylene **14** could be regioselectively hydrated by utilization of a gold catalyst to give the acetophenone **16a**.[15] Compound **16b** bearing a nitrile group instead of the ester group was obtained from *o*-methylacetophenone by a four-step sequence. The introduction of the mesyloxy group took place again with the hypervalent iodine reagent PhI(OMs)OH and provided the ketones **1n**,**o**.

Synthesis of 1-Indanones: Known Methods. To classify the photochemical route to 1-indanones described herein, the hitherto known methods to prepare these bicyclic ketones should be briefly outlined. These methods may be systematized regarding C−C bonds tied to construct the five-membered ring of the indane skeleton (**A**−**D**). Scheme 6 depicts a selection of methods. One of the oldest methods is the intramolecular Friedel−Crafts acylation of 3-arylpropionic acid derivatives (**A1**[16]). Another method to form the arene−carbonyl-C bond of 1-indanones is based on the Pd-catalyzed cyclization of 3-(2-iodoaryl)propionitriles (**A2**[17]). The formation of the C1−C2 bond (**B**) was relatively seldom used and was performed by an intramolecular Claisen condensation (Dieckmann condensation, **B1**[18]). Most methods are based on the formation of the C2−C3 bond (**C**) and include intramolecular S_N reactions (**C1**[19]), the cyclization of 2-(alkynylaryl)allenes (**C2**[20]), or the insertion of ketocarbenes, generated from diazoketones by Rh-catalysis, in C−H bonds of *o*-alkyl groups (**C3**[21]). There exist also some photochemical routes to 1-indanones. Thus, 1,2-diketones were cyclized in the course of a Norrish−Yang reaction (**C4**[22]) and also enones (**C5**[23]) and inones (**C6**[24]) were used as reactants for the preparation of 1-indanones. Furthermore, the simultaneous formation of two C−C bonds form the basis of some methods (**AB1**,[25] **AD1**,[26] and **BC1**[27]).

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SCHEME 6. Selected Methods for the Preparation of 1-Indanones

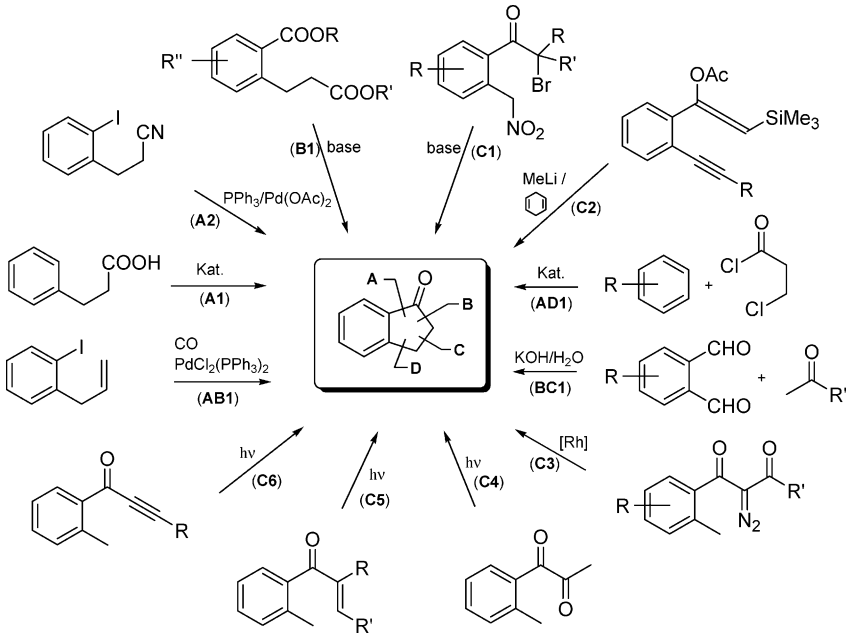

TABLE 1. Photochemical Behavior of Ketones 1

entry	reactant	R^1	R^2	R^3	X	**20**[a]	**21**[a]	condition	remarks
1	**1a**	H	H	H	OMs	39 (**a**)	0	A	+**22a** (47%)
2	**1a**	H	H	H	OMs	42 (**a**)	0	C	
3	**1b**	Me	H	H	OMs	71 (**b**)	0	A	
4	**1b**	Me	H	H	OMs	73 (**b**)	0	C	
5	**1c**	Et	H	H	OMs	69 (**c**)	0	B	+**20a** (3%)
6	**1c**	Et	H	H	OMs	35 (**c**)	0	C	+**20a** (20%)
7	**1d**	Ph	H	H	OMs	66 (**d**)	0	A	
8	**1d**	Ph	H	H	OMs	20 (**d**)	0	C	
9	**1e**	COOEt	H	H	OMs	30 (**e**)	67 (**a**)	C	
10	**1e**	COOEt	H	H	OMs	82 (**e**)	0	D	
11	**1f**	$CON(CH_2)_4$	H	H	OMs	46 (**f**)	43 (**b**)	C	
12	**1f**	$CON(CH_2)_4$	H	H	OMs	70 (**f**)	21 (**b**)	D	
13	**1g**	*i*Pr	H	H	OMs	46 (**g**)	0	A	+**20a** (27%)
14	**1g**	*i*Pr	H	H	OMs	5 (**g**)	0	C	+**20a** (32%)
15	**1h**	Me	Me	H	OTs	0	0	B	
16	**1i**	Me	H	H	$OPO(OEt)_2$	62 (**b**)	0	A	
17	**1j**	Me	H	H	OCOO*i*Bu	40 (**b**)	0	A	
18	**1k**	Me	H	H	OCOOEt	52 (**b**)	0	A	
19	**1*l***	Me	H	H	Ac	0	0	A	
20	**1m**	H	H	Me	OMs	31 (**h**)	0	A	+**22b** (36%)
21	**1m**	H	H	Me	OMs	24 (**h**)	0	D	+**22c** (24%)
22	**1m**	H	H	Me	OMs	42 (**h**)	0	C	
23	**1n**	H	H	COOMe	OMs	77 (**i**)	0	A	
24	**1n**	H	H	COOMe	OMs	73 (**i**)	0	C	
25	**1o**	H	H	CN	OMs	58 (**j**)	0	A	
26	**1o**	H	H	CN	OMs	41 (**j**)	0	C	

[a] Yields and compound index. Conditions: (A) MeOH/NMI (2 equiv), (B) MeOH, (C) DCM/NMI, (D) *t*-BuOH.

Photochemical Behavior of Ketones 1. The UV−vis spectra of ketones **1** exhibit a weak absorption band between 320 and 360 nm assigned to the n−π* transition of the keto carbonyl group. Irradiation of ketones **1** with a high-pressure mercury arc lamp in Pyrex vessels, which absorb light with wavelength <300 nm, mainly affords three types of products. The results of various irradiation experiments are summarized in Table 1. To explore the synthetic scope of the reaction, we varied the substituents R^1−R^3 and the leaving group X. Furthermore, we used different solvents to find out the optimal reaction conditions. Because a very strong acid is liberated during the irradiation we added the acid scavenger *N*-methylimidazole (NMI), which proved to be worthwhile in recent investigations.[3]

1-Indanones **20** were almost always the main products of the irradiation of ketones **1**. If the ketones **1** bear an electron-withdrawing substituent in the α-position with respect to the carbonyl group we obtained 2-alkylidene benzo[*c*]furane **21** besides the isomeric 1-indanones **20**. This is probably due to a shift of the mesomer equilibrium between **XIIIa** and **XIIIb** by the acceptor substituent (see

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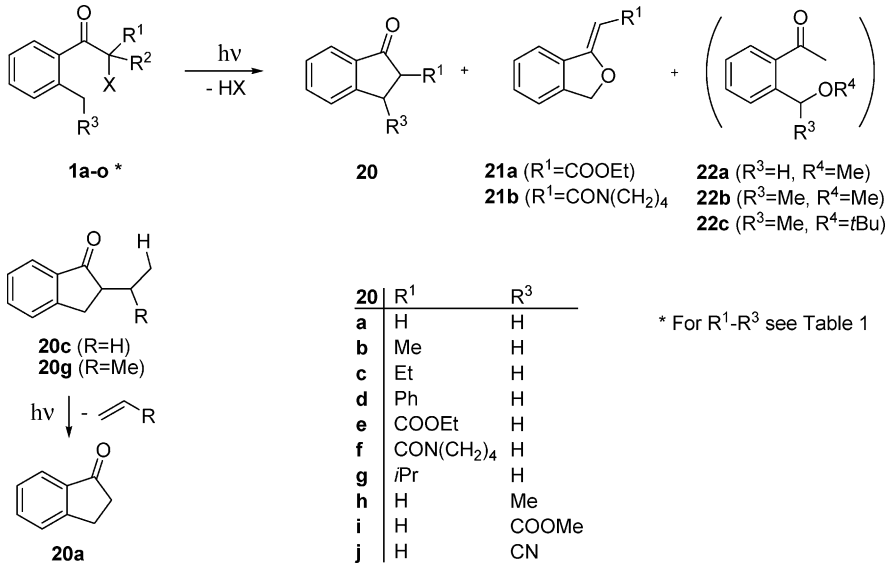
SCHEME 7. Photochemical Behavior of Ketones 1



20	R^1	R^3
a	H	H
b	Me	H
c	Et	H
d	Ph	H
e	COOEt	H
f	$CON(CH_2)_4$	H
g	*i*Pr	H
h	H	Me
i	H	COOMe
j	H	CN

Scheme 2). Upon irradiation of ketones **1** in protic solvents such as MeOH or *t*BuOH the solvent adducts **22** can be formed as described earlier.[5−8] In two cases (**20c**,**g**) the primarily formed 1-indanones can undergo a second photochemical process by abstraction of a hydrogen atom from the γ-position by the excited carbonyl group. The resulting 1,4-diradicals are subjected to a Norrish-Type-II cleavage giving the parent 1-indanone **20a** (Scheme 7).

As seen in Table 1, the ratio of products **20**−**22** depends considerably on the solvent used. MeOH in the presence of NMI is mostly preferred compared with dichloromethane (DCM), due to shorter irradiation periods and higher yields. On the other hand, we observed the formation of methanol adducts **22a**,**b** (entries 1 and 20) in some cases. It should be noted that these products are only formed from acetophenones (**1a**,**m**) but not if there is an electron-withdrawing substituent (**1n**,**o**). The Norrish-Type-II cleavage of indanones **20c**,**g** giving the parent indanone **20a** proceeds to a much higher extent in DCM than in MeOH (entries 5, 6 and 13, 14). The β-ketoester **1e** and the β-ketoamide **1f** are the only reactants which cyclize both from the C−C centered diradical **XIIIa** and from the O−C centered diradical **XIIIb** (entries 9 and 11, cf. Scheme 2). Interestingly, this reaction outcome may be substantially influenced by the solvent. Whereas in DCM both products **20** and **21** are observed, the utilization of *tert*-butyl alcohol strongly diminishes the yields of 2-alkyliden benzo[*c*]furanes **21** (entries 10 and 12). The photochemical behavior of ketone **1h** demonstrates the limits of the method. We could not isolate any defined products. Obviously, the Norrish-Type-I cleavage with unspecific following reactions of the thus formed radicals predominates, if the atom adjacent to the carbonyl group is a quaternary carbon atom (entry 15). If the mesyloxy group in **1b** (entry 3) is replaced by phosphate (entry 16) or by carbonates (entries 17 and 18) the yields of indanone **20b** are decreased a little. On the other hand, the photochemical behavior of compounds **1i**−**k** demonstrates the ability to use compounds **1** as a photoreleasable protecting group for phosphates (**1i**) and alcohols (**1j**,**k**). Recently, 2,5-dimethylphenacyl esters were used as photolabile protecting groups for carboxylic acids.[7] Notably, the structurally similar ketone **1l**, which mainly differs from the 2,5-dimethylphenacyl esters by the presence of a methyl group at the leaving group bearing carbon atom, does not undergo any photoinduced cleavage reaction. This result underlines the sensible dependence of photochemical reactivity on steric factors.

In summary, from the results shown in Table 1 it can be concluded that it is not possible to state ideal reaction conditions for all reactants **1** irrespective of the substituents R^1−R^3. Rather three competing processes can diminish the yields of 1-indanones, all of which depend on the solvent. Although protic solvents are more favorable than aprotic solvents in many cases (**1c**,**d**,**e**,**f**,**g**,**n**), solvent adducts **22** were formed in two cases (**1a**,**m**). If R^1 is an electron-withdrawing group (**1e**,**f**), benzo[*c*]-furanes **21** are formed as byproducts. If the substituent R^1 bears a hydrogen atom in the γ-position with respect to the carbonyl group (**1c**,**g**), a second photochemical transformation can take place (Norrish-Type-II cleavage) giving the parent 1-indanone **20a** as byproduct.

Mechanism of the 1-Indanone Formation. The mechanism of the formation of 1-indanones and methanol adducts upon irradiation of *o*-alkyl-substituted aromatic ketones has controversially been discussed in the literature. First of all it should be emphasized that the previously investigated molecules of type **1** containing chloride[5,6,8] or carboxylate,[7] which are much poorer leaving groups than sulfonates, are used mostly in this work. Bergmark et al.[5] proposed that a homolytic cleavage of the C−Cl bond is the first step of the photochemical reaction, still before the hydrogen transfer takes place. Netto-Ferreira and Scaiano investigated the reaction by laser flash photolysis.[6] On the basis of the assumption that all the reactivity of ketones **1** (X = Cl) arises from the triplet excited state, they concluded that its lifetime must be unusually short. A recently published thorough reinvestigation[8] revealed that the reaction proceeds, at least partly, through singlet excited states and that triplets are not involved in the reaction outcome. To find out whether these results are fully applicable to our reactants we reinvestigated the reaction mechanism by

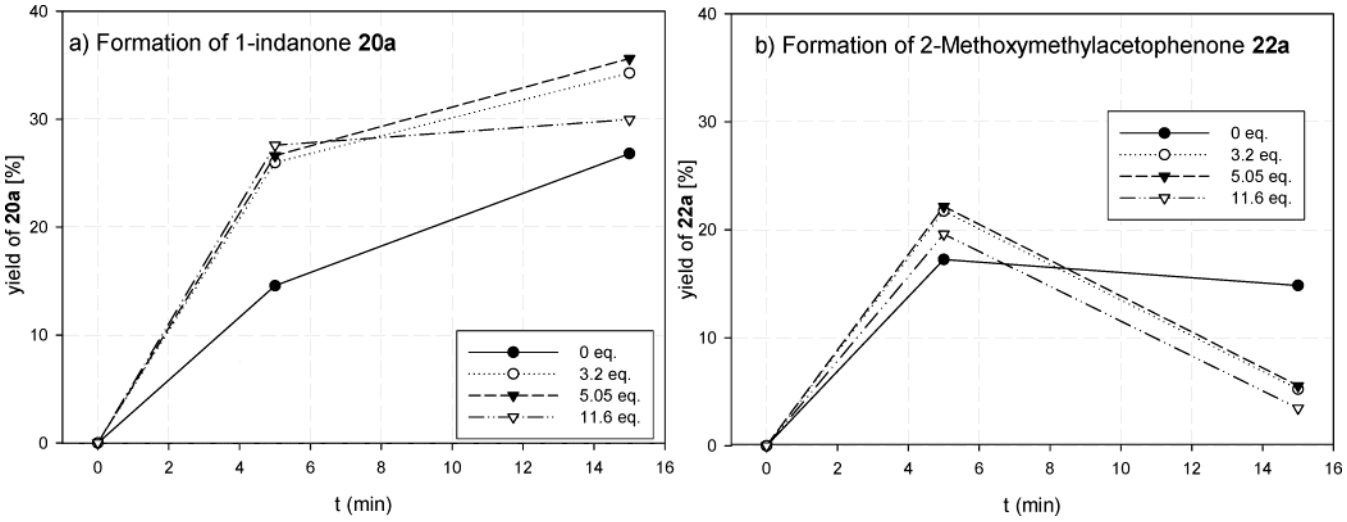


FIGURE 1. Influence of acetophenone on the photochemical behavior of **1a**.

means of kinetic measurements and quantum chemical calculations. We concentrated our attention on the question of which role the triplet excited state plays. By a variety of previous investigations it was established that alkyl aryl ketones undergo a very rapid intersystem crossing to the triplet state ($k > 10^{10}$ s^{-1}) so that product formation from the singlet excited state must not be discussed.[1] On the other hand, we found out previously[3c] that the presence of a leaving group adjacent to the carbonyl group lowers the activation barrier of the hydrogen transfer considerably.

There are principally two ways to clarify the participation of the singlet or triplet excited state in the product formation. The singlet pathway may be forced by addition of suitable triplet quenchers (e.g., 1,3-dienes) and the triplet pathway may be preferred in the presence of triplet sensitizers. The first approach was already pursued and it was found that the reaction cannot be suppressed by triplet quenchers. This could indicate that the reaction only proceeds from the singlet excited state, but it could also be an indication of an extremely fast initial step of the reaction. The sensitization of the triplet pathway, which was to the best of our knowledge hitherto not undertaken, is more instructive. We determined the product distribution of compound **1a** in the presence of different amounts of acetophenone as triplet sensitizer. Acetophenone is particularly suitable as a triplet sensitizer for compounds **1** because its triplet energy should be very similar and its ISC quantum yield amounts to unity. The results are summarized in Figure 1.

Interestingly, the rate of formation of 1-indanone **20a** is considerably increased by the addition of acetophenone (Figure 1a), whereas the rate of formation of the methanol adduct **22a** is hardly influenced in the initial period of the irradiation (Figure 1b). During further reaction, the amount of **22a** was evenly diminishing. This can be explained by a remarkable higher reactivity of triplet **22a** in following photochemical reactions compared with the singlet excited state of **22a**. Naturally, we cannot rule out that the small influence of acetophenone on the rate of formation of **22a** in the first minutes is at least partly induced by two contrary effects. It is possible that the rate of formation of **22a** is just as accelerated as those of **20a**, but this effect is compensated through the faster following reaction of **22a**. The important conclusion from the sensitization experiments is that 1-indanone **20a** is much more efficiently formed by a triplet reaction. It should be noted that, despite the reasonable influence of acetophenone in analytical scale irradiations, it is not recommended to use these conditions in a preparative scale because it is difficult to separate the products from the large excess acetophenone and its photochemical products.

To obtain detailed information about the triplet pathway we have undertaken some quantum chemical calculations.[28] For comparison purposes, we have evaluated the mechanism of *o*-methylacetophenone **23** without the presence of a leaving group at first. The photochemical behavior of **23** is well-known and the mechanism of the photochemical behavior of *o*-alkylaryl alkyl ketones was thoroughly investigated.[31] The primarily formed product from the irradiation of **23** is the *E*-xylenole *E*-**28**, and this process is therefore called *photoenolization*. *E*-**28** may either cyclize to the benzocyclobutene **30** or be captured by dienophiles, according to a Diels−Alder reaction.[32]

In this work, we have calculated the geometry and the energy of all relevant species on the way from the ground-

(28) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.9; Gaussian, Inc., Pittsburgh PA, 1998.

(29) B3PW91 is Becke's 3-parameter functional (Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648), with the nonlocal correlation provided by the Perdew 91 expression (Perdew, J. P.; Chevary, J. A.; Vosko, S. H.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, 46).

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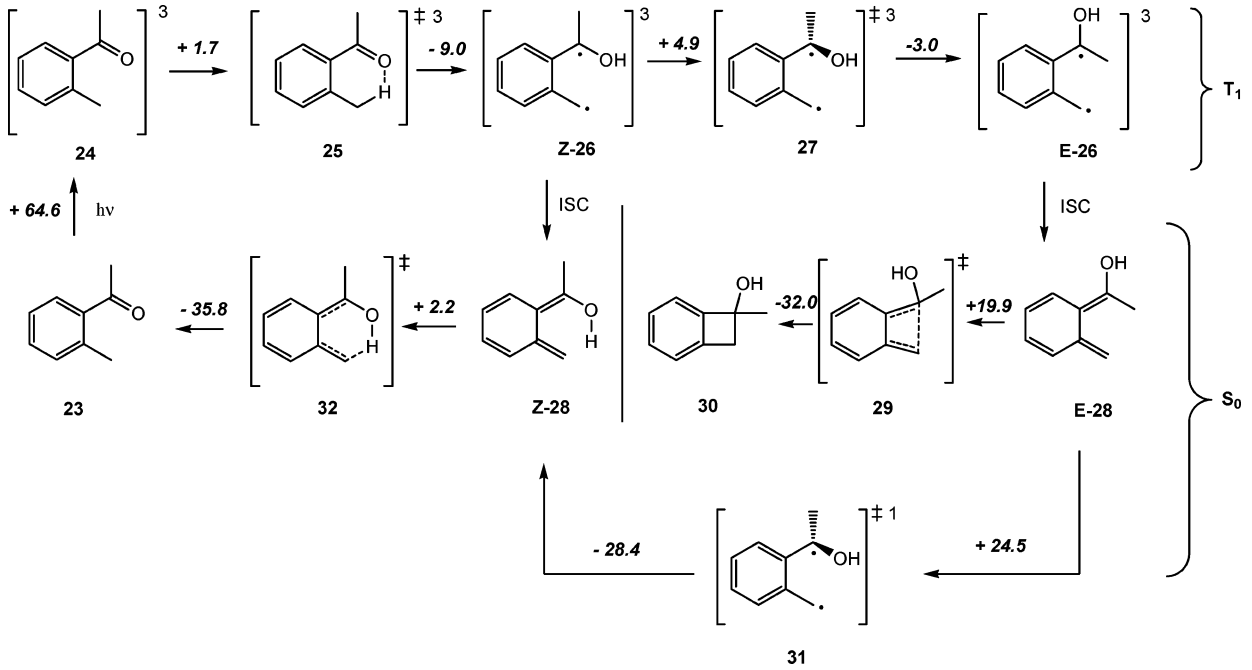
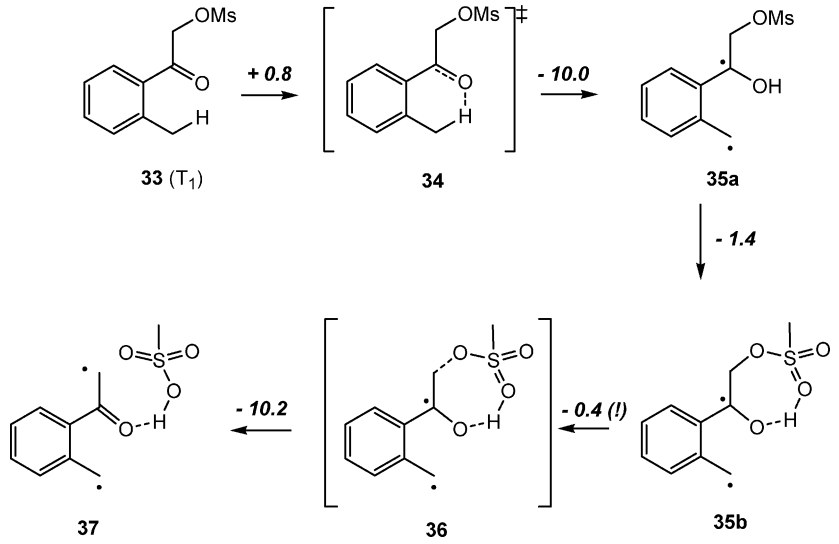
(31) (a) Gebicki, J.; Krantz, A. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1623. (b) Wagner, P. J.; Subrahmanyam, D.; Park, B. *J. Am.Chem. Soc.* **1991**, *113*, 709. (c) Marcinek, A.; Michalak, J.; Rogowski, J.; Tang, W.; Bally, T.; Gebicki, J. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1353.

SCHEME 8. DFT Calculation of the Photochemical Behavior of 23[a]



[a] UB3PW91/6-311++G**//UB3PW91/6-31G*, energy differences in kcal/mol.

SCHEME 9. DFT Calculation of the Photochemical Behavior of 33[a]



[a] UB3PW91/6-311++G**//UB3PW91/6-31G*, energy differences in kcal/mol.

state ketone **23** to the benzocyclobutene **30** as well as the regeneration of the starting ketone via the *Z*-xylenole *Z*-**28** by means of density functional theory methods[29] (for details see the Supporting Information). The calculated energy differences are summarized in Scheme 9. After photochemical excitation and intersystem crossing (ISC) a hydrogen abstraction of the carbonyl group of triplet ketone **24** from the *o*-methyl group takes place. The activation barrier of this hydrogen migration is very low (1.7 kcal/mol). The thus formed triplet xylenole *Z*-**26** can either isomerize to the *E* form (*E*-**26**), which is more stable than *Z*-**26** by 1.9 kcal/mol, or return back to the singlet state (*Z*-**28**) by ISC. *Z*-**28** undergoes an 1,5-sigmatropic hydrogen shift over a small activation barrier of 2.2 kcal/mol (Scheme 8).

The *E*-xylenole *E*-**28**, which is formed from *E*-**26** after ISC, should be a relatively stable species, because it is separated from benzocyclobutene **30** by an activation barrier of 19.9 kcal/mol. The alternative way, the rotation around one of the exocyclic double bonds, demands 24.5 kcal/mol and is, therefore, relatively unlikely. The stability of *E*-**28** is also demonstrated by successful [$2\pi-4\pi$] cycloaddition reactions with various dienophiles.[32]

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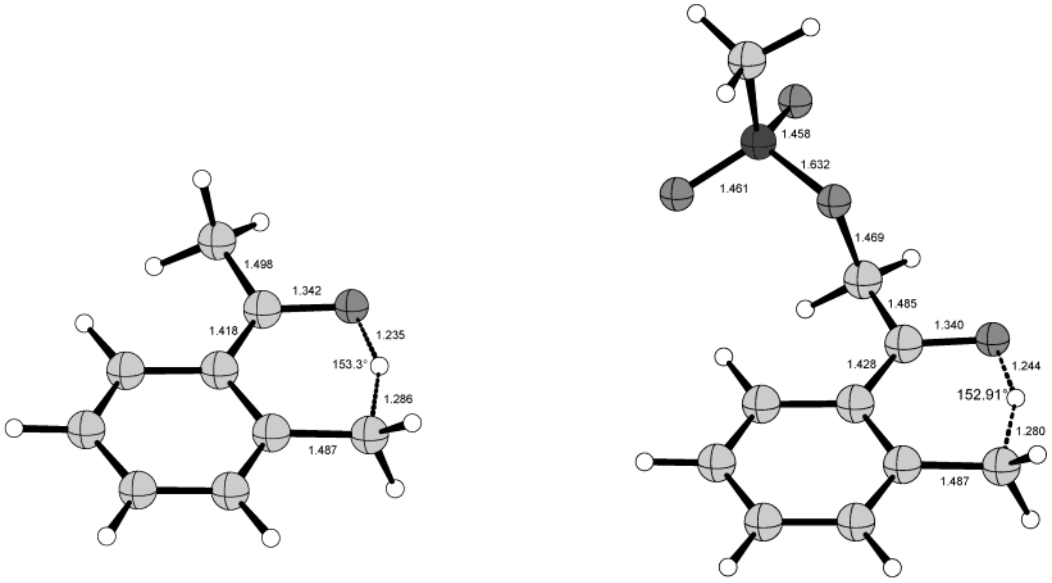
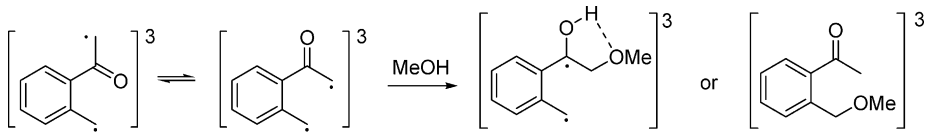


25 34

FIGURE 2. Transition states **25** and **34** of the intramolecular hydrogen transfer.

SCHEME 10. Addition of MeOH onto Diradicals 38[a]



anti-**38** (0.0) *syn*-**38** (+ 0.74) **39** (- 0.04) **40** (+ 5.7)

[a] Calculated relative energies in parentheses.

The introduction of a leaving group (mesyloxy) at the carbon atom, adjacent to the carbonyl group, causes crucial changes in the mechanism. The activation barrier of the initial hydrogen transfer in the triplet excited ketone **33** is considerably lowered compared with that of the parent ketone **24** and amounts to only 0.8 kcal/mol. This phenomenon was already observed for other α-mesyloxy ketones and could be explained by a hyperconjugative interaction between the semifilled π^*-orbital of the excited carbonyl group and the σ^*-orbital of the α-C−OMs single bond.[3c] Consequently, the initial hydrogen transfer should occur extremely fast, which could explain why the reaction could not be suppressed by addition of triplet quenchers.[6] The thus formed diradical **35** may exist in two conformers **35a** and **35b** in which **35b**, characterized by an intramolecular hydrogen bond, is slightly more stable than **35a**. The most remarkable result of the calculations concerns the activation barrier of the subsequent elimination of methane sulfonic acid. After consideration of the zero-point vibrational energy, the energy of transition state **36** drops below that of transition state **35b**. This means that the diradical **35b** is not truly a minimum of the potential energy surface and that the lifetime of the 1,4-diradical **35** should be extremely short. It may be concluded from these calculations that the hydrogen transfer from **33** to **35**, followed by the immediate elimination of methane sulfonic acid, proceeds very efficiently and that the 1,5-diradical **37** is the first really stable species along the reaction pathway. It should be noted that 1,5-diradicals of type **37** were not considered in previous investigations of the reaction mechanism[6−8] (Scheme 9).

The difference between the transition states **25** and **34** is also discernible in the comparison of their geometries. The distance between the oxygen atom of the carbonyl group and the transferred hydrogen atom is remarkably increased in **34** compared with **25** (1.244 Å vs 1.235 Å) whereas the C−H bond length of the breaking bond is shorter in **34** than in **25** (1.280 Å vs 1.286 Å). This means that the transition state **34** is of earlier nature than the transition state **25**, which is in good agreement with the lowering of the action barrier upon introduction of the leaving group (Figure 2).

Finally, we wish to discuss the possibility that the solvent adducts **22** may be formed at the triplet potential energy surface. According to the DFT calculation of the photochemical behavior of **33**, the only reasonable intermediates, which can react with the solvent, are 1,5-diradicals **38** (corresponding to diradicals **37** without solvating MsOH). Interestingly, we found that the addition of MeOH onto the enolate radical moiety of **38**, giving triplet xylenoles **39**, is essentially thermoneutral whereas the addition onto the other radical center, giving the triplet ketone **40** (which corresponds to the observed ketone **22a**), is endothermic. This means that if solvent adducts would originate from triplet 1,5-diradicals **38**, then the alkoxy group would be tethered at the carbon

atom adjacent to the carbonyl group and not to *o*-alkyl group as in **22**. Accordingly, it is very likely that the solvent adducts **22** are solely formed from singlet intermediates, even though we cannot rule out that they are formed by a diabatic process through an T_1-S_0 intersection. In summary, we have described a versatile synthetic route to substituted 1-indanones. We have shown that the photochemical key step, which is another application of the previously established principle of *spin center shift*, may be optimized by the proper choice of solvent, leaving group, and acid scavenger. Extensive DFT calculations revealed that 1-indanones **20** are formed from triplet intermediates, whereas the occasionally obtained solvent adducts **22** result probably from the singlet excited state of ketones **1**. We will report on the application of this interesting ring closure reaction on the synthesis of natural products soon.

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Supporting Information Available: Experimental procedures and analytical data of all prepared compounds; Cartesian coordinates and electronic and zero-point vibrational energies of all calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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