21. Photochemical Cyclization of Allylated Anisole and N-Alkyl Aniline Derivatives

Preliminary Communication[1])

by **Ursula Koch-Pomeranz**[2]), **Hans-Jürgen Hansen***) and **Hans Schmid**

Organisch-chemisches Institut der Universität Zürich, Rämistrasse 76, 8001 Zürich

*) Institut de chimie organique de l'Universite de Fribourg, Pérolles, 1700 Fribourg

(12. XII. 74)

Summary. The allyl anisole derivatives **1**, d_2-**1**, **3**, **5** and **7** (*Scheme 1*), on exposure to UV. light in benzene, acetone or methanol solution, cyclize to yield the corresponding cyclopropyl anisole derivatives **2**, d_2-**2**, *cis*- and *trans*-**4**, **6** and **8**, respectively. Under the above conditions the N,N-dialkyl-2-allyl anilines **9**, **10** and **11** give similar results (*Scheme 2*). On the other hand, N-alkyl-2-allyl anilines (**15** and **19**, *Scheme 3*) are transformed by UV. light in cyclohexane or benzene solution into 2-methyl-indolines (**16** and **20**, resp.), whereas in methanol solution the corresponding 2'-methoxy compounds **18** and **21** are formed in addition to **16** and **20**, respectively.

Very recently it was reported [2] that the photochemical cyclization of 2- and 4-allyl anisole give 2-cyclopropyl (21% chemical yield) and 4-cyclopropyl anisole (25% chemical yield), respectively. This prompts us to publish our results which we have so far obtained in this field. These results are connected with earlier investigations on the photocyclization of 2-allyl phenols to 2-methyl cumaranes and chromanes [3] (*cf.* also [4]).

Irradiation (11 h) of 2-allyl-4-methyl anisole (**1**) in methanol solution with a mercury high pressure lamp (quartz vessel) under argon gave 2-cyclopropyl-4-methyl anisole (**2**)[3]) in a yield of 70%[4]) (quantum yield *ca.* 0,05) (*Scheme* 1). Similar yields were obtained when irradiations of **1** were performed in benzene of acetone solution. The 1',1'-dideuterio anisole derivative $\mathbf{d_2}$-**1** afforded on exposure to UV. light in methanol solution exclusively $\mathbf{d_2}$-**2** with both deuterium atoms at C(2'). Irradiation of 4-methyl-2-(1'-methylallyl) anisole (**3**) in benzene solution led to a 2,4:1 mixture of 4-methyl-2-(2'-*cis*- and 2'-*trans*-methyl-cyclopropyl) anisole (*cis*- and *trans*-**4**)[5]) in a yield of 80%.

The photocyclization of 4-allyl-2,6-dimethyl anisole (**5**) did not occur as well as that of the previously mentioned 2-allylated species: After irradiating **5** for 50 h some starting material was still present. 4-Cyclopropyl-2,6-dimethyl anisole (**6**) was isolated by preparative gasphase chromatography (prep. GC.) in a yield of 20%. Most ineffective was the photocyclization of 3-allyl anisole (**7**): The time of irradiation had to be

---

1) 39. Commun. on photoreactions. A full paper will be published in this journal. 38. Commun.: See [1].

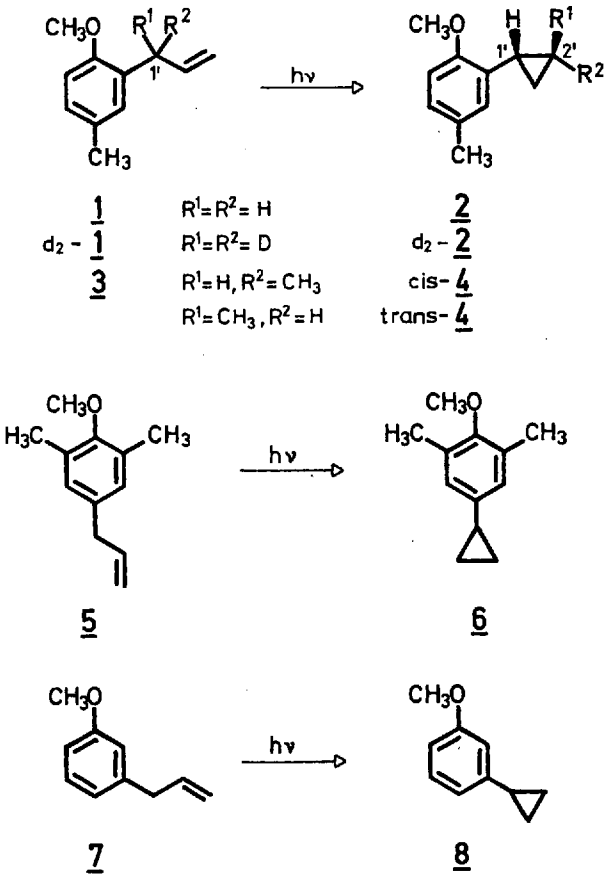
2) Part of the planned thesis, University of Zurich.

3) All new photoproducts gave correct NMR., IR., UV. and mass spectra as well as elemental analyses.

4) Given yields are with respect to isolated and purified material.

5) Both isomers are interconvertible under the conditions of the irradiation of **3**.

Scheme 1



prolonged to 135 h. After this time a 3:1 mixture of starting material **7** and 3-cyclopropyl anisole (**8**) was isolated in 41% yield, from which pure **8** (4%) was obtained by prep. GC.

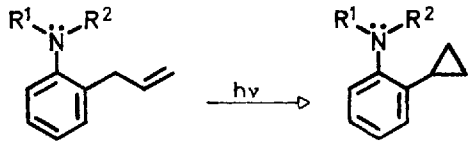
No cyclopropane derivatives were formed when 4-methyl-2-(2'-methylallyl) anisole or 2-(2'-butenyl) anisole were irradiated. The latter compound showed only (*E*)/(*Z*) isomerization. All attempts to photocyclize 1-allyl-2-methoxy and 2-allyl-1-methoxy naphthalene in methanol or acetone solution also failed.

On the other hand, a smooth photochemically induced 'cyclopropanization' occurred when N,N-dialkyl-2-allyl anilines were irradiated (5–12 h in methanol). From the N,N-dimethyl, N-ethyl-N-methyl and N,N-diethyl aniline derivatives **9**, **10** and **11** (*Scheme 2*) the corresponding 2-cyclopropyl anilines **12**, **13** and **14** were formed in 77, 60 and 52% yield, respectively. No reaction was observed, however, when 2-allyl-1-N,N-dimethylamino-naphthalene was irradiated in methanol.

The photochemical 'cyclopropanization' of allylated aromatic ethers or amines seems to have only a limited scope as preparative method.

Until now, the photochemical transformation of allyl benzene derivatives into their cyclopropyl isomers has been described only for such compounds that are substituted at C(3') with aryl [5], vinyl [6], carbomethoxy [7] or cyano groups [8]. The photochemically induced transformation of **1**, **3** and **5** into **2**, **4** and **6** and of **9–11** into **12–14**, respectively occurs presumably in all cases – this is shown by the rearrangement of d_2-**1** to d_2-**2** – by a 1,2 aryl migration and thus representing (at least in a formal sense) a di-π-methane rearrangement (*cf.* [9] and literature cited therein). However, there can also be envisaged rearrangements which are initiated by a one electron transfer from the oxygen or nitrogen of the excited aryl chromophore to the C,C double bond of the allyl group (*cf.* later)[6]).

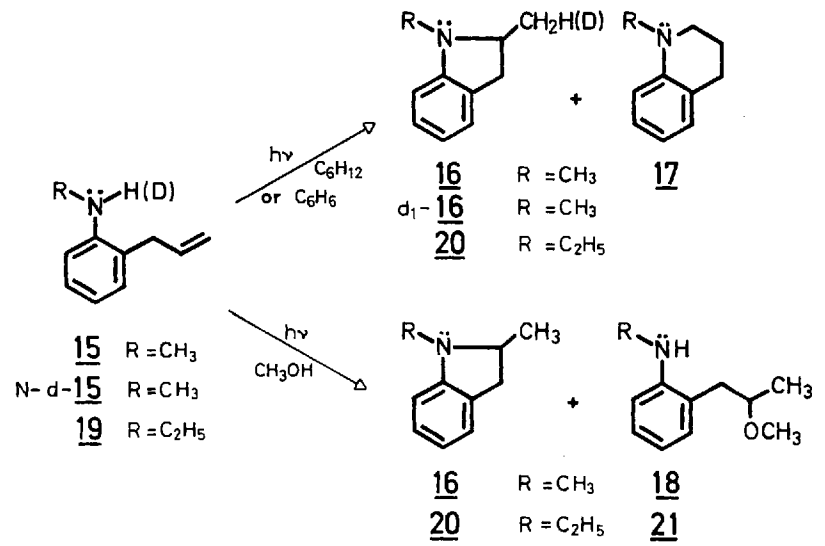
Scheme 2



9	$R^1=R^2=CH_3$	**12**
10	$R^1=CH_3, R^2=C_2H_5$	**13**
11	$R^1=R^2=C_2H_5$	**14**

Whereas, as mentioned above, N,N-dialkyl-2-allyl anilines form the corresponding cyclopropyl anilines, the N-mono-alkylated 2-allyl anilines cyclize under the influence of UV. light to give indolines (*Scheme* 3). Thus, irradiation (quartz vessel) of the N-

Scheme 3



15	$R=CH_3$	**16**	$R=CH_3$
N-d-**15**	$R=CH_3$	d1-**16**	$R=CH_3$
19	$R=C_2H_5$	**20**	$R=C_2H_5$

16	$R=CH_3$	**17**	
20	$R=C_2H_5$	**18**	
		21	

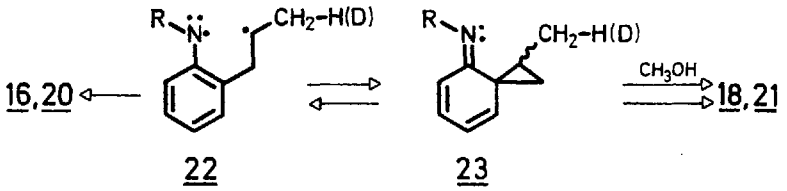
[6]) A more detailed discussion will be given in the full paper.

methyl compound **15** in cyclohexane for 4 h under argon led to the formation of 1,2-dimethyl indoline (**16**) in 84% yield and 1-methyl 1,2,3,4-tetrahydroquinoline (**17**) in 0,7% yield. The N-deuteriated compound N-d-**15** yielded under the same conditions d_1-**16** with the deuterium label in the methyl group at C(2). Different results were obtained in methanol. Irradiation of **15** yielded, in addition to the expected product **16** (41%), the methanol addition product **18** (28%) which was formed regiospecifically. Similarly, the N-ethyl derivative **19** yielded after irradiation in benzene only the indoline **20** (87%) whereas in methanol, in addition to **20** (32%), the methoxy compound **21** (34%) was formed. As mentioned, the N,N-dialkyl-2-allyl anilines yield by irradiation in methanol solution no methanol addition products but only cyclopropane derivatives. Under the conditions of irradiation neither **16** and **20** are converted into their corresponding methoxy compound **18** and **21**, nor is **18** or **21** transformed into the indoline **16** or **20**.

The photocyclization of a 2-allyl aniline derivative to an indoline was observed some time ago [10].

The following mechanism can be discussed for these cyclizations[6]: An electron transfer occurs from the excited aniline chromophore to the C,C double bond of the allyl side chain (*cf.* [11]). This is followed by a proton transfer from the anilinium radical to C(3′) whereby the biradical **22** is formed (*Scheme 4*). This cyclises to give

Scheme 4



the indolines **16** and **20**, respectively or to give reversibly the spiro[5.2]dien-imine **23**. The methanol adducts can be derived from the addition of methanol to **23** (*cf.* [1b] [12] [13] and literature cited therein).

Support of this work by the *Swiss National Research Foundation* is gratefully acknowledged.

REFERENCES

[1] *P. Gilgen, B. Jackson, H.-J. Hansen, H. Heimgartner & H. Schmid,* Helv. *57,* 2634 (1974).
[2] *T. Clark & D. A. M. Watkins,* J. chem. Soc. (Perkin I) *1974,* 2124; *N. Miyamoto & H. Nozaki,* Tetrahedron *29,* 3819 (1973).
[3] a) *Gy. Fráter & H. Schmid,* Helv. *50,* 255 (1967); b) *E. Schmid, Gy. Fráter, H.-J. Hansen & H. Schmid,* Helv. *55,* 1625 (1972).
[4] *W. M. Horspool & P. L. Pauson,* Chem. Commun. *1967,* 195.
[5] *S. S. Hixson & T. P. Cutler,* J. Amer. chem. Soc. *95,* 3032 (1973) and literature cited therein.
[6] *H. Kristinsson & G. S. Hammond,* J. Amer. chem. Soc. *89,* 5968 (1967); cf. *M. J. Bullivant & G. Pattenden,* Tetrahedron Letters *1973,* 3679.
[7] a) *D. DeKeukeleire, E. C. Sanford & G. S. Hammond,* J. Amer. chem. Soc. *95,* 7904 (1973); b) *S. S. Hixson & J. C. Tausta,* Tetrahedron Letters *1974,* 2007.
[8] *R. C. Cookson, A. B. Ferreira & K. Salisbury,* Chem. Commun. *1974,* 665.

[9] *S. S. Hixson, P. S. Mariano & H. E. Zimmerman*, Chem. Rev. *73*, 531 (1973); *H. E. Zimmerman*, Symposium on Photochemistry of Hydrocarbons, Division of Petroleum Chemistry, Inc., Amer. chem. Soc., Dallas, April 1974.
[10] *N. Paillous & A. Lattes*, Tetrahedron Letters *1971*, 4945.
[11] *H.-D. Becker* in S. Patais 'The Chemistry of the Hydroxyl Group', Interscience Publ., New York 1971, Part 2, p. 917ff.
[12] *A. Habich, R. Barner, W. v. Philipsborn & H. Schmid*, Helv. *48*, 1297 (1965).
[13] *S. Farid*, Chem. Commun. *1970*, 303.

22. Varianten im Zuckerteil des Streptozotocins

von **Niklaus Gassmann. Fred Stoos. Arthur Meier, Gürol Büyük, Salah Eldin Helali** und **Emil Hardegger**

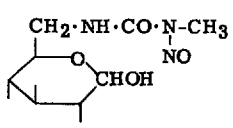
Organisch-chemisches Laboratorium der Eidg. Technischen Hochschule, Zürich

(25. XI. 74)

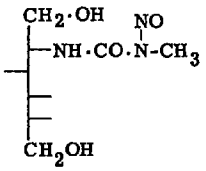
Zusammenfassung. Wir beschreiben die Synthese von krist. Analogen des Streptozotocins, welche sich von 6-Amino-D-glucose, D-Glucosaminol, D-Glucamin, D-Galactosamin, D-Arabinamin, D-Mannamin und D-Galactamin ableiten. Die meisten der krist. Präparate wurden als Acetylderivate charakterisiert.

Japanische Forscher variierten den Zuckerteil des Streptozotocins, indem sie Nitrosomethylharnstoffe der Inosamin-Reihe [1] und Streptozotocin-methylglykoside [2] herstellten, die gegen bösartige Tumoren wirksam waren. Über weitere Abwandlungen des Zuckerteils nach der *Upjohn*-Methode berichtete *Bannister* [3], der aus D-Galactosamin das 4-*epi*-, aus D-Mannosamin das 2-*epi*-Streptozotocin, die von D-Glucosylamin, D-Galactosylamin, D-Glucamin abgeleiteten Nitrosomethylharnstoffe und ebenfalls die Streptozotocin-methylglykoside herstellte und auf antibakterielle, diabetogene und cytotoxische Wirkung prüfte. Über weitere, im Nitrosoharnstoffteil modifizierte Streptozotocine vgl. [4].

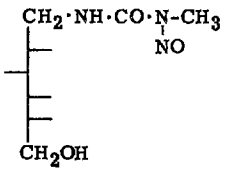
In der vorliegenden Arbeit berichten wir über neue, bereits in der Zusammenfassung erwähnte Varianten **1**, **2**, **5**–**7** im Zucker-Teil des Streptozotocins, die ausnahms-



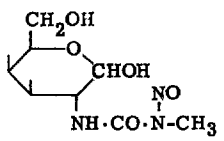
1



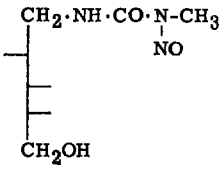
2



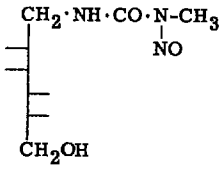
3



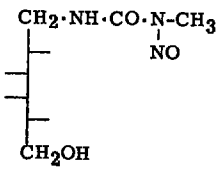
4



5



6



7