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PHOTOCHEMICAL TRANSFORMATIONS OF DIENES—VI[1]

PHOTOLYSIS OF SEMICARBAZONE AND OXIME DERIVATIVES OF 6-FORMYLTESTOSTERONE METHYL ENOL ETHER ACETATE[2]

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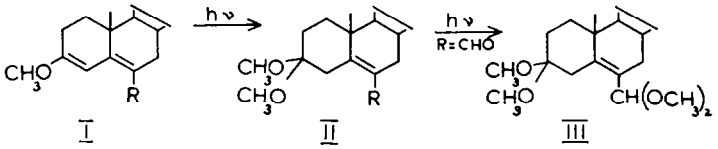
Abstract—Irradiation of *syn*-semicarbazone enol ether (IV) in methanol with 2537 Å light leads to a mixture of syn-ketal (VI) and anti-ketal (VII); anti-semicarbazone enol ether (V) is also formed. Irradiation of IV with 3500 Å light leads very rapidly to an almost quantitative conversion to *anti*-semicarbazone enol ether (V). It therefore seems that excitation of the long wavelength band (313 mμ) of IV gives rise to *syn* ⇌ *anti* isomerization, whereas the short wavelength band (228 mμ) is responsible for ketalization. Irradiation of *syn*-oxime enol ether (VIII) leads to *syn*-oxime ketal (XI), *anti*-oxime ketal (XII), nitrile enol ether (X) and nitrile ketal (XIII). The formation of the latter two compounds constitutes, to our knowledge, the first example of a photo-dehydration of oximes to nitriles. *anti*-Oxime enol ether (IX) could only be obtained upon irradiation of VIII with 3500 Å light.

INTRODUCTION

IRRADIATION of enol ethers of type I (R = H, CH_3, F[4,5] and CHO[1]) has been shown to produce ketals of type II in good yield. In the case where R = CHO, the final product of irradiation is the ketal acetal (III).



I II III

I R = H, CH_3, F
Ia R = CHO

This photoreaction has been extended to nitrogen containing derivatives of I (R = CHO), such as oximes and semicarbazones. It is known that aromatic oximes can be photoisomerized to their geometrical isomers.[6] The oximes and semicarbazones of type I (R = CH=NOH and CH=NNHCONH$_2$) have two strong bands in their electronic spectrum. These transitions may be linked with reactions such as the *syn-anti* isomerism or ketal formation. This paper describes the results obtained in the photolysis of semicarbazone IV and oxime VIII.

[1] Part V. G. Just and C. Pace-Asciak, *Tetrahedron* **22**, 1063 (1966).

[2] This work was supported by the National Research Council of Canada.

[3] Holder of a National Research Council of Canada Bursary, 1962–3, and Studentships, 1963–5.

[4] C. C. Leznoff and G. Just, *Canad. J. Chem.* **42**, 2919 (1964).

[5] G. Just and C. C. Leznoff, *Canad. J. Chem.* **42**, 79 (1964).

[6] O. L. Brady and G. P. McHugh, *J. Chem. Soc.* **125**, 547 (1924).

RESULTS

Semicarbazones

The semicarbazone of 17β-acetoxy-6-formyl-3-methoxyandrosta-3, 5-diene (III) was irradiated[7] in absolute methanol until less than 5% of the original chromophore could be detected in the UV spectrum. The resulting mixture was separated by TLC giving three products (V, VI and VII) in good yield. The structure of these compounds was elucidated through an examination of their NMR[8] and UV spectra, which are summarized in Table 1.

TABLE 1. SOME SPECTRAL DATA OF *syn*- AND *anti*-SEMICARBAZONES

Compound	H—C=N—R* ppm	—OCH$_3$† ppm	λ_{max}^{meOH} mμ	(ε)
syn-Semicarbazone enol ether (IV)	8·12	3·7 (3H)	313 228	(28,000) (8,600)
syn-Semicarbazone ketal (VI)	8·06	3·25 (3H) 3·10 (3H)	272	(28,800)
anti-Semicarbazone enol ether (V)	6·81	3·56 (3H)	284 230	(7,600) (15,000)
anti-Semicarbazone ketal (VII)	6·74	3·23 (6H)	233	(8,400)

* R = —NHCONH$_2$

† Tetramethylsilane was used as internal reference = 0 ppm

The *syn*-compounds[9] (IV and VI) show a signal at 8·12 and 8·06 ppm respectively (H—C=N—), whereas the *anti*-compounds (V and VII) absorb at 6·81 and 6·74 ppm.[14] These signals have a chemical shift similar to those observed in the corresponding oximes tabulated in Table 2 (See also Ref. 10, 11, 12, 13). *syn*-Semicarbazone ketal VI was also identified by comparison with a sample prepared from ketal aldehyde II with semicarbazide hydrochloride. The UV spectra are consistent with the assignment. In particular, models show that only the *syn*-isomers (IV and VI) can exist in a planar arrangement, and hence absorb at longer wavelength than the corresponding *anti*-isomers (Vand VII) in which the ureido group is sterically hindered. The IR spectrum is not very informative in distinguishing between the *syn*- and the *anti*-isomers except in that the *anti*-isomers displayed a peak at 1410 cm^{-1}, the intensity of which is far greater than that of the *syn*-compounds.

Owing to the considerable overlap of the UV bands of the four compounds, the photolysis could not be followed in a quantitative manner. Nevertheless, the following

[7] Rayonet Photochemical Reactor, 2537 Å light.

[8] We wish to thank Mr. K. Valentin for taking the spectra.

[9] E. L. Eliel, *Stereochemistry of Carbon Compounds* p. 320, McGraw-Hill. "In an aldoxime, the *syn*-isomer is the one in which the hydroxyl group of the oxime is on the same side as the hydrogen of the aldehyde carbon".

[10] N. S. Bhacca, L. F. Johnson and J. N. Shoolery, *NMR spectra Catalogue*, Vol. 2; No. 420. Varian Associates, Palo Alto, California (1963).

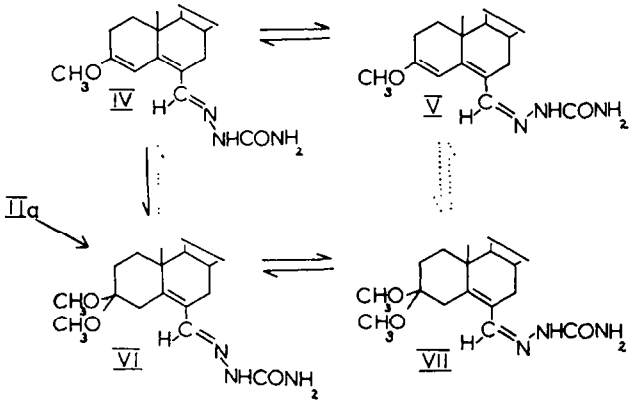
[11] W. D. Phillips, *Ann. N.Y. Acad. Sci.* **70**, 817 (1958).

[12] D. Y. Curtin, J. A. Gourse, W. H. Richardson and K. L. Rinehart, Jr., *J. Org. Chem.* **24**, 93 (1959).

[13] G. Karabatsos, F. Vane, R. Taller and N. Hsi, *J. Am. Chem. Soc.* **86**, 3351 (1964).

[14] The HC=N and =NNHCO NMR signals of the aldehyde semicarbazones were distinguished from each other by means of deuterium oxide exchange experiments.

semi-quantitative results were obtained. Irradiation[7] of a $2{\cdot}5 \times 10^{-5}$ molar methanolic solution of *syn*-semicarbazone enol ether (IV) resulted in a rapid disappearance of IV. Analysis of the UV spectrum of the reaction mixture indicated the fairly rapid appearance of ketals VI and VII, together with a somewhat slower appearance of *anti*-semicarbazone enol ether (V). When V was irradiated[7], a rapid conversion to *syn*-semicarbazone enol ether (IV) was observed with a subsequent reaction of IV to give ketals as discussed. Irradiation[7] of either ketal (*syn*- or *anti*-) resulted in the establishment of a photoequilibrium in which the *anti*- to *syn*- ratio was approximately 2:3; since the amount of enol ether formed was below 5% in each case, it could not be determined accurately. Based on this data, the following scheme is proposed in which dotted arrows indicate slow and therefore uncertain paths.



In an attempt to find out which of the two bands (313 or 228 mμ) in the UV spectrum of IV gave rise to isomerization or ketalization after excitation with UV light, IV was irradiated[15] with 3500 Å light in which the energy output of the lamps at 228 mμ is negligible. *anti*-Semicarbazone enol ether (V) was obtained in almost quantitative yield in 30 seconds. It therefore seems reasonable to assume that the excitation of the 313 mμ band in IV leads to isomerization of the *syn* $\rightleftharpoons$ *anti* type. The excitation of the 228 mμ band is therefore most likely responsible for ketal formation.

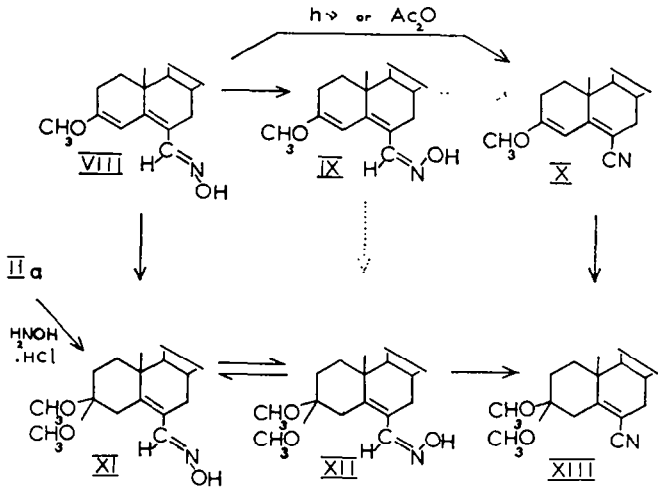
Oximes

Irradiation[7] of the oxime[16] of 17β-acetoxy-6-formyl-3-methoxyandrosta-3,5-diene (VIII) in absolute methanol gave a mixture, from which were isolated *syn*-oxime ketal (XI), identical with that obtained by oximation of ketal aldehyde (II), *anti*-oxime ketal (XII), enol ether nitrile (X), identical with a sample obtained by dehydration of VIII with acetic anhydride, and ketal nitrile (XIII). No *anti*-oxime enol ether (IX) could be detected. However, IX could be isolated in low yield when VIII was irradiated with 3500 Å light.

The products were identified as follows: all *syn*-oximes had NMR signals (H—C=N\) at approximately 8·4 ppm, whereas the *anti*-oximes showed a corresponding signal at higher field[11] at approximately 7·3 ppm (Table 2). All enol ethers showed a

[15] Rayonet Photochemical Reactor, 3500 Å light.

[16] D. Burn, G. Cooley, M. T. Davies, J. W. Ducker, B. Ellis, P. Feather, A. K. Hiscock, D. N. Kirk, A. P. Leftwick, V. Petrow and D. M. Williamson, *Tetrahedron* **20**, 597 (1964).



signal around 3·6 ppm due to the presence of one methoxyl group, whereas the ketals absorbed around 3·25 and 3·13 ppm corresponding to two methoxyl groups. The enol ether nitrile and ketal nitrile had a band in the IR at around 2200 cm^{-1} corresponding to the —CN group.

The *anti*-oxime compounds (ketal and enol ether) were converted to their *syn*-isomers upon crystallization from ether–pyridine. Prolonged irradiation of all oximes resulted in the formation of ketal nitrile, which slowly decomposed upon further irradiation to a mixture of unidentified products.

TABLE 2. SOME SPECTRAL FEATURES OF THE OXIMES AND NITRILES

Compound	H—C=N—R* ppm	OCH_3 ppm	λ_{max}^{meOH} mμ	(ε)
syn-Oxime enol ether (VIII)	8·45	3·68 (3H)	296 219	(20,000) (9,800)
syn-Oxime ketal (XI)	8·40	3·28 (3H) 3·13 (3H)	247	(17,600)
anti-Oxime enol ether (IX)	7·30	3·65 (3H)	284 218	
anti-Oxime ketal (XII)	7·25	3·25 (3H) 3·13 (3H)	(245)[a]	
Enol ether nitrile (X)		3·68 (3H)	282 216	(22,300) (10,000)
Ketal nitrile (XIII)		3·20 (3H) 3·18 (3H)	220	(21,900)

[a] The spectrum of XII was taken on a mixture containing XI. Irradiation of *syn*-oxime ketal (XI) produces a rapid photoequilibrium in which the *anti*- to *syn*-ketal ratio is 4·6 as determined by the relative area of the HC=N—NMR signals at 7·25 and 8·40 ppm respectively.

* R = —OH.

EXPERIMENTAL[17]

Semicarbazone of 17β-*acetoxy*-6-*formyl*-3-*methoxyandrosta*-3,5-*diene* (IV)

Water was added dropwise to a hot methanolic solution (25 ml) of 17β-acetoxy-6-formyl-3-methoxyandrosta-3,5-diene[16] (500 mg) until crystals appeared. The aqueous methanolic solution was then heated and semicarbazide hydrochloride (500 mg) and sodium acetate (700 mg) were added. The contents were swirled until a solution was obtained. Upon cooling, small light yellow needles of IV separated. Filtration gave 457 mg, m.p. 237–239° (dec) ν ($CHCl_3$) 3530, 3410, 3350 cm^{-1} (NH—CO—NH_2), 1725 cm^{-1} (—OAc), 1685 cm^{-1} (N—CO—N), 1630 cm^{-1} (C=C—OCH_3), 1560 cm^{-1} (C=N); δ ($CDCl_3$) 10·3 (singlet, 1H, = N—NH—CO), 8·12 (singlet, 1H, H—C=N), 6·0 (broad singlet, 2H, N—CO—NH_2), 5·71 (singlet, 1H = C_4H), 3·7 (singlet, 3H, —OCH_3), 2·08 ppm (singlet, 3H, acetate). (Found: C, 67·04; H, 7·97; N, 9·59. $C_{24}H_{35}N_3O_4$ requires: C, 67·10; H, 8·21; N, 9·78%.)

Irradiation of IV

A solution of IV (350 mg) in abs MeOH (75 ml) was irradiated for 3 hr at which time the rate of disappearance of the 313 mμ band in the UV decreased appreciably and IV (170 mg) crystallized upon concentration of the photolysis solution. Purification of the mother liquor by preparative TLC using ether–MeOH (96%) as the developing solvent, gave an amorphous compound (48 mg) identified as *anti*-semicarbazone enol ether (V). ν ($CHCl_3$) 3534, 3410, 3350 cm^{-1} (NH—CO—NH_2), 1725 cm^{-1} (—OAc), 1685 cm^{-1}; (N—CO—N), 1641 cm^{-1} (C=C—OCH_3), 1560 cm^{-1} (C=N), 1425 cm^{-1}; δ ($CDCl_3$) 7·8 (singlet, 1H, N—NH—CO), 6·81 (singlet, 1H, H—C=N), 5·83 (broad singlet, 2H, N—CO—NH_2), 4·93 (singlet, 1H, =C_4H), 3·56 (singlet, 3H, —OCH_3), 2·05 ppm (singlet, 3H, acetate). (Found: C, 66·31; H, 8·49; N, 10·15. $C_{24}H_{35}N_3O_4$ requires: C, 67·10; H, 8·21; N, 9·78%.)* A further irradiation of IV (170 mg) for 13 hr gave, after separation by TLC *anti*-enol ether V (9 mg); an amorphous *anti*-ketal VII (52 mg), ν ($CHCl_3$) 3525, 3405, 3240 cm^{-1} (NH—CO—NH_2), 1725 cm^{-1} (—OAc), 1690 cm^{-1} (N—CO—N), 1560 cm^{-1} (C=N), 1425 cm^{-1}, and 1100 cm^{-1} (ketal); ν (CCl_4) 1105 and 1055 cm^{-1} (ketal); δ ($CDCl_3$) 9·15 (singlet, 1H, N—NH—CO), 6·74 (singlet, 1H, H—C=N), 5·61 (broad singlet, 2H, N—CO—NH_2), 3·23 (singlet, 6H, ketal), and 2·1 ppm (singlet, 3H, acetate). (Found: C, 64·55; H, 8·69; N, 9·21. $C_{35}H_{39}N_3O_5$ requires: C, 65·05; H, 8·52; N, 9·10%);* *syn*-ketal VI (35 mg), m.p. 223° (dec), ν ($CHCl_3$) 3525, 3405, 3345 cm^{-1} (C=N), 1100 cm^{-1} (ketal); ν (CCl_4) 1100 and 1050 cm^{-1} (ketal); δ ($CDCl_3$) 9·50 (broad singlet, 1H, N—NH—CO), 8·06 (broad singlet, 1H, N—NH—CO), 5·75 (broad signal, 2H, N—CO—NH_2), 3·25 (singlet, 3H, —OCH_3), 3·1 (singlet, 3H, —OCH_3), 2·05 ppm (singlet, 3H, acetate). (Found: C, 64·84; H, 8·61; N, 9·68. $C_{35}H_{39}N_3O_5$ requires: C, 65·05; H, 8·52; N, 9·10%.)

Preparation of syn-*semicarbazone ketal* VI *from* 17β-*acetoxy*-6-*formyl*-3,3-*dimethoxyandrost*-5-*ene* (IIa)

The procedure was the same as that used in the preparation of IV. The compound obtained had an IR spectrum superimposable with that of the photoproduct VI. No depression in m.p. was observed when the two compounds were admixed.

Kinetic experiments

Magnetically stirred solutions (200 ml) of IV, V, VI, VII ($2·5 \times 10^{-5}$ molar) in abs MeOH were separately irradiated in a He atm. in a quartz cell fitted with a cold water jacket and a cold water condenser. The photochemical reaction was followed by the withdrawal of a 3 ml aliquot at various time intervals and the recording of the disappearance of the original chromophore on a Beckman DKI recording spectrophotometer. In a separate experiment IV was irradiated with 3500 Å light, in which case the spectrum recorded, after 30 sec of irradiation, displayed a curve almost identical in shape and intensity with that obtained from a $2·5 \times 10^{-5}$ molar solution of V, indicating an almost complete transformation to this compound.

17β-*Acetoxy*-6-*cyano*-3-*methoxyandrosta*-3,5-*diene* (X)

A mixture of enol ether oxime[16] VIII (104 mg) in acetic anhydride (4 ml) was heated at 98° on a water bath for 80 min, after which time the acetic anhydride was stripped off *in vacuo*, giving an oil from which crystals appeared upon addition of MeOH. Recrystallization from MeOH containing

* This compound could only be obtained in an amorphous state. Its simple NMR and IR spectra, however, were so clear-cut as to permit no doubt concerning its structure.

[17] See Ref. 1 for general procedures.

a few drops pyridine gave 62 mg X, m.p. 194·5–195°; ν (CCl_4) 2200 cm^{-1} (—CN), 1740, 1230, 1050 cm^{-1} (—OAc), 1630 cm^{-1} (CH_3O—C=C), 1180, 1155, 1125 cm^{-1} (ether); δ (CCl_4) 5·65 (singlet, 1H, =C_4—H), 3·68 (singlet, 3H, CH_3O—), 1·95 (singlet, 3H). (Found: C, 74·79; H, 8·46; N, 3·66; $C_{22}H_{31}NO_3$ requires: C, 74·76; H, 8·46; N, 3·79%.)

17β-Acetoxy-6-cyano-3,3-dimethoxyandrost-5-ene (XIII)

A solution of X (150 mg) was irradiated in abs MeOH (37 ml) for 15 hr, until no starting material could be detected by TLC using benzene–ether (8:2) as developing solvent. The photoproduct consisted of one component, as revealed by TLC. Evaporation of the solvent gave an oil which was purified by preparative TLC. Recrystallization from MeOH containing a few drops of pyridine gave XIII, m.p. 183–184°; ν (CCl_4) 2210 cm^{-1} (—CN), 1740, 1240 cm^{-1} (—OAc), 1640 cm^{-1} (C=C), 1110, 1050 cm^{-1} (ketal); δ (CCl_4) 3·2 (singlet, 3H, —OCH_3) 3·13 (singlet, 3H, —OCH_3), 2·0 ppm (singlet, 3H); λ_{max}^{MeOH} 220 mμ (ε 21,875). (Found: C, 71·54; H, 8·68; N, 3·43; $C_{24}H_{35}NO_4$ requires: C, 71·79; H, 8·79; N, 3·49%.)

Oxime of 17β-acetoxy-6-formyl-3,3-dimethoxyandrost-5-ene (XI)

A solution of IIa (194 mg) in MeOH (30 ml) containing pyridine (10 ml) and hydroxylamine hydrochloride (194 mg) was refluxed for 0·5 hr, followed by an ether extraction and washing of the organic layer with water several times. The organic phase was dried over $MgSO_4$, filtered and evaporated to dryness giving a crystalline residue. Two recrystallizations from ether–pyridine gave XI, m.p. 204° (dec); ν ($CHCl_3$) 3570, 3300 cm^{-1} (=NOH), 1725 cm^{-1} (—OAc), 1630 cm^{-1} (C=C), 1100 cm^{-1} (ketal), δ ($CDCl_3$) 8·41 (singlet, H—C=N), 3·3, 3·15 (ketal), 2·10 ppm. (Found: C, 68·45; H, 9·22; N, 3·31. $C_{24}H_{37}NO_5$ requires: C, 68·70; H, 8·89; N, 3·79%.) A decomposition of XI to enol ether VIII took place upon heating XI in $CDCl_3$.

Irradiation of the oxime of 17β-acetoxy-6-formyl-3-methoxyandrosta-3,5-diene (VIII)

A solution of VIII (171 mg) in abs MeOH (80 ml) was irradiated in a He atm. After 3 hr the UV spectrum showed a band at 284 mμ instead of the 294 mμ band present in the starting material VIII. TLC using benzene–ether (8:2) revealed the presence of four compounds. The faster moving product was identified as X since its IR was superimposable with that obtained by dehydration of the *syn*-oxime enol ether (VIII) described above. No depression in m.p. was evident upon admixture of the two compounds. The next component was identified as ketal nitrile XIII, by its IR spectrum and mixture m.p. Elution of the slowest moving compound (R_f approx. 0·1) gave a semi-crystalline oil which exhibited two spots by TLC (R_f = 0·1 and 0·2 approx.). Upon recrystallization from ether containing a few drops of pyridine the original compound (R_f = 0·1) was converted completely to the higher R_f component (R_f = 0·2), m.p. 198–199°. Two recrystallizations from ether pyridine gave pure *syn*-oxime ketal XI, m.p. 204° (dec) identical with *syn*-oxime ketal prepared by oximation of IIa, described above. The compound with R_f = 0·1 (*anti*-oxime ketal XII)* could also be obtained in a mixture with ketal *syn*-oxime XI by irradiation of XI.

Irradiation of XI

Photoequilibrium between ketals XI *and* XII. Ketal *syn*-oxime XI (45 mg) was irradiated in abs MeOH (10 ml) for 10 min after which time TLC (benzene–ether 8:2) revealed two components (R_f = 0·1, 0·2 approx.) and a faint spot (R_f = 0·5 approx.) due to the formation of XIII. The solvent was stripped off, giving a crystalline residue; δ ($CDCl_3$) 8·40 (syn, H—C=N), 7·25 (anti, HC=N), 3·28, (syn, —OCH_3) 3·13 (syn, —OCH_3), 3·25 (anti, —OCH_3), 3·13 (anti, —OCH_3 2·18 ppm (acetate). The relative area of the signals at 8·40 and 7·25 ppm indicated a *syn*:*anti* ratio of 1:4·6.

* The *anti*-oxime ketal (XII) could not be obtained in a pure form since TLC converted it to a mixture of *syn*- and *anti*-isomers and any attempt to crystallize the compound led to its conversion to pure *syn*-oxime ketal. Characterization of the mixture was easily achieved by NMR spectra.