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Photochemical Preparation of Tricyclic Hydroxyketones by Transanular Cyclization of Bridged 4-Benzoylcyclohexanones

P. Wessig[1,*], **J. Schwarz**[1], **D. Wulff-Molder**[2], and **G. Reck**[2]

[1] Institut für Chemie der Humboldt-Universität zu Berlin, D-10115 Berlin, Germany
[2] Bundesanstalt für Materialforschung und -prüfung (BAM), D-12489 Berlin, Germany

Summary. The bridged 4-benzoyl-cyclohexanones **3a–f** were synthesized by α,α'-annelation of cyclic ketones. Irradiation of **3a–f** revealed a strong dependence of the photochemical behaviour on the ring size and the introduction of a nitrogen atom. Ketones which are able to form 1,6-biradicals (**3b,c,e**) undergo unselective photolytic decomposition, whereas **3a,d,f** afforded tricyclic hydroxyketones. The diastereoselectivity of ring closure is remarkably improved by introduction of a protected nitrogen atom (**3d,f**) in comparison to the carbocyclic diketone **3a**. Moreover, the N protective group of 4-azatricyclo-[4.3.1.$0^{3,8}$]decan-7-one (**7**) could be removed affording the free hydroxy amino ketone **8** in good yields. An explanation of the diastereoselective cyclization of **3a** and of the surprisingly low quantum yield of **3d** was found by conformational analysis of the corresponding triplet biradicals.

Keywords. Photocyclization, transanular; Tricyclic hydroxyketones; Triplet biradicals, conformational analysis of; Quantum yields; Aminoalcohols.

Photochemische Darstellung tricyclischer Ketone durch transanulare Cyclisierung verbrückter 4-Benzoylcyclohexanone

Zusammenfassung. Die verbrückten 4-Benzoyl-cyclohexanone **3a–f** wurden durch α,α'-Anellierung cyclischer Ketone synthetisiert. Das photochemische Verhalten von **3a–f** hängt in starkem Maße von der Ringgröße und von der Einführung eines Stickstoffatoms ab. Ketone, die in der Lage sind, 1,6-Biradikale zu bilden (**3b,c,e**), unterliegen einer unselektiven photolytischen Zersetzung, während **3a,d,f** tricyclische Hydroxyketone liefern. Die Diastereoselektivität des Ringschlusses wird durch Einführung eines Stickstoffatoms (**3d,f**) im Vergleich zum carbocyclischen Analogon **3a** deutlich gesteigert. Weiterhin gelang es, die N-Schutzgruppe im 4-Azatricyclo-[4.3.1.$0^{3,8}$]decan-7-on (**7**) unter Bildung des freien Hydroxyaminoketons **8** in guten Ausbeuten zu entfernen. Eine Erklärung für die diastereoselektive Cyclisierung von **3a** und für die überraschend geringe Quantenausbeute von **3d** wurde durch Konformationsanalyse der entsprechenden Triplett-Biradikale gefunden.

Introduction

The formation of C–C bonds is one of fundamental problems of organic chemistry. Among the various modern methods, photochemical reactions have obtained an

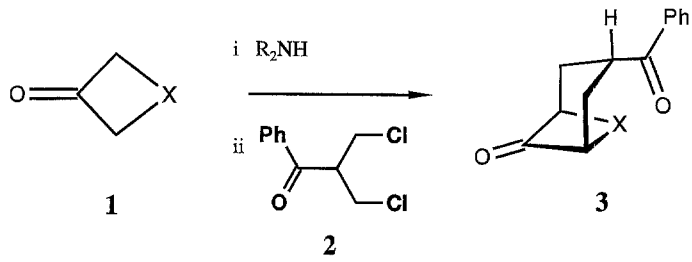


Fig. 1. α, α'-Anellation of cycloalkanones **1**

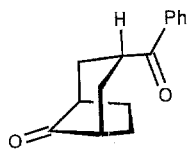
increasing importance. A reason of this trend seems to be that their regio- and stereoselectivity often differs substantially from that of thermal reactions. The preparative value of the *Norrish* Type II reaction [1, 2], one of the best investigated photochemical reactions, has been proven in many cases (*e.g.* Ref. [3]). Nevertheless, the course of an irradiation is often not foreseeable. Although many mechanistical investigations have been published [4], a theory which is easy to handle for preparative chemists is missing at present. Therefore it is necessary to obtain more informations from the investigation of suitable reactants.

In continuation of our previous work on stereoselective photocyclization [5–7], we were interested in conformationally rigid reactants. The restriction of conformational degrees of freedom should allow conclusions about the mechanism, especially an explanation of regio- and stereoselectivity. In this connection we became aware of a previous work of *Stetter et al.* [8] who have described the α, α'-annelation of cycloalkanones **1** after converting them into the appropriate enamines using 2-benzoyl-1,3-dichloropropane (**2**). Whereas this work provided no information about diastereoselectivity, few years later *Momose* and *Muroka* proved the *endo* configuration of the benzoyl group in the formed bicyclic diketones **3** and proposed a mechanistic explanation of the observed high diastereoselectivity [9] (Fig. 1). Recently, this cyclization method has been extended to a heterocyclic ketone, and the same *endo* selectivity as described for carbocyclic reactants was observed [10].

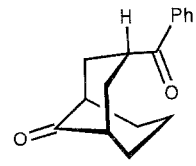
Diketones **3** meet ideal geometric requirements for an intramolecular photochemical hydrogen abstraction by the n-π^* excited benzoyl group, followed by a recombination of the formed two radical centres. Furthermore, it should be noted that the usually favoured γ position with respect to the excited carbonyl group is blocked due to the conformational rigidity of the reactants. In the present work we describe the photochemical behaviour of the six bicyclic diketones **3a–f**.

Results and Discussion

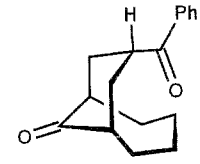
Carbocyclic ketones **3a–c** were prepared as described earlier [8]. The exclusive *endo* orientation of the benzoyl group could be verified by NMR investigations (NOE experiments). Heterocyclic ketones **3d–f** were prepared analogously by α, α'-anellation of the appropriate N-protected heterocyclic ketones. The benzyloxycarbonyl group (*Z*) was chosen in view of its easy removability after photolytic ring closure.



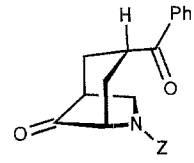
3a



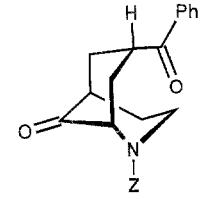
3b



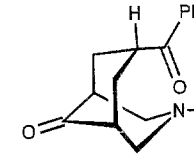
3c



3d



3e



3f

Spectroscopic properties, quantum yields and reactivity

Before dealing with preparative results, we wish to report on the photophysical properties of ketones **3a–f**. All of them contain two functional groups which are known to be photochemically reactive. Therefore, it is important to note that the n-π^* bands of the two ketocarbonyl groups are separated. Absorbtion of light with wavelength above 300 nm ensures excitation of the benzoyl group only. The UV/Vis data are summarized in Table 1. It can be seen that nitrogen atoms have no remarkable influence on the UV/Vis spectra. It both cases, the absorption behaviour is mainly determined by the benzoyl chromophor. The assignments in Table 1 result from a comparison with known spectra of alkyl aryl ketones [11]. The molar extinction coefficients of the benzoyl n-π^* band are similar for the six compounds. This fact is important in so far as different rates of decay really reflect the decay quantum yields which will be designated in the following as quantum yields for simplicity.

We have determined the quantum yields of **3a–f** in order to investigate the relationship of structure and photochemical reactivity. The results are summarized

Table 1. UV/Vis data and quantum yields of **3a–f**

	$\lambda_{max}(\epsilon)$ $(\pi - \pi^*)$	$\lambda_{max}(\varepsilon)$ $(\pi - \pi^*\text{-CT})$	$\lambda_{max}(\varepsilon)$ $(n - \pi^*)$	Φ_D
3a	240 (10752)	276 (829)	314 (127)	0.18
3b	243 (12671)	279 (986)	312 (89)	0.27
3c	242 (12685)	279 (957)	313 (94)[b]	0.35
3d	239 (9575)	–[a]	314 (137)	0.04
3e	243 (11774)	279 (928)	311 (178)	0.43
3f	243 (13050)	278 (1019)	313 (90)[b]	0.45

[a] Superimposed by $\pi - \pi^*$ band; [b] shoulder

in Table 1. The carbocyclic ketones **3a–c** show a similar reactivity ($\phi_D = 0.2$–0.4). Nevertheless, a correlation of quantum yields and ring size is noticeable. Thus, the bicyclo[4.3.1]decanone **3c** is twice as reactive as bicyclo[3.2.1]octanone **3a**. For alkyl aryl ketones, it is commonly accepted that quantum yields of decay less than unity result from a reversion to the starting ketone by internal radical disproportionation [2]. Recently, *Klessinger* and *Michl* have described the importance of geometries of triplet biradicals with high spin-orbit coupling (SOC) both for cyclization and disproportionation [11]. According to the rules first summarized by *Salem* and *Rowland* [12], SOC increases with increasing overlap of the orbitals participating in singlet product formation. Hence, cyclization demands an overlap of the two *p*-orbitals of spin-bearing C-atoms, whereas disproportionation is favoured if the *s*-orbital of the transferred hydrogen atom overlaps with the *p*-orbital of the radical centre. Obviously, the increasing flexibility of the biradicals with enlargement of ring decreases the probability of disproportionation.

These mechanistic considerations have been proved by the behaviour of the heterocyclic ketones **3d–f**. We observed surprising differences in the reactivity of these ketones. The quantum yields of **3e,f** are in the order of 0.45, whereas the reactivity of **3d** is one order of magnitude smaller ($\phi_D = 0.04$). To achieve an explanation of this phenomenon, we investigated the preferred conformation of the triplet biradical formed from **3d** using semiempirical methods (AM1 [13]; the benzyl group was replaced by a methyl group). Fig. 2 shows a low energy conformer of this biradical. It differs from its carbocyclic analogue (**3a**) by a sp^2-hybridized nitrogen atom instead of a methylene group, leading to the possibility of establishing a hydrogen bond. The result is a short distance between the hydrogen atom of the hydroxyl group and the radical centre adjacent to the N atom (3.19 Å), accompanied by a larger distance between the two radical centres (3.5 Å). Consequently, disproportionation is the predominant reaction pathway of the biradical shown in Fig. 2, and the low quantum yields are easily understandable.

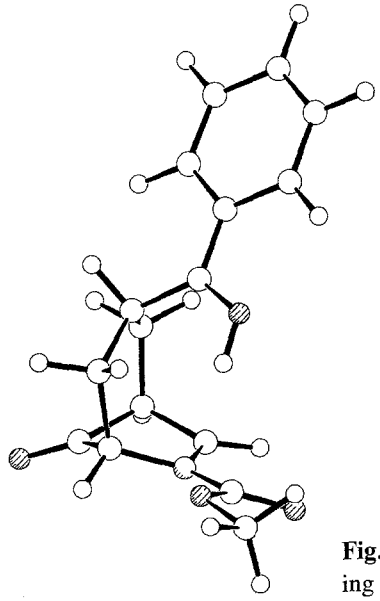


Fig. 2. AM1-optimized structure of a triplet biradical corresponding to **3d**

In the course of determination of quantum yields using the *E,E*-1,4-diphenylbutadiene as standard [14], a problem became obvious. Very small molar extinction coefficients at the irradiation wavelength (313 nm) in comparison with those of the actinometer led to long irradiation periods of **3a–f** even if very short irradiation periods were used for the actinometer. This fact is true for most of the established actinometers. The often used valerophenone actinometer [15], which lacks the described disadvantage, demands GLC detection of product build-up and is not suitable for detection by UV/Vis spectroscopy. From our experience, ketone **3a** would be a suitable actinometer, especially applicable for alkyl aryl ketones. The advantages are that 1) **3a** is a crystalline substance which can easily be prepared and purified, 2) **3a** is stable in daylight, 3) **3a** has a small molar exinction coefficient at 313 nm, and 4) (*dc/dt*) can easily be determined by UV/Vis spectroscopy.

Photopreparative behaviour

Ketones **3a–f** differ by the position from which a hydrogen atom could be abstracted by the triplet excited carbonyl group. Considering the pseudo C_s-symmetry of ketones **3a–c,f**, the hydrogen abstraction by the triplet excited benzoyl group could take place from two equivalent methylene groups in the case of **3a** and **3f**, whereas **3b,c** and **3e** bear two different positions each. **3d** contains only one hydrogen atom for abstraction. These structural features are reflected by the photochemistry of **3a–f**

According to their behaviour, the ketones **3a–f** can be subdivided in two classes. Thus, we found an unselective decay upon irradiation of ketones **3b,c,e**. DC and HPLC investigations indicated a broad variety of products. During irradiation of **3b**, a solid of very low solubility was obtained in low yields (*ca.* 9%). Spectroscopic data suggest an adamantane structure, though a final evidence could not yet be produced.

Although a clear explanation of this result is pending at time, a connection is obvious. All three ketones **3b,c,e** are able to form 1,6-biradicals which should be able to undergo a radical fragmentation (*homo-Norrish* Type II cleavage) as shown in Fig. 3 for **3b**. The resulting primary products would also be photochemically reactive and could undergo further thermal and photochemical reactions.

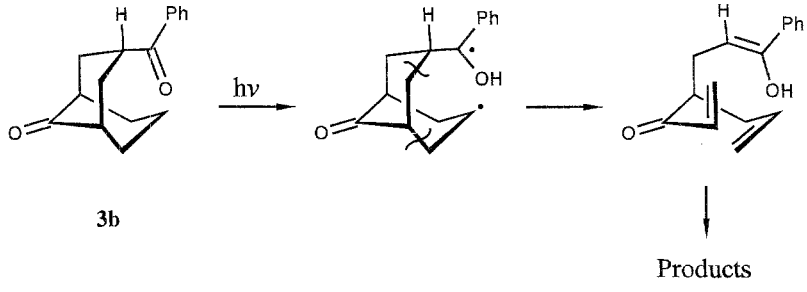
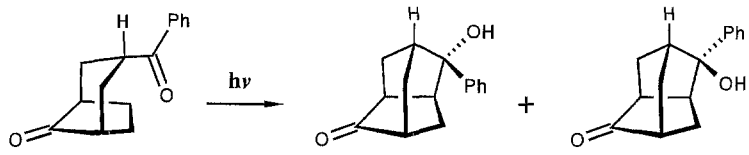


Fig. 3. Mechanistic proposal for the photochemical cleavage of **3b,c,e**



3a **4a** (47%) **4b** (24%)

Upon irradiation of **3a** in aprotic solvents we have isolated two diastereomeric noradamantanes (**4a** and **4b**) which could be easily separated by flash chromatography. Whereas structural assignment of **4a** and **4b** by NMR spectroscopy failed due to signal overlap, the structure could be solved by X-ray analysis of **4a** (Fig. 4). Furthermore, the arrangement of **4a** in the crystal was determined. The molecules are related by *n* glide plane forming chains in the [101] direction. Between the molecules of a chain there are hydrogen bondings which have a length of 2.01 Å (Fig. 5). The chains consist of alternating enantiomers of **4a**.

The difference between **4a** and **4b** is expressed in the positions of the phenyl and the OH group with respect to the noradamantane framework. As shown above, the phenyl group adopts *endo* position in the preferred product.

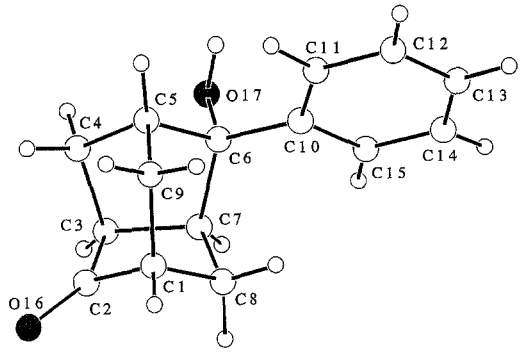


Fig. 4. X-ray crystal structure of **4a**

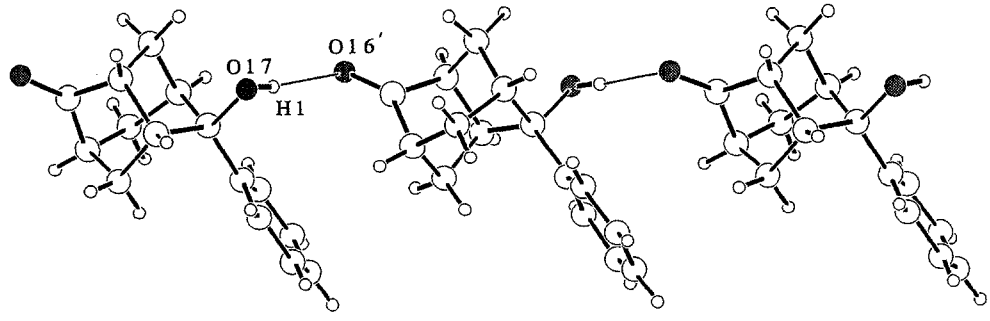
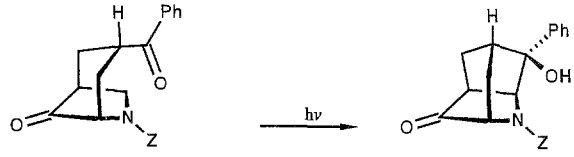


Fig. 5. Crystal packing of **4a**

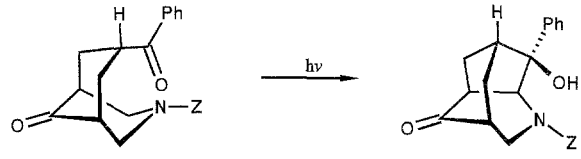
Despite of the moderate diastereoselectivity we were interested in an explanation of this result. It should be noted, however, that it is difficult to argue about stereoselectivity in connection with energy differences of less than 1 kcal/mol. Nevertheless, the authors will attempt to provide a speculative discussion. *Ab initio* calculations at high level of theory (MP2/6-31G*//HF/6-31G*) [16] provided that the preferred product **4a** is by 1.4 kcal/mol less stable than **4b**. On the other hand, a conformational analysis of the corresponding triplet biradicals showed that a conformation **5a**, the precursor of **4a**, is by 0.5 kcal/mol more stable than the biradical conformer **5b** which gives **4b**.

We are well aware of the fact that a discussion of such small energy differences is problematical. Nevertheless, the results reflect the experimental outcome correctly. The relative energies of biradical conformers have also been used in other investigations in order to explain the stereoselectivity of photocyclizations [17].

The cyclization of heterocyclic ketones **3d** and **3f** provided the azatricycles **6** and **7** respectively.



3d **6** (55%)



3f **7** (37%)

In contrast to the carbocyclic reactant **3a**, the cyclization of **3d** and **3f** occurred stereoselectively yielding products with *endo* oriented hydroxyl group only. Despite of the moderate yields, the other diastereomers could not be detected. Besides products **6** and **7** only polymer decomposition products were formed. The relative configurations of **6** and **7** were elucidated by NOE experiments. Moreover, X-ray structure analysis of the 4-azatricyclo[4.3.1.$0^{3,8}$]decan-7-one **7** was performed which corroborated the assignment assessed from NMR investigations (Fig. 6). The arrangement of molecules in crystals of **7** differs from that found for **4a**. The molecules are related by a 2_1 screw axis forming two different chains in the [010] direction. In contrast to **4a**, each of the chains contains only one enantiomer of **7** (Fig. 7). The upper chain is composed of the *R*-enantiomer, wheras the lower one is formed by molecules of *S*-configuration.

The highly diastereoselective formation of **6** and **7** could be explained by a hydrogen bonding between the hydroxyl group and the *Z* group which fixes the

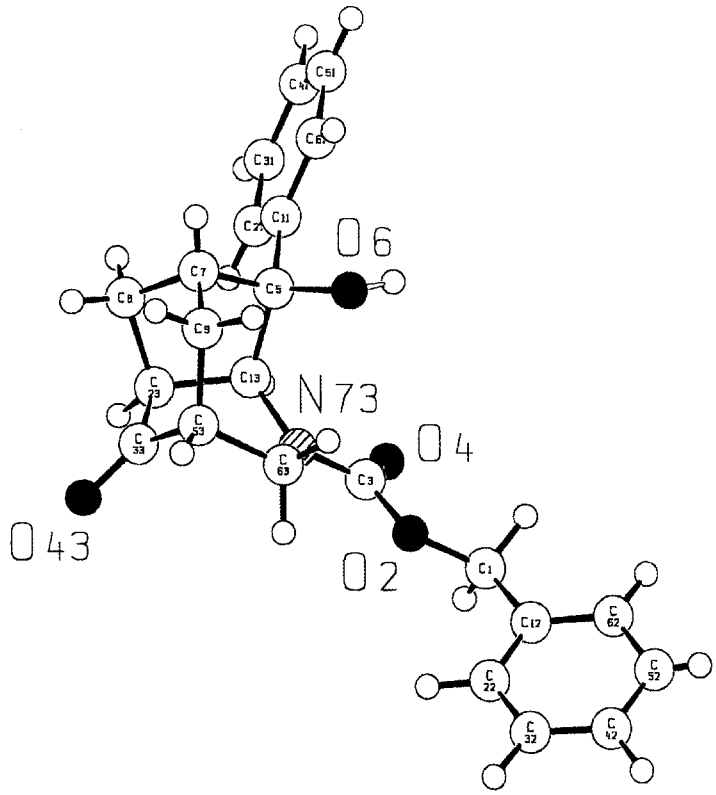


Fig. 6. X-ray crystal structure of **7**

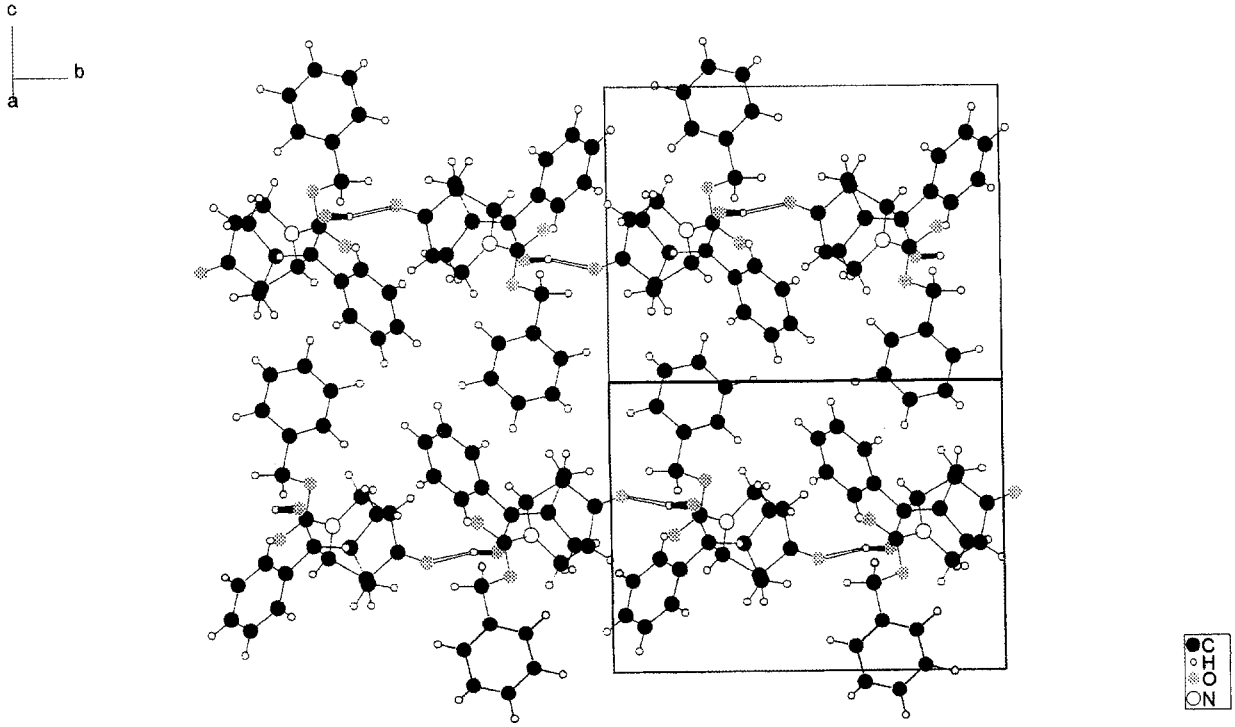
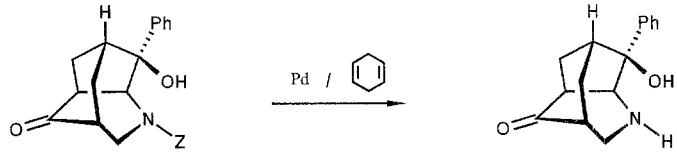


Fig. 7. Crystal packing of **7**

conformation and forces the observed *endo* position of the hydroxyl group in the corresponding products. We assume the hydrogen bond to exist in these products because the NMR spectra of **6** and **7** contain one set of signals indicating that only one rotamer with respect to the amide bond appears. In the NMR spectra of **3d–f**, in contrast, almost all signals appear twice.

Finally, we would like to demonstrate the accessability of free hydroxy amino ketones by reductive cleavage of **6** and **7**. Due to the presence of the keto group, we treated **6** and **7** with palladium/1,4-cyclohexadiene instead of palladium/hydrogen. The benzyloxy carbonyl group in **7** could be easily removed affording aminoketone **8** in 84% yield. Analogous hydrogenolysis of **6** provided a mixture of many products which could not be separated.



7 **8**

Conclusions

In the present work we report on the photochemical and photophysical properties of six bicyclic ketones. These ketones show a different behaviour depending on ring size and replacement of a methylene group by a protected nitrogen atom. Ketones which are able to form 1,6-biradicals (**3b,c,e**) undergo unselective decomposition upon irradiation. However, a clear explanation of this behaviour is pending at time. Ketones **3a,d,f** provided tricyclic compounds. The diastereoselectivity of ring closure is remarkably higher in the case of the heterocyclic reactants **3b** and **3f** in contrast to **3a**. We suppose that strong hydrogen bondings in the respective biradicals give rise to these results.

The synthesis of the tricyclic hydroxy amino ketone **8** should be of special interest. Although **8** is formed in rather low yields, our route provides a highly functionalized conformationally rigid tricyclic molecule in few steps and fully diastereoselective. **8** contains the substructures of the physiologically active aminoalcohols ephedrine and amphetamine. We will report on a enantioselective approach of this reaction soon.

Experimental

General

All solvents were distilled and dried before use. The reagents were of reagent grade and used without further purification. Organic extracts were dried (Mg_2SO_4) and evaporated below 50°C. TLC: silica gel 60 F_{254} (*Merck*); flash chromatography (FC): silica gel (35–70 μm, *merck*); m.p.: *Büchi 530* uncorrected; IR: *Perkin Elmer 881*, cm^{-1}; NMR: *Bruker AM300, DPX300*; δ in ppm rel. to internal

TMS, *J* in Hz; photochemistry: 150 W mercury arc lamp (Hanau); UV: 1 × 1 cm cuvet, filter *WG 295 (Schott)*; MS: *Hewlett-Packard GCMS-5995-A*, 70 eV.

Quantum yields

The photolyses were carried out using a 500 W high-pressure mercury arc lamp (*OSRAM HBO-500*) with controlled light intensity and a metal interference filter of 313 nm (*Carl Zeiss*). Decay quantum yields Φ_D, defined as ratio of decomposed reactant molecules to the amount of photons absorbed, were determined by the relative method [21] according to the equation $\Phi_x = (dc/dt)_x \times (dc/dt)_s^{-1} \times \Phi_s \times (I_{abs})_s \times (I_{abs})_x^{-1}$ and using *E,E*-1,4-diphenylbutadiene ($\Phi = 0.11$) [14]. Subscripts *s* and *x* refer to standard and sample, respectively. The values of the reaction rate (d*c*/d*t*) were calculated from the initial slope of the decomposition curves. Decomposition of both standard and samples were monitored by UV/Vis spectroscopy using a *UVICON 930* spectrometer (*Kontron Instruments*). The decay of the standard was recorded at 327 nm, whereas the π, π^* bands of **3a–f**, summerized in Table 1, served for the observation of sample decay.

The bicyclic ketones **3a–f** were synthesized following the procedure of *Stetter et al.* [8]. The preparation of **3a–c** starting from cyclopentanone, cyclohexanone and cycloheptanone, has already been described there. **3d–f** were prepared from the appropriate N-benzyloxycarbonyl-heterocycloalkanones which were obtained according to literature procedures: *N-benzyloxycarbonyl-pyrrolidin-3-one* [18], *N-benzyloxycarbonyl-piperidin-3-one* [19], and *N-benzyloxycarbonyl-piperidin-4-one* [20].

(1S, 3S, 5S)-(±)-3-Benzoyl-6-benzyloxycarbonyl-6-azabicyclo[3.2.1]octan-8-one (**3d**)

Yield: 70% from *N-benzyloxycarbonyl-pyrrolidin-3-one*; M.p.: 50°C; IR (KBr): $\tilde{\nu} = 2952, 2893$ (= CH), 1768 (CO), 1704 (CO), 1692 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.24$–2.36 (m, 1H), 2.45–2.60 (m, 1H), 2.62–2.65 (m, 1H), 3.04–3.18 (m, 2H), 3.35–3.55 (m, 2H), 3.80–4.10 (M, 2H), 4.63–5.19 (m, 2H), 6.93–7.45 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 34.1$, 34.5 (CH_2), 37.6, 38.1 (CH), 38.6, 39.5 (CH_2), 44.7, 45.1, 46.3, 46.8 (CH_2), 58.1 (CH), 66.9, 67.1 (CH_2), 127.6, 127.8, 127.9, 128.0, 128.2, 128.3, 128.5, 128.6, 132.5, 132.6, 135.8, 135.9, 136.2, 136.4 (arom. C), 153.8, 153.9, (CO), 201.1, 201.8 (CO), 211.3, 211.7, (CO); almost all signals appear twice due amide rotamers; MS (70 eV): *m/z* (%) = 335 (1.9) [M^+-CO], 228 (5.0) [M^+-Z], 200 (9.8), 144 (14.9), 105 (33.9) [$PhCO^+$], 91 (100) [$PhCH_2^+$].

(1S, 5S, 7S)-(±)-7-Benzoyl-2-benzyloxycarbonyl-2-azabicyclo[3.3.1]nonan-9-one (**3e**)

Yield: 75% from *N-benzyloxycarbonyl-piperidin-3-one*; **3e** oil; IR (KBr): $\tilde{\nu}$ = 2910 (CH), 1738 (CO), 1701 (CO), 1692 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.11$ (s_{br}, 2H), 2.34–2.51 (m, 4H), 2.73–2.78 (m, 1H), 3.32–3.35 (m, 1H), 3.68–3.75 (m, 1H), 4.5–4.8 (m_{br}, 1H), 5.00–5.15 (m, 2H), 7.26–7.57 (m, 8H), 7.86 (d, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 31.8$ (CH_2), 32.8 (CH_2) 33.9 (CH_2), 35.6 (CH_2), 37.4 (CH), 41.4 (CH), 56.9, 57.6 (CH), 67.9 (CH_2), 128.2, 128.3, 128.4, 128.5, 128.8, 129.1, 133.7, 135.9, 136.4 (arom. C), 155.2 (CO), 201.2 (CO), 211.8 (CO); some signals appear twice due to amide rotamers; MS (70 eV): *m/z* (%) = 286 (0.7) [M^+-$PhCH_2$], 242 (3.5) [M^+-Z], 144 (1.2), 105 (31.5) [$PhCO^+$], 91 (100) [$PhCH_2^+$].

(1S, 5R, 1r, 3c)-(±)-3-Benzoyl-7-benzyloxycarbonyl-7-azabicyclo[3.3.1]nonan-9-one **3f**

Yield: 70% from *N-benzyloxycarbonyl-piperidin-4-one*; M.p.: 119–121°C; IR (KBr): $\tilde{\nu} = 2959$, 2869 (CH), 1720 (CO), 1701 (CO), 1677 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.10$–2.50 (m_{br}, 4H), 2.55–2.70 (m_{br}, 2H), 3.07–3.46 (m, 3H), 4.36–4.52 (q_{br}, 2H, J = 12Hz), 5.22 (d, 2H, J = 3Hz),

7.26–7.53 (m, 8H), 7.88 (d, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.7, 32.0 (CH_2), 38.9 (CH), 44.5, 44.8 (CH), 51.7 (CH_2), 67.9 (CH_2), 128.0, 128.1, 128.5, 128.7, 133.2, 135.6, 136.2 (arom. C), 156.3 (CO), 200.4 (CO), 215.8 (CO); some signals appear twice due to amide rotamers; MS (70 eV): m/z (%) = 286 (1.2) [M^+-$PhCH_2$], 242 (5.1) [M^+-Z], 142 (3.4), 105 (6.2) [$PhCO^+$], 91 (100) [$PhCH_2^+$].

Preparation of **4a**, **4b**, **6**, **7** *(general procedure)*

A solution of ketone **3** in 500 ml dry diethylether (10^{-2} mol/l) was degassed with dry O_2-free argon for 30 min. The solution was irradiated until practically no reactant was detectible by TLC (approximate irradiation time see below). After evaporation of solvent, the crude photoproducts were purified by FC (mobile phase: CH_2Cl_2:MeOH = 100:2).

(1R, 3S, 5R, 6R, 7S)-(±)-6-Hydroxy-6-phenyl-tricyclo[3.3.1.0^{3,7}]nonan-2-one **4a** [22]

Irradiation time: *ca.* 2 h; yield: 0.53 g (47%) after FC (1.14 g **3a** were irradiated); m.p.: 84–86°C; IR (KBr): $\tilde{\nu}$ = 2994, 2977 (CH), 1734 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (d, 1H, J = 12.8 Hz), 1.65–1.70 (m, 1H), 1.75–1.88 (m, 2H), 2.05 (s, br, 1H, OH), 2.32 (d, 2H), 2.48–2.61 (m, 2H), 2.75 (d, 1H, J = 12.0 Hz), 2.97 (t, 1H, J = 6 Hz), 7.20–7.50 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.7 (CH_2), 33.3 (CH_2), 38.4 (CH_2), 40.6 (CH), 44.3 (CH), 45.7 (CH), 47.2 (CH), 81.8 (C_6), 125.6, 127.7, 128.5, 146.4 (arom. C), 218.0 (CO); MS (70 eV): m/z (%) = 228 (10, [M^+]), 210 (6, [M^+-H_2O]), 159 (4), 145 (6), 133 (13), 105 (100). 91 (51) [$PhCH_2^+$].

(1R, 3S, 5R, 6S, 7S)-(±)-6-Hydroxy-6-phenyl-tricyclo[3.3.1.0^{3,7}]nonan-2-one **4b** [22]

Irradiation time: *ca.* 2 h; yield: 0.27 g (24%) after FC (1.14 g **3a** were irradiated); m.p.: 133–135°C; IR (KBr): $\tilde{\nu}$ = 2992, 2975 (CH), 1735 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60–1.72 (m, 2H), 1.84–2.14 (m, 5H), 2.74–2.81 (m, 2H), 2.95–3.04 (m, 2H), 7.27–7.47 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.8 (CH_2), 35.0 (CH_2), 41.1 (CH_2), 42.5 (CH), 44.3 (CH), 45.1 (CH), 47.5 (CH), 85.4 (C_6), 127.5, 127.8, 129.2, 142.2, (arom. C), 217.5 (CO); MS (70 eV): m/z (%) = 228 (15, [M^+]), 210 (9, [M^+-H_2O]), 159 (5), 145 (6), 133 (7), 115 (13), 108 (13), 105 (100) [$PhCO^+$].

(1S, 3S, 5S, 6S, 7S)-(±)-6-Hydroxy-6-phenyl-8-benzyloxycarbonyl-8-azatricyclo[3.3.1.0^{3,7}]nonan-2-one (**6**)

Irradiation time: *ca.* 8 h; yield: 1.0 g (55%) after FC (1.82 g **3d** were irradiated); m.p.: 116–118°C; IR (KBr): $\tilde{\nu}$ = 2953, 2952 (CH), 1762 (CO), 1693 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62–1.79 (m, 3H), 2.45 (s_{br}, 1H), 2.70–2.85 (m, 1H), 3.00 (m, 1H), 4.29 (s_{br}, 1H), 4.96 (d, 1H, J = 6 Hz), 5.13 (d, 2H, J = 3 Hz), 7.29–7.38 (m, 10 H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 32.1 (CH_2), 37.3 (CH_2), 43.7 (CH), 49.3 (CH), 60.6 (CH), 67.7 (CH_2), 81.1 (C_q), 126.0, 128.6, 128.7, 129.0, 129.2, 136.7, 143.6 (arom. C), 155.3 (CO), 206.3 (CO); MS (70 eV): m/z (%) = 335 (0.6) [M^+-CO], 228 (2.3) [M^+-Z], 144 (3.2), 105 (22.9), 91 (100).

(1R, 2S, 3S, 6R, 8S)-(±)-2-Hydroxy-2-phenyl-4-benzyloxycarbonyl-4-azatricyclo[4.3.1.0^{3,8}]decan-7-one (**7**)

Irradiation time: *ca.* 1 h; yield: 0.7 g (37%) after FC (1.89 g **3f** were irradiated); m.p.: 159–161°C; IR (KBr): $\tilde{\nu}$ = 2952 (CH), 1727 (CO), 1689 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59–1.66 (m, 1H), 1.90–2.15 (m, 2H), 2.25 (1H, OH), 2.46–2.50 (m, 1H), 2.62–2.70 (m, 2H), 2.99–3.04 (m, 1H), 3.80–4.06 (m, 2H), 5.02–5.41 (m, 3H), 7.26–7.65 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 33.4

(CH_2), 34.8 (CH_2), 41.9 (CH), 44.1 (CH), 52.8 (CH_2), 67.4 (C_q), 126.2, 126.4, 127.6, 128.0, 128.1, 128.3, 128.5, 128.6, 128.7, 128.9, 136.1, 136.4, 145.1 (arom. C), 156.9 (CO), 212.6 (CO); MS (70 eV): m/z (%) = 242 (19.0) [M^+-Z], 214 (2.4), 187 (3.1), 141 (5.2), 131 (13.9), 115 (11.2), 108 (21.4), 105 (57.8), 91 (100).

(1R, 2S, 3S, 6R, 8S)-(±)-2-Hydroxy-2-phenyl-4-azatricyclo-[4.3.1.$0^{3,8}$]decan-7-one **8**

Compound **7** (0.5 g, 1.33 mmol) was dissolved in 10 ml MeOH, and 1,4-cyclohexadiene (0.23g, 2.33 mmol) and Pd/C (0.5 g, content 10% Pd) were added. The mixture was refluxed under N_2 until no **7** could be detected by TLC (*ca.* 15 min). Filtration through a pad of celite followed by evaporation of the solvent *in vacuo* afforded **8** (0.27 g, 84%) as a white solid.

Table 2. X-ray data for **4a** and **7**

	4a	**7**
Empirical formula	$C_{15}H_{16}O_2$	$C_{23}H_{23}NO_4$
Molecular mass	228.29	377.42
a (pm)	1077.9(2)	2486.2(4)
b (pm)	1029.2(2)	1418.2(2)
c (pm)	1079.0(3)	1104.2(3)
β(deg)	90.11(2)	94.23(3)
V(pm^3)	$1196.9 \cdot 10^6$	$3882.7(13) \cdot 10^6$
Z	4	8
d(calcd) (g cm^{-3})	1.267	1.291
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$ (No. 14)	C2/c (No. 15)
Diffractometer	CAD-4 (Enraf-Nonius)	STADI 4 (Stoe)
Radiation	MoKα(λ = 0.71069 Å)	
Monochromator	graphite	
Crystal size (mm)	0.42 × 0.42 × 0.10	0.74 × 0.30 × 0.06
Data collection mode	ω-2θ-scan	ω-2θ-scan
θ range (deg)	1.5 → 25.0	1.64 → 22.47
Recip. latt. segment	$h = -12 \rightarrow 12$	$h = -26 \rightarrow 26$
	$k = 0 \rightarrow 12$	$k = 0 \rightarrow 15$
	$1 = 0 \rightarrow 12$	$1 = 0 \rightarrow 10$
No. of refl. measd.	2112	2379
No. of unique refl.	2112	2376
No. of refl. $I > 2\sigma(I_0)$	1769 ($I > 1\sigma(I_0)$)	1091
Lin. abs. coeff. (mm^{-1})	0.077	0.088
Abs. correction	no	no
Solution by	direct methods	direct methods
Method of refinement	full-matrix LSQ, hydrogens refined isotropically	full-matrix LSQ, hydrogen positions riding and free
Data-to-parameter ratio	1769/219 = 8.07	1929/316 = 6.10
R, R_w	0.051, 0.064	0.0615, 0.1131 (wR_2)
Weighting scheme	$w = 1/[\sigma(I)^2 + (0.05F_2)^2]$	$w = 1/[\sigma(F_o^2) + (0.0326P)^2 + 8.46P)$ with $P = (\max(F_o^2) + 2F_c^2)/3$
Largest difference peak (e Å^3)	0.25	0.198
Largest difference hole (e Å^3)	−0.15	−0.170
Program used	ENRAF-NONIUS MOLEN	SHELXS-86, SHELXL-93

M.p.: 170–176°C; IR (KBr): $\tilde{\nu}$ = 3389 (NH), 2952, 2938 (CH), 1720 (CO); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, 1H, J = 12.8 Hz), 1.68–1.89 (m, 2H), 2.08 (s_{br}, OH), 2.20–2.30 (m, 1H), 2.34–2.39 (m, 1H), 2.42–2.44 (m, 1H), 2.87 (t, 1H, J = 7.8 Hz), 3.19 (q, 1H, J = 7.2 Hz), 3.56 (d, 1H, J = 9 Hz), 3.91 (d, 1H, J = 6.6 Hz), 7.20–7.48 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 34.1 (CH_2), 35.2 (CH_2), 44.1 (CH), 45.9 (CH), 53.6 (CH_2), 54.1 (CH), 66.2 (CH), 82.0 (C_q), 127.1, 127.4, 128.6, 149.6 (arom. C), 215.9 (CO); MS (70 eV): m/z (%) = 243 (7.2) [M^+], 148 (4.2), 139 (5.6), 138 (50.3), 123 (8.8), 115 (12.5), 110 (20.9), 105 (96.4), 96 (87.2), 77 (100).

X-ray structure analysis of **4a** *and* **7**

The X-ray structures of **4a** and **7** are shown in Fig. 4 and 7 respectively. Crystal data and parameters of the data collection are compiled in Table 2. Unit cell parameters were determined by accurate centering of 25 strong independent reflections by the least-squares method. Reflection intensities were collected at r.t. on a four-circle diffractometer CAD4 (*Enraf-Nonius*) for **4a** and a STADI 4 (*Stoe*) for **7** using MoK_α radiation.[1]

References

[1] Wagner PJ (1994) In: Horspool WM, CRC Handbook of Organic Photochemistry and Photobiology. CRC Press, New York
[2] Wagner PJ (1989) Acc Chem Res **22**: 83
[3] Yang NC, Yang DH (1958) J Am Chem Soc **80**: 2913
[4] Wagner PJ (1971) Acc Chem Res **4**: 168
[5] Wessig P, Legart F, Hoffmann B, Henning HG (1991) Liebigs Ann Chem 979
[6] Wessig P, Wettstein P, Giese B, Neuburger M, Zehnder M (1994) Helv Chim Acta **77**: 829
[7] Steiner A, Wessig P, Polborn K (1996) Helv Chim Acta **79**: 1843
[8] Stetter H, Rämsch KD, Elfert K (1974) Liebigs Ann Chem 1322
[9] Momose T, Muraoka O (1978) Chem Pharm Bull **26**: 2217
[10] Nemes P, Janke F, Scheiber P (1993) Liebigs Ann Chem 179
[11] Klessinger M, Michl J (1990) Lichtabsorption und Photochemie organischer Moleküle. VCH, Weinheim
[12] Salem L, Rowland C (1972) Angew Chem Int Ed Engl **11**: 92
[13] Semiempirical Calculations were performed with the program MOPAC7, Seiler FJ (1995) Res Lab, US Air Force Academy, Colorado Springs, CO 80840
[14] Schöneich R, Bendig J, Kreysig D (1979) Z Naturforsch **34A**: 1344
[15] Wagner PJ (1967) J Am Chem Soc **89**: 5898
[16] *Ab initio* calculations were performed with the program packet Gaussian 92, Revision G.2, Frisch MJ, Trucks GW, Head-Gordon M, Gill PMW, Wong MW, Foresman JB, Johnson BG, Schlegel HB, Robb MA, Replogle ES, Gomperts R, Andres JL, Raghavachari K, Binkley JS, Gonzalez C, Martin RL, Fox DJ, Defrees DJ, Baker J, Stewart JJP, Pople JA (1992) Gaussian Inc, Pittsburgh PA
[17] Wagner PJ, Park BS (1991) Tetrahedron Lett **32**: 2126
[18] Cooper CS, Clock PL, Chu DTW, Hardy DJ, Swanson RN, Plattner JJ (1992) J Med Chem **35**: 1393
[19] Krogsgaard-Larsen P, Hjeds H (1976) Acta Chem Scand Ser B **30**: 884

[1] Additional material to the structure determination may be ordered from Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen, Federal Republic of Germany, referring to the depository numbers CSD-406357 (**4a**) and CSD-406303 (**7**).

[20] Stetter H, Reinhartz W (1972) Chem Ber **105**: 2773
[21] Kuhn HJ, Braslavsky SE, Schmidt R (1989) Pure Appl Chem **61**: 187
[22] In *Chemical Abstracts*, noradamantanes are called 2,5-octahydro-methano-pentalenes

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