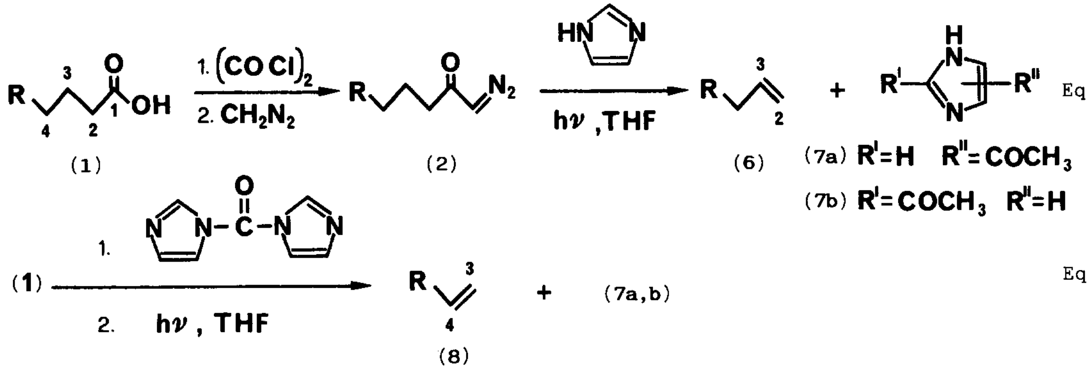
Tetrahedron Letters,Vol.25,No.29,pp 3103-3106,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

PHOTOLYSIS OF α-DIAZO CARBONYL COMPOUNDS IN THE PRESENCE OF IMIDAZOLE. A NEW METHOD FOR THE PREPARATION OF NOR OLEFINS AND ITS APPLICATION TO BILE ACID SIDE CHAIN DEGRADATION

Roberto Pellicciari,* Benedetto Natalini, Sergio Cecchetti and Sergio Santucci
Istituto di Chimica Farmaceutica e Tecnica Farmaceutica,
Università degli Studi, Perugia, Italy

Summary: α-Diazomethyl ketones derived from carboxylic acids are photolyzed in the presence of imidazole to give the corresponding nor olefins or, in the case of aryl diazo ketones, the corresponding, stable imidazolides. The application of the method to a novel degradation of bile acid side chain is reported.

The conversion of a carboxylic acid (or derivative) to the corresponding nor olefin with loss of one carbon atom is a valuable synthetic transformation. We report herein that this degradation is efficiently achieved by photolysis[1] in the presence of imidazole[2] of α-diazo carbonyl compounds routinely prepared from carboxylic acids.[3] The overall reaction sequence is represented in Eq 1.

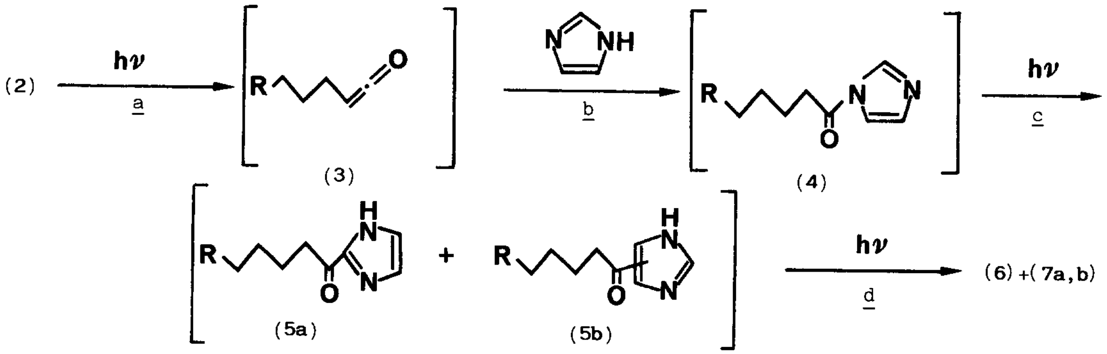


Eq 1

Eq 2

The crucial, 'one pot' conversion of α-diazo carbonyl compound (**2**) into the corresponding olefin (**6**) involves the following steps (Scheme I):[1] a)formation of ketene (**3**) by photochemical Wolff rearrangement of diazoketone (**2**);[4] b) N-acylation of imidazole by the ketene (**3**) leading to the imidazolide (**4**); c) N-acyl migration converting (**4**) into the corresponding 2-substituted and 4 (or 5)-substituted imidazoles (**5a**) and (**5b**); d) Norrish type II elimination converting (**5a**) and (**5b**) into olefin (**6**) and 2-, 4 (or 5) acetylimidazoles (**7a**) and (**7b**).

Scheme I



This sequence deserves a few comments. It is known that ketenes such as (**3**), generated in our case by photolysis of diazo ketones (**2**) (step a),[4] react with nucleophiles such as water, alcohols, amines[5] and with carbon-nitrogen double bond.[6] In analogy with the step b of our sequence, moreover, one report has described the preparation of N-acylimidazoles by reaction of ketenes with imidazoles having a free amino group.[7] Imidazolides such as (**4**), however, are radiation-sensitive, and under the condition of our experiment they undergo further photo-rearrangements (steps c, d, Scheme I).[8] These latter steps are amenable to the Iwasaki method which allows the preparation of the homologous bisnor olefins (**8**) by photochemical cleavage between carbon atoms C_2-C_3 of imidazolides bearing a γ-hydrogen atom, prepared by reaction of alkanoic acids (**1**) with N,N'-carbonyldiimidazole (Eq 2).[9a-f]

The results from the photolysis of α-diazo carbonyl compounds **2a-c** prepared[3] from stearic acid (**1a**) and from the diformyl derivatives of ursodeoxycholic acid (**1b**) and hyodeoxycholic acid (**1c**), respectively, are shown in the Table.[10]

Table

α-Diazoketone[a]	Irradiation time (h)	Olefin	Yield (%)[b]
(**2a**)	60	(**6a**)[c]	54.7
(**2b**)	3	(**6b**)[d]	40.6
(**2c**)	3	(**6c**)[d]	35.7

[a] See Ref. 3. [b] The yields quoted refer to isolated samples of at least 98% purity. [c] See Ref. 11.

[d] See Ref. 12.

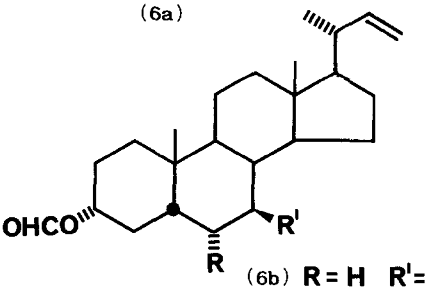
$n\text{-}C_{17}H_{35}COR$

(1a) **R = OH**

(2a) **$R = CHN_2$**

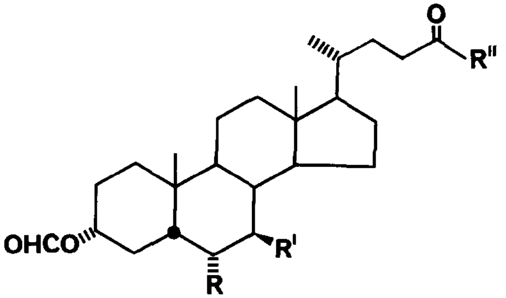
$n\text{-}C_{15}H_{31}CH{=}CH_2$

(6a)



(6b) **R = H R' = OCHO**

(6c) **R = OCHO R' = H**



(1b) **R = H R' = OCHO R'' = OH**

(1c) **R = OCHO R' = H R'' = OH**

(2b) **R = H R' = OCHO $R'' = CHN_2$**

(2c) **R = OCHO R' = H $R'' = CHN_2$**

In the course of yield optimisation studies it was observed that the optimum irradiation time is dependent upon the structure of the substrate. Thus, in the case of (**2a**), the best yield of olefin (**6a**) was obtained with an irradiation time of 60 h. Conversely, in the case of the α-diazo methyl derivatives of bile acids (**2b**) and (**2c**), the best results were obtained with an irradiation time of 3 h. Previously, Δ^{22}-24-norcholene derivatives such as (**6b**) and (**6c**), valuable intermediates for structural elaboration of the steroidal side chain, have been obtained by oxidative decarboxylation of the starting steroidal acids with lead tetra-acetate.[12] Our procedure, giving yields comparable to the above, is a contribution to the general problem of degradation of steroid side chain and complements currently available photochemical procedures so far developed for this important task.[9b-f, 13a-e]

General Procedure. A solution of α-diazo carbonyl compound (**2**) (3 mmol) and imidazole (6 mmol) in anhydrous THF (200 ml) is photolyzed under nitrogen and stirring at T ranging from -5° to -10°C. The solvent is then evaporated under vacuo and the residue purified by column chromatography. Elution with petroleum ether-diethyl ether 9:1 and evaporation of the solvent yields the pure olefin (**6**).

Acknowledgment. This research was assisted by a grant from Ministero della Pubblica Istruzione (Rome, Italy).

References and Notes

1. Irradiations were performed with a Hanau TNN 15/32 15 W low-pressure mercury lamp contained in a quartz immersion well.

2. For results of the Cu-bronze catalyzed decomposition of α-diazo carbonyl compounds in the presence of imidazole, see: R. Pellicciari, M. Curini, N. Spagnoli and P. Ceccherelli, Synthesis, 629 (1981); R. Pellicciari, M. Curini and N. Spagnoli, Arch. Pharm. (Weinheim), **317**, 38 (1984).

3. α-diazo carbonyl compounds (2) were prepared in excellent yield by reaction of the appropriate carboxylic acid (1) with oxalyl chloride followed by treatment of the resulting acid chloride with diazomethane in the presence of tertiary amine.

4. For reviews of Wolff rearrangement of ketocarbenes, see: H. Meier and K. P. Zeller, Angew. Chem. Int. Ed. Engl., **14**, 32 (1975); W. Ando in "The Chemistry of Diazonium and Diazo groups", S. Patai, Ed., Wiley, New York, 1978, Vol. I.

5. D. P. N. Satchell and R. S. Satchell, Chem. Soc. Rev., **4**, 231 (1975).

6. R. Huisgen, B. A. Davies and M. Morikawa, Angew. Chem. Int. Ed. Engl., **7**, 826 (1968).

7. W. E. Erner (Air Products and Chemicals, Inc.), U. S. 3,197,476, July 27, 1965; Chem. Abstr **63**, 13273c (1965).

8. Irradiations of diazoketones not possessing γ-hydrogens favorably oriented for photochemical fragmentation (such as diazoacetophenone) in the presence of imidazole are currently under study in our laboratory.

9. (a) S. Iwasaki, Helv. Chim. Acta, **59**, 2738 (1976); (b) ibidem, 2753 (1976). For applications of the Iwasaki method, see: (c) P. Welzel and H. Stein, Tetrahedron Lett., **22**, 3385 (1981); (d) P. Welzel, H. Stein and T. Milkova, Liebigs Ann. Chem., 2119 (1982); (e) P. Welzel, H. Stein, T. Milkova (Hoechst A.-G) Ger. Offen. DE 3,143,090 (Cl. C07J19/00) May 11, 1983; Chem. Abstr., **99**, 158725u (1983); (f) J. La Mattina, R. T. Suleske and R. L. Taylor, J. Org. Chem., **48**, 897 (1983).

10. Satisfactory infrared and nmr spectra and analytical data were obtained on purified samples of reactions products described herein.

11. (**6a**) has previously been obtained by reaction of $C_{14}H_{29}MgBr$ with allyl bromide: A. W. Schmidt, V. Schoeller and K. Eberlein, Chem. Ber., **74**, 1313 (1941).

12. A. S. Narula and S. Dev, Tetrahedron, **27**, 1119 (1971); G. L. Carlson, D. T. E. Belobaba, A. F. Hofmann, Steroids, **30**, 787 (1977). For a general review, see: R. A. Sheldon and J. K. Kochi, Org. React., **19**, 279 (1972).

13. (a) M. Fetizon, F. J. Kakis and V. Ignatiadou-Rogoussis, J. Org. Chem., **38**, 4308 (1973); (b) ibidem, **39**, 1959 (1974); (c) B. Ganem and M. S. Kellog, J. Org. Chem., **39**, 575 (1974); (d) J. M. Bernassau and M. Fetizon, Synthesis, 796 (1975); (e) M. Audouin and J. Levisalles, Tetrahedron, **39**, 2799 (1983).

(Received in UK 14 May 1984)