Tetrahedron Letters No.7, pp. 827-830, 1968. Pergamon Press. Printed in Great Britain.

ACETAL FORMATION BY THE USUAL METHOD OF OXIME FORMATION FROM ALDEHYDES.

(STUDIES ON HETEROAROMATICITY XI)

Tadashi Sasaki and Toshiyuki Yoshioka

Institute of Applied Organic Chemistry, Faculty of Engineering,
Nagoya University, Chikusa-ku, Nagoya, Japan

(Received in Japan 21 September 1967)

It is the well-known procedure for identification of aldehydes to prepare their oximes by the general method (1) that an aldehyde is treated in alcohol with hydroxylamine hydrochloride in the presence of a base such as sodium acetate, sodium carbonate, sodium hydroxide, pyridine etc.. In the course of our studies on heterocyclic carbonitrile oxides (2,3), we have found an interesting phenomenon that the main product of the routine procedure for the oxime formation from 5-nitro-2-furylacrolein (I) is the acetal (II) instead of the expected oxime (III) as shown by the following experiment: 3.3 g (0.02 mol) of I and 2.8 g (0.04 mol) of hydroxylamine hydrochloride were dissolved in 100 ml of methanol, followed by addition of 2.6 g (0.02 mol) of anhydrous sodium carbonate or 3.6 g (0.02 mol) of sodium acetate with stirring at 0°∿5° under ice cooling. After one hour's stirring, precipitated crystals were collected and recrystallized from petroleum ether to give yellow crystals of mp 61° in almost quantitative yield. Its elemental analysis shows a chemical formula of $C_9H_{11}O_5N$ (4). In the IR spectrum there's no absorption in a 3200-3600 cm^{-1} region due to ν_{OH} and in the NMR spectrum in $CDCl_3$ it shows a singlet at 6.62τ (6 H) assignable to two $-OCH_3$. II was easily convertible to I by heating with dilute hydrochloric acid. The above-mentioned properties suggest II to be 5-nitro-2-furylacrolein dimethylacetal, which was already prepared by Saikachi and Ogawa (5) by heating I with methyl orthoformate and p-toluenesulfonic acid as catalyst, though I was recovered when heatid with large amounts of methanol in the presence of concd. hydrochloric acid as catalyst. 5-Nitro-2-furylacrolein dimethylacetal thus obtained was identical with II in every respect. When I was refluxed in methanol with hydroxylamine hydrochloride in the absence of base, precipitation occurred spontaneously. After half an hour, the precipitate was collected and recrystallized from ethanol to give yellow crystals of mp 145-155°, a mixture of the syn and anti oxime (6), in quantitative yield and this mixture was easily convertible all to the anti oxime of mp 164° only by longer heating. The same oxime formation had occurred exclusively when I was treated in ethanol in place of methanol under the above experimental conditions or when free hydroxylamine in methanol was added to a methanolic solution of I, while only the starting material(I)was recovered when I was treated in methanol with pyridine, triethylamine, sodium acetate or 2% aqueous sodium carbonate without hydroxylamine hydroxhloride. It should be mentioned here that II was also formed when I was treated in methanol with hydrochloric acid, directly followed by addition of an equimolecular amount of sodium carbonate in the absence of hydroxylamine hydrochloride.

In order to investigate the relationship between the chemical structure and the reaction scheme, several aldehydes involving a furan or a benzene ring were treated under the same reaction conditions as described in the above experiment. Their results are summarized in the Table.

From this table, it could be concluded that the similar reaction scheme might be applicable to furaldehydes and benzene analogues. Both the existence of an ethylenic linkage between an aldehyde group and a furan or a benzene ring and the introduction of a nitro group in the ring seem to play important roles for determining the main product being either oxime or acetal; the introduction of a nitro group favors the formation of acetal to some extent as observed in comparison of Ex 1-2 with Ex 3-5 and this trend becomes more remarkable by further introduction of an ethylenic linkage as seen in Ex 8-9. In comparison of Ex 1-2 with Ex 6-7, the oxime formation is seemingly favored by the presence of an ethylenic linkage. Considering from the fact that the acidity of nitrocinnamic acid becomes stronger than that of benzoic acid by the presence of an ethylenic linkage conjugated with nitrophenyl while benzoic acid is a stronger acid than

TABLE

Ex No	REACTANT	PRODUCTS (YIELDS %)	
1	C_4H_3O-CHO	oxime, mp 73-75$^{\circ *1}$ syn form (30)	acetal, bp 177-178$^{\circ *8}$ (60)
2	C_6H_5-CHO	oxime, mp 33-35$^{\circ *2}$ syn form (30)	acetal. bp 206-207$^{\circ *9}$ (60)
3	5-NO_2-C_4H_2O-CHO	oxime, mp 100-110$^{\circ *3}$ mixture (20)	acetal. bp 113-115°/2 mmHg^{5} (70)
4	4-NO_2-C_6H_4-CHO	oxime, mp 109-118$^{\circ *4}$ mixture (20)	acetal, mp 28$^{\circ *10}$ (70)
5	3-NO_2-C_6H_4-CHO	oxime, mp 121$^{\circ *5}$ anti form (20)	acetal, bp 145-146°/9 mmHg^{*10} (70)
6	C_4H_3O-CH=CH-CHO	oxime, mp 110-111$^{\circ *6}$ anti form (90)	———
7	C_6H_5-CH=CH-CHO	oxime, mp 70-90$^{\circ *7}$ mixture (92)	———
8	5-NO_2-C_4H_2O-CH=CH-CHO	———	acetal (II), mp 59$^{\circ 5}$ (95)
9	2-NO_2-C_6H_4-CH=CH-CHO	———	acetal, mp 30$^{\circ *11}$ (75)

[*1] O. L. Brady and R. F. Goldstein, J. Chem. Soc., 1927, 1959. syn form, mp 75-76°; anti form, mp 90-92°

[*2] T. W. J. Taylor and D. C. V. Roberts, J. Chem. Soc., 1933, 1433. syn form, mp 35°; anti form, mp 131-133°.

[*3] H. Gilman and G. F. Wright, J. Am. Chem. Soc., 52, 2550 (1930). syn form, mp 120-121°; anti form, mp 161-164°.

[*4] B. König, Ann., 268, 350 (1892). syn form, mp 121°; anti form, mp 173-175° (The literature described their mps reversely.)

[*5] G. Ciamician and P. Silber, Chem. Ber., 36, 4266 (1903). anti form, mp 121° but no description about that of syn form.

[*6] anti form, mp 110-111° by Gilman^{*3}.

[*7] O. L. Brady and C. D. Thomas, J. Chem. Soc., 121, 2104 (1922). syn form, mp 64°; anti form, mp 138.5° (The literature described their mps reversely)

[*8] N. C. Kaas, F. Limberg and K. Glens, Zhur. Obshch. Khim., 29, 106 (1959). Bp 178°.

[*9] R. D. Haworth and A. Lapworth, J. Chem. Soc., 121, 80 (1922). Bp 207°.

[*10] E. Schmitz., Chem. Ber., 91, 410 (1958).

[*11] Anal. Calcd for $C_{11}H_{13}O_4N$: C, 59.18; H, 5.87; N, 6.28%. Found : C, 59.22; H, 5.74; N, 6.12%. IR(KBr) : 1610 ($\nu_{C=C}$), 1530 (ν_{NO_2}) and 1350 cm^{-1} (ν_{NO_2}).

cinnamic acid (6), it can be concluded that the stronger the acidity of the aldehyde becomes, the more the formation of acetal is favored and this conclusion is supported by our experimental results that the oximes were formed exclusively in Ex 6-7 and the acetals were produced in Ex 8-9.

The fact that II was convertible to an anti form of the oxime, mp 164° (7), by longer heating with hydroxylamine hydrochloride in methanol indicates low reaction temperature to be another factor for determining the acetal formation.

It is generally believed (8) that the conversions of aldehydes to oximes probably proceed in much the same manners as does the formation of hemiacetals but to the best of authors' knowledge, there have been no reports dealing with the simultaneous formation of acetal and oxime from aldehyde. The detailed mechanism whether acetal and oxime are formed by parallel or by consecutive reaction is uncertain at the present stage, which is under investigation.

REFERENCES

(1) For example, L. F. Fieser, "Experiments in Organic Chemistry", 3rd Ed., p 103, D. C. Heath and Company, Boston (1955)

(2) T. Sasaki and T. Yoshioka, Bull. Chem. Soc. Japan, **40**, (1967) as Part IV of Studies on Heteroaromaticity.

(3) T. Sasaki and T. Yoshioka, Bull. Chem. Soc. Japan, **40**, (1967) as Part VIII of Studies on Heteroaromaticity.

(4) Calcd for this formula: C, 50.70; H, 5.20; N, 6.57%. Found: C, 50.44; H, 5.26; N, 6.48%.

(5) H. Saikachi and H. Ogawa, J. Am. Chem. Soc., **80**, 3642 (1958)

(6) M. Charton and H. Meislich, J. Am. Chem. Soc., **80**, 5941 (1958)

(7) M. Ikeda, Chem. Abstr., **50**, 10701 (1956)

(8) E. S. Gould, "Mechanism and Structure in Organic Chemistry", p 539-544, Holt, Rinehart and Winston, New York (1959)