CHEMISTRY LETTERS, pp. 1295-1298, 1979. Published by the Chemical Society of Japan

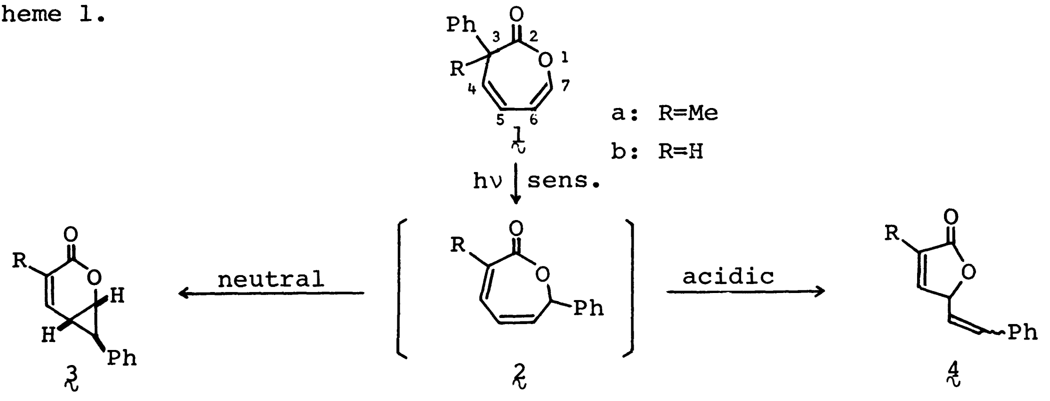
EVIDENCE FOR THE PHOTOLYTIC REACTION PATHWAY OF 3-PHENYL-2(3*H*)-OXEPINONES. SYNTHESIS, REACTION, AND ISOLATION OF 7-PHENYL-2(7*H*)-OXEPINONES

Nobuto HOSHI, Hisahiro HAGIWARA, and Hisashi UDA*
Chemical Research Institute of Non-Aqueous Solutions,
Tohoku University, Katahira-2, Sendai 980

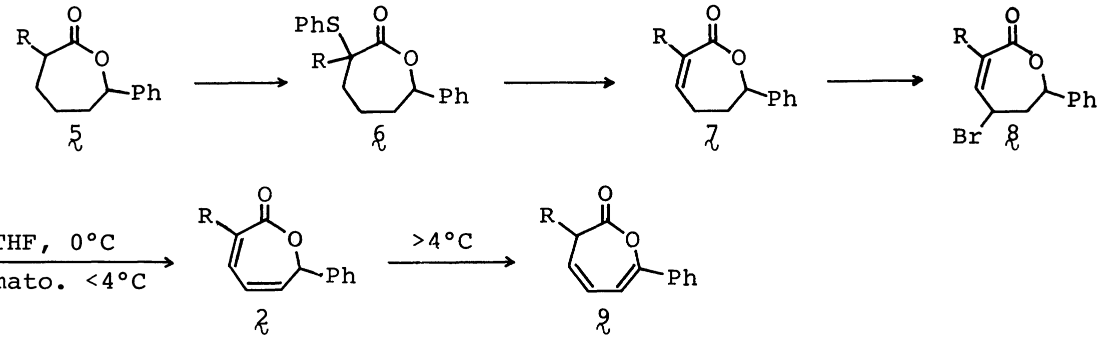
7-Phenyl-2(7*H*)-oxepinones are shown to be the initial photoproducts of 3-phenyl-2(3*H*)-oxepinones by the synthesis and reaction, and finally by the success of the actual isolation of the 3-methyl derivative from photolysis.

In the preceding paper,[1] we have postulated that the sensitized photolysis of 3-phenyl-2(3*H*)-oxepinones **1** would produce initially 7-phenyl-2(7*H*)-oxepinones **2** through a 1,5-phenyl shift, which subsequently undergo two modes of rearranging pathways depending on the medium employed, giving 7-phenyl-2-oxabicyclo[4.1.0]hept-4-en-3-ones **3** as the major products in neutral or protophilic media,[2] whereas 5-styryl-2(5*H*)-furanones **4** in acidic non-protophilic ones (Scheme 1). We now wish to report the synthesis and reaction of **2** and the success of the actual isolation of **2a** from the photolysis of **1a** under the selected conditions.

Scheme 1.



The synthetic sequence of **2** is outlined in Scheme 2. The Baeyer-Villiger oxidation of 2-phenylcyclohexanone[3] with MCPBA afforded **5b**, which was methylated to give **5a**. Sulfenylation of **5**, followed by dehydrosulfenylation[4] of the resulting α-(phenylthio)lactones **6** gave 5,6-dihydro-2(7*H*)-oxepinones **7**. Compounds **7** were brominated with NBS to the precursors **8**.[5] Dehydrobromination of **8** with DBU in tetrahydrofuran at 0°C afforded, after preparative tlc on silica gel below 4°C, 7-phenyl-2(7*H*)-oxepinones **2a** in 43% and **2b** in 20% yields, respectively.[7] Compounds **2** were found to be thermally very unstable, isomerizing completely to 7-phenyl-2(3*H*)-isomers **9**[5] within several hours at room temperature.[8] The structures of **2** were apparent from the nmr spectra taken at -20°C: **2a**: δ ($CDCl_3$) 2.22 (3H, d, J=1.5 Hz), 5.46 (1H, d, J=4.5 Hz), 6.15–6.60 (2H, m), 6.62 (1H, d of quintet, J=4.5 and 1.5 Hz, Scheme 2.

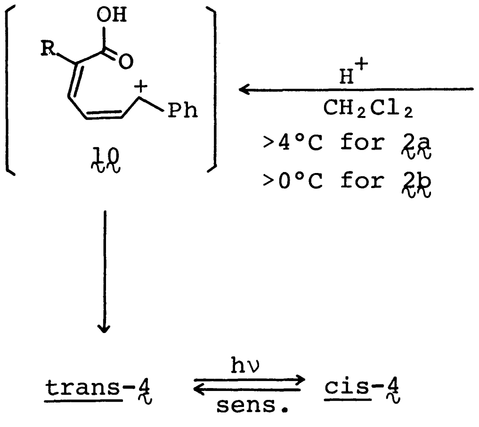


changed to dd, J=4.5 and 1.5 Hz, upon irradiation at 2.22), and 7.37 (5H, m), and 2b: δ ($CDCl_3$) 5.56 (1H, dd, J=4.0 and 1.5 Hz), 6.25–6.60 (3H, m), 6.77 (1H, ddd, J=11.0, 4.0, and 1.5 Hz), and 7.44 (5H, m). Thus, compounds 2 were subjected, immediately after isolation, to subsequent reactions.

The results of the reactions of 2 are summarized in Scheme 3. Treatment of 2a with conc hydrochloric acid in methylene chloride above 4°C gave, as expected, *trans*-4a in 70% yield. No rearrangement was observed in an acetone solution even at room temperature. These results are consistent with the findings on the photolysis of 1a in acidic media.[1] Similarly, 2b gave *trans*-4b.[10] The fact that 3-phenyl-2(7*H*)-oxepinone was stable upon prolonged treatment with acidic methylene chloride at room temperature indicates that a phenyl substituent at C-7 is essential to proceed this translactonization in the 2-oxepinone system, cleavage of the O–C-7 bond leading to a cationic intermediate such as 10 being probably facilitated. Compounds *trans*-4 were photo-equilibrated by acetophenone sensitization to produce a mixture of *cis*- and *trans*-4 with a *cis*/*trans* ratio of 1.1∼1.4 almost equal to the value of 1.5 obtained from the photolysis of 1.[1]

As shown in Scheme 3, the sensitized photolysis[11] of 2a afforded the 2-oxabicyclo[4.1.0]hept-4-en-3-one derivative 3a as the major product, except in hexane, through a formal di-π-methane rearrangement, along with the small amounts of 9a and its cyclized product 11a. Among several experiments, the rearrangement proceeded most efficiently by the use of 2-acetonaphthone in methanol similar to the case of the photolysis of 1a.[1,2b,12] Similarly, 2b gave 3b. These results also

Scheme 3.



$$\mathbf{2} \xrightarrow{h\nu,\ 0°C,\ 2\ h} \mathbf{3}$$

2a	2-acetonaphthone*	–CH_2Cl_2	3a	54%
	"	–MeOH	"	70
	"	–hexane	"	trace + 1a
	acetophenone*	–CH_2Cl_2	"	40
	"	–MeOH	"	23
	acetone		"	33
2b	2-acetonaphthone* (−40∼−30°C)	–CH_2Cl_2	3b	53

* 1 equiv

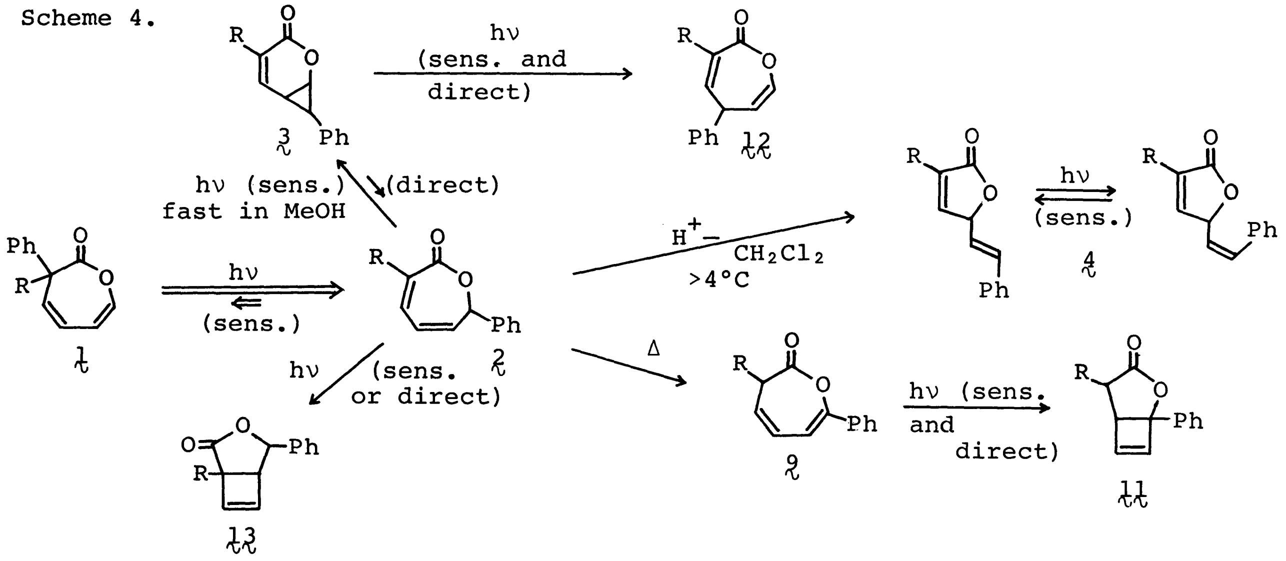
strongly support the intervention of **2** in the photolytic reaction pathway of **1**.

Moreover, two following important findings were observed in the photoreactions of **2a**. The first one is the observation of the signals assignable to **1a**, together with the intense signals of **9a**, in the nmr spectrum of the fraction of **9a** obtained from the reaction in hexane. If the formation of **1a** from **2a** is true, the 1,5-phenyl shift between **1a** and **2a** would be reversible, providing further evidence for the photolytic reaction pathway of **1a** to **3a**. Indeed, we could obtain **1a** from the following experiment. A scale-up photolysis of **2a** under the same conditions, followed by standing the photolysate at room temperature for 1 day to complete the thermal isomerization of unchanged **2a** afforded, after preparative tlc, an inseparable mixture of **1a** and **9a** (ca. 1 : 3.4). Upon direct irradiation of the mixture in methylene chloride, only the cyclization of **9a** took place giving rise to a mixture of **1a** and **11a**, from which **1a** could be isolated in 15% yield.

Secondary, it was found that at low temperature below -30°C the reaction of **2a** was greatly suppressed.[13] It should be noted that this finding would provide possibility of the actual detection or isolation of **2a** from the photolysis of **1a** under the appropriate conditions preventing further rearrangement and permitting easy isolation. In fact, an acetone solution of **1a** was irradiated at -78°C for 4 h afforded, after preparative tlc below 4°C, **2a** in 81% yield.[14] Thus, for the formation of **3** from **1** two sequential sensitized processes, the 1,5-phenyl shift leading to **2** and the subsequent di-π-methane rearrangement, are definitely confirmed, the one-step vinylogous di-π-methane rearrangement proposed previously[2a] being ruled out.

From these results, combined with the previous[15] and additional[16] ones, the photochemical reaction pathway of 3-phenyl-2(3H)-oxepinones **1** may be summarized in Scheme 4. It is now clear that the diversity of the photochemical behaviors of **1** is due to the high and diverse reactivities, depending on sensitizers, solvents, acidity, and temperature, of the initial photoproduct, 7-phenyl-2(7H)-oxepinones **2**.

Scheme 4.



References and Notes

1) N. Hoshi, H. Hagiwara, and H. Uda, Chem. Lett., 1291(1979).

2) (a) K. Sato, H. Hagiwara, H. Uda, M. Sato, and N. Harada, J. Am. Chem. Soc., **98**, 8281 (1976); (b) K. Sato, H. Hagiwara, and H. Uda, Chem. Lett., 175 (1977).

3) M. S. Newman and M. D. Farbman, J. Am. Chem. Soc., **66**, 1550 (1944). For the preparation of 2-phenylcyclohexanone, 2-bromocyclohexanone was used instead of 2-chlorocyclohexanone.

4) B. M. Trost, T. N. Salzman, and K. Hiroi, J. Am. Chem. Soc., **98**, 4887 (1976).

5) Satisfactory analytical (except compounds **2**) and spectral results were obtained for all new compounds. Compound **9b** is known.[6]

6) M. Foa, L. Cassar, and M. Tacchi Venturi, Tetrahedron Lett., 1357 (1968).

7) When dehydrobromination or isolation was carried out at room temperature, only compounds **9** were obtained.

8) The high stability of the 2(3*H*)-isomers **9** is reasonable from the fact that the more stable 4,6-diene system is further stabilized by conjugation with the C-7 phenyl group.[9]

9) A. Kawamoto, H. Kosugi, and H. Uda, Chem. Lett., 807 (1972).

10) *Trans*-**4b** could be isolated by preparative tlc below 4°C. At room temperature *trans*-**4b** was isomerized on a silica gel plate to the 2(3*H*)-isomer.

11) Irradiated externally with a 500 W high-pressure Hg lamp through a Pyrex filter in both sensitized and direct photolyses.

12) This finding allows us to estimate the E_T value of about 59 Kcal/mole for **2**, being approximately equal to 2-acetonaphthone.

13) This finding, temperature dependence, may be ascribed to the conformational mobility of **2a**. The conformation, in which the 7-phenyl group is axial-like, seems to be the favorable one for the rearrangement, being unable to exist below -30°C in sufficient content. Such a temperature dependence was also observed in the photolysis of **1b**, the reaction did not occur at -60°C.

14) In all experiments at -78°C using 2-acetonaphthone or acetophenone in CH_2Cl_2, MeOH, or hexane, the formation of **2a** in *ca.* 62–80% yields could be detected, after thermal isomerization, as **9a** by nmr analysis.

15) It was already shown that compounds **12**, the minor products from **1**, were produced slowly from **3** by sensitized photolysis, but rapidly and efficiently by direct one.[2b] In the case of the direct photolysis, compound **11a** (7.7%) from **3a** and compound **13b** (trace) from **3b** were also produced. This indicates that the reverse process from **3** to **2** also took place in low efficiency.
The cyclization of **2** to **13** was an extremely low efficient process, only the formation of **13b** (7%) was observed in the photolysis of **1b** at -40∿-30°C.[2]

16) The great ease and preference of the di-π-methane rearrangement of **2** to **3** in methanol beyond the thermal isomerization to **9** was shown by the photolysis of **1a** in methanol at 60∿70°C, giving **3a** as an almost sole product. Contrary to this, the photolysis in hexane at the same temperature afforded **11a** in 72% yield, indicating that the reaction rate of **2a** to **3a** was greatly slow down in hexane, the thermal isomerization to **9a** became the main reaction path.
The cyclization of **9** to **11** was found to be effected by both sensitized and direct irradiation.

(Received June 25, 1979)