

Substituted gamma-Lactones. XIV¹⁾

Nitration of 2-Phenyl- and 2-Methyl-4-benzylidene-5-(4H)-oxazolones

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Summary

The nitration of 2-phenyl-4-alkoxybenzylidene-5-(4H)-oxazolones to yield the corresponding mononitrobenzylidene derivatives is described. During nitration of the analogue 2-methyl-derivatives hydrolysis occurs simultaneously to give α -acetylaminocinnamic acids.

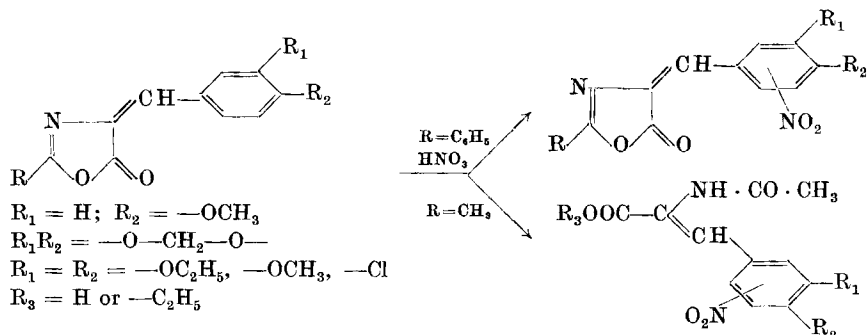
A great number of 4-benzylidene-5-oxazolones (azlactones) with a nitro group as substituent in the benzylidene ring are described in the literature²⁾. Without exception these compounds were obtained by ERLLENMEYER's method through condensation of the N-substituted glycine with the appropriate nitrobenzaldehyde.

Since azlactones are important intermediates in the synthesis of aromatic amino acids, we should like to report briefly on another method which also affords certain nitroazlactones. In spite of the general opinion concerning the sensitivity of this class of compounds towards hydrolysis, it was found that direct nitration of 2-phenyl-4-benzylidene-5-(4H)-oxazolones could indeed be accomplished. The nitration was carried out with concentrated nitric acid ($d = 1.42$) and proved successful only with 2-phenyl-4-benzylidene-5-(4H)-oxazolones which possessed activating substituents in the benzylidene group. With these compounds the yields were almost quantitative. No nitration occurred in the case of 2-phenyl-4-(3,4-dichloro)-benzylidene-5-(4H)-oxazolone under the described conditions. Due to increased sensitivity toward hydrolysis the 2-methyl-azlactones failed to yield the expected nitro substituted azlactones; instead, hydrolysis took place during the reaction to yield the corresponding α -acetylamine-2-nitrocinnamic acid derivatives.

¹⁾ Part XIII of this series: H. ZIMMER, R. WALTER and D. GENGE, J. Org. Chem. 29, 925 (1964).

²⁾ H. E. CARTER, Organic Reactions, J. Wiley and Sons, Inc., New York, p. 232.

The structures of the obtained compounds were proven by condensation of hippuric acid or acetylglycine with 3-nitro-4-methoxybenzaldehyde, 6-nitropiperonal, 2-nitro-4,5-dimethoxy-, and 2-nitro-4,5-diethoxybenzaldehyde, along with elementary analyses, comparison of IR-spectra, undepressed mixed melting points with authentic materials, and preparation of derivatives. The results of the nitration are summarized in scheme 1.



Experimental

Microanalyses by A. BERNHARDT, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mülheim Ruhr, Germany. The azlactones have been recrystallized from ethyl acetate, the cinnamic acids and ethyl cinnamates from ethyl alcohol.

2-Phenyl-4-(2-nitro-4,5-methylenedioxy)benzylidene-5-(4H)-oxazolone. Concentrated nitric acid ($d = 1.42$) (200 ml.) was cooled to about (-25°). While being stirred 20 gm. of carefully powdered 2-phenyl-4-(3,4-methylenedioxy)benzylidene-5-(4H)-oxazolone was added. Over a period of eight hours the temperature of the mixture was allowed to rise to 0°C . and was then poured into 1000 ml. of water. The orange precipitate was filtered and thoroughly washed with water until the washings were neutral. The melting point of the crude product was 195°C . Yield: 22.5 g. = 97%, m. p.: 199°C . (Ref. 4 m. p. 196°C . from glacial acetic acid). Mixed melting point with a sample prepared by ERLÉNMEYER'S method³) showed no depression.

Anal. Calcd. for $C_{17}H_{10}N_2O_6$: C 60.36, H 2.98, N 8.28; found: C 60.23, H 2.82, N 8.17.

Its hydrolysis product, α -benzoylamino-2-nitro-4,5-methylenedioxy-cinnamic acid (m. p. 215°), and its alcoholysis product, ethyl α -benzoylamino-2-nitro-4,5-methylenedioxy-cinnamate (m. p. 178°), also agreed with the values already reported in the literature⁴).

2-Phenyl-4-(2-nitro-4,5-diethoxy)benzylidene-5-(4H)-oxazolone was similarly obtained from 2-phenyl-4-(3,4-diethoxy)benzylidene-5-(4H)-oxazolone. Yield: 20.5 g. = 90%, m. p.: $172-173^\circ$. A sample which was obtained by condensation of hippuric acid with 2-nitro-4,5-diethoxybenzaldehyde, melted at $171-172^\circ$, Mixed melting point showed no depression.

Anal. Calcd. for $C_{20}H_{18}N_2O_6$: C 62.82, H 4.75, N 7.33; found: C 63.50, H 4.90, N 7.07.

α -Benzoylamino-2-nitro-4,5-diethoxycinnamic acid obtained through hydrolysis of the above nitration product; m. p.: 227° . It was shown to be identical with the

³) F. McDONALD, J. chem. Soc. London 1948, 376; E. HOVINGA and E. T. M. SPITZER, Rec. Trav. chem. Pays-Bas 76, 173 (1957).

⁴) D. BAIN, W. H. PERKIN and R. ROBINSON, J. chem. Soc. London 105, 2392 (1913).

hydrolysis product of the azlactone, prepared by ERLLENMEYER's method; m. p.: 228°. Mixed melting point was 226°.

Anal. Calcd. for $C_{20}H_{20}N_2O_7$: C 59.99, H 5.04, N 7.00; found: C 58.87, H 5.00, N 7.06.

Ethyl- α -benzoylamino-2-nitro-4,5-diethoxycinnamate obtained through alcoholysis from the corresponding azlactone; m. p.: 178°.

Anal. Calcd. for $C_{22}H_{24}N_2O_7$: C 61.67; H 5.65, N 6.54; found: C 62.18, H 5.63, N 6.39.

2-Phenyl-4-(3-nitro-4-methoxy)benzylidene-5-(4H)-oxazolone was obtained by nitration of 2-phenyl-4-(4-methoxy)benzylidene-5-(4H)-oxazolone; m. p.: 209–210° (lit. m. p.: 206)⁵⁾, yield 93%.

Anal. Calcd. for $C_{17}H_{13}N_2O_5$: C 62.96, H 3.73, N 8.64; found: C 63.43, H 4.14, N 8.78.

α -Benzoylamino-3-nitro-4-methoxycinnamic acid obtained through hydrolysis of the nitration product and from a sample prepared by ERLLENMEYER's method, both of which melted at 255–256°.

Anal. Calcd. for $C_{17}H_{13}N_2O_6$: C 59.65, H 4.12, N 8.18; found: C 59.77, H 4.31, N 8.20.

Ethyl- α -benzoylamino-3-nitro-4-methoxycinnamate obtained through alcoholysis from the corresponding azlactone; m. p.: 171°.

Anal. Calcd. for $C_{19}H_{13}N_2O_6$: C 61.61, H 4.90, N 7.56; found: C 62.20, H 4.96, N 7.48.

2-Phenyl-4-(2-nitro-4,5-dimethoxy)benzylidene-5-(4H)-oxazolone was obtained by nitration of 2-phenyl-4-(3,4-dimethoxy)benzylidene-5-(4H)-oxazolone; m. p.: 227–228° (lit. 227–228°)⁶⁾; the yield was quantitative.

Anal. Calcd. for $C_{18}H_{13}N_2O_6$: C 61.01, H 3.98, N 7.91; found: C 60.76, H 4.02, N 8.02.

Ethyl- α -benzoylamino-2-nitro-4,5-dimethoxycinnamate obtained through alcoholysis from the above azlactone; m. p.: 169–170°.

Anal. Calcd. for $C_{20}H_{20}N_2O_7$: C 59.99, H 5.04, N 7.00; found: C 60.19, H 4.48, N 6.95.

2-Phenyl-4-(3,4-dichloro)benzylidene-4-(4H)-oxazolone obtained by ERLLENMEYER's method; m. p.: 173°.

Anal. Calcd. for $C_{16}H_9Cl_2NO_2$: C 60.40, H 2.85, N 4.40, Cl 22.29; found: C 60.23, H 2.76, N 4.31, Cl 22.19.

2-Methyl-4-(6-nitro)-piperonylidene-5-(4H)-oxazolone, m. p.: 157°.

Anal. Calcd. for $C_{12}H_8N_2O_6$: C 52.18, H 2.92, N 10.14; found: C 52.14, H 3.15, N 10.21.

α -Acetylamino-2-nitro-4,5-methylenedioxcinnamic acid. This experiment was carried out under the same conditions mentioned above. 70 ml. of nitric acid and 5 gm. of 2-methyl-4-piperonylidene-5-(4H)-oxazolone, were reacted, but only the hydrolysis product could be isolated; m. p.: 228°C.

Anal. Calcd. for $C_{12}H_{10}N_2O_7$: C 48.98, H 3.43, N 9.52; found: C 49.41, H 3.51, N 9.39.

The melting point agreed with the sample obtained by hydrolysis of 2-methyl-4-(6-nitro)piperonylidene-5-(4H)-oxazolone which was obtained by ERLLENMEYER's method.

⁵⁾ J. A. McRAE and C. Y. HOPKINS, Can. J. Chem. 7, 257 (1932).

⁶⁾ A. OLIVERIA, Gazz. chim. Ital. 65, 143 (1935).

This work was supported by the NIH, Bethesda 14, Maryland, through grant RG-8797.

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Bei der Redaktion eingegangen am 6. November 1963.