Studies on Nitration of Furan Derivatives. Part II. On the Nitration of Furfurylidene-type Compounds***

By Tadashi SASAKI*

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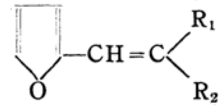
The earliest reported nitro-substituted furan compounds were obtained by the nitration of furan-carboxylic acid[1] or by that of other stable furan compounds such as the products obtained by condensation of furfural with compounds possessing reactive methylene group[2, 3, 4]. In Part I of these studies the former reaction was studied and in the present study the nitration of some furfurylidene compounds belonging to the latter reaction were studied by using two kinds of nitrating reagents, fuming nitric acid (d=1.46) and the mixture of acetic anhydride and fuming nitric acid (d=1.46). Furfurylidene compounds to be nitrated, having a general formula  (where R_1 and R_2 are both electrophilic radicals as shown in the experimental part) were prepared by the condensation of furfural with the corresponding reactive methylene compounds.

Experimental

Nitration was carried out on 13 kinds of furfurylidene compounds described below (shown in Table II) by the following two methods of nitration. In method 1, nitration was carried out at -5~-10° by using the starting material, acetic anhydride and fuming nitric acid in a ratio of 1:5.6:5.6 in mol. unit. In method 2, the starting material was added portionwise at -5° to a stirred fuming nitric acid which was thrice the amount of the starting material. In both cases, stirring was continued for one hour after the addition. When the nitration product was suspended in the reaction mixture, it was filtered. But when the nitration product was dissolved in the reaction mixture, the reaction mixture was poured on cracked ice, and the resulting oil was treated with the solvent suitable to separate the nitration product in a pure state.

(1) Nitration of Ethyl Furylacrylate.—Ethyl furylacrylate was prepared by Claisen condensation[5].

Method 1: Gilman[4] reported already on this nitration by using the starting material, nitric acid and acetic anhydride in mol. ratio of 1:3.2:5.5, yielding 51%. But the present author's experiment with the same mol. ratio resulted in only 29.5%. Furthermore, the yield of the reaction with 1:5.6:5.6 mol. ratio was 49.5%. The m.p. of the product was in good accordance with that described by Gilman, m.p. 123°[4]. In the second method decomposition occurred and the nitrated product was not obtained.

(2) Nitration of Furfurylideneacetone.—Furfurylideneacetone was prepared by the method of Organic Syntheses[6].

Method 1: When the nitration temperature was -5~-10°, no crystalline product could be isolated from the red oil which was obtained by pouring the clear red reaction mixture on cracked ice. But when nitration was carried out at -25°, a very small amount of a yellow crystalline product, m.p. 120–135°, was obtained by the addition of a very small amount of alcohol to the red oil which was obtained by pouring the reaction mixture on cracked ice. Its semicarbazone, decomposition point 224°, was identified with that prepared by another method[7].

In the second method decomposition occurred.

(3) Nitration of bis-Furfurylideneacetone.—Bis-furfurylideneacetone was prepared by the method of Organic Syntheses[6].

Method 1: 4.3 g. of bis-furfurylideneacetone, m.p. 52–4°, was dissolved in 10 cc. of acetic anhydride and this solution was nitrated at -5° by the mixture of fuming nitric acid (20g.) and acetic anhydride (30 cc.). In a while, precipitation occurred in the stirred reaction mixture. After stirring was continued for two hours, the reaction mixture was filtered off to give a crude product which was recrystallized twice from acetic acid to a yellow needle crystal, m.p. 198–200° (decomp.) with 5% yield.

Found: N, 8.98, Calcd. for $C_{13}H_8O_7N_2$: N, 9.21%.

In the second method decomposition occurred.

(4) Nitration of Furylacrolein.—Furylacrolein was prepared by König's method[8].

Method 1: When the nitration temperature was -5~-10°, the nitrated product could not be isolated. The nitration was carried out below -15° and the resulting red solution was poured on cracked ice. The red oil, separated, was dissolved in ethylacetate and the solution was left to stand in an ice box for several days to give a small amount

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* Part I, this Bulletin, **27**, 395 (1954).

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[1] H. B. Hill and Palmer, ***Am. Chem. J.***, **10**, 380 (1888); H. B. Hill and R. White, Ibid., **27**, 196 (1905).

[2] B. Priebs, *Ber.*, **18**, 1362 (1885).

[3] R. Heuck, Ibid., **28**, 2256 (1895).

[4] H. Gilman, *J. Am. Chem. Soc.*, **52**, 2550 (1930).

[5] L. Claisen, *Ber.*, **24**, 143 (1891).

[6] Org. Syn., Col. Vol. I, 301.

[7] This will be reported in Part IV of this study.

[8] W. König, *Ber.*, **58**, 2559 (1925).

of a red needle-like crystal, m.p. 112–4°, which was recrystallized from methanol to result in a brilliant red crystal, m.p. 114–5°; the yield was as low as 0.4%. This compound was identical with the specimen prepared by another method which is a more suitable preparation for this compound[9].

In the second method decomposition occurred.

(5) Nitration of Furylacrylic Acid.—Furylacrylic acid was prepared by the method of Organic Syntheses[10].

Method 1: Nitration of furylacrylic acid, F.A.A., was carried out in detail as a standard for nitration of other furfurylidene compounds. Gilman's procedure, slightly modified, was used[4]. The results by changing the ratio of F.A.A. and the nitration mixture are given in Table I, which shows that the maximum yield was obtained when F.A.A., nitric acid and acetic anhydride were in mol. ratio of 1:5.6:5.6. The yield in this mol. ratio was 48.5% at the nitration temperature of -7° and 55% at that of -15°, which seems to indicate that the yield is higher when the nitration temperature is lower. Both yields were higher than that of Gilman whose yield was 40%[4]. In this case, however, the addition of a small amount of conc. sulfuric acid made the yield less and the color of the reaction mixture more reddish. Excess of the nitration mixture decreased the yield and especially the excess of nitric acid resulted in the oxidative destruction occurring during the filtration of the nitration product. On the contrary, the yield became greater when F.A.A. was added directly to the nitrating mixture than when it was added in the form of a solution in acetic anhydride according to the procedure of Gilman[4].

In the second method decomposition occurred.

(6) Nitration of Nitrovinylfuran. Nitrovinylfuran was prepared by Thiele's method[11].

Method 1: The nitration product appeared in the form of a suspension in a red colored nitration mixture. The precipitate was filtered and washed with cold water to give a crude product, m.p. 134–9°, which was identical with that prepared by method 2.

Method 2: Priebs[2] reported on this nitration, in which the yield was not described. A dark red solution, obtained by nitration, was poured on cracked ice and the resulting brown precipitate was filtered and washed with water to give a crude product, m.p. 132–5°, which was identified by mixed melting point with the specimen of Priebs, m.p. 143°, after recrystallization from alcohol.

(7) Nitration of Ethyl Furfuralmalonate.—Ethyl furfuralmalonate was prepared by Knoevenagel's condensation[12].

Method 1: A yellow solution which was obtained by nitration, was poured on cracked ice and the resulting yellow oil gradually solidified. It was filtered to result in a crude product, m.p. 75–83°, which was recrystallized from ethanol and identified with the specimen prepared by method 2.

Method 2: Heuck[3] reported on this nitration qualitatively. The dark blue solution which resulted from the nitration was poured on cracked ice and the resulting oil gradually solidified to give a crude product, m.p. 84–89°, which was identified after recrystallization from ethanol with the specimen prepared by Heuck, m.p. 106–8°[3].

(8) Nitration of Ethyl 3-(2-furyl)-2-Acetylacrylate.—Ethyl 3-(2-furyl)-2-acetylacrylate was prepared by Claisen condensation[13].

Method 1: The reddish blue reaction mixture was poured on cracked ice and the resulting red oil was washed several times with cold water by decantation and mixed with a small amount of ethanol. A crystalline product was separated from the mixture and it was purified by recrystallization from ethanol to give a light yellow, corn-like crystal, m.p. 127–9°.

Found: N, 5.62, Calcd. for $C_{11}H_{11}O_6N$: N, 5.57.

Method 2: The reaction mixture changed to dark red. By the same procedure as method 1, a crude product was obtained. This was recrystallized from ethanol and identified by mixed melting point with the specimen prepared by method 1.

(9) Nitration of Ethyl 3-(2-furyl)-2-Cyanoacrylate. — Ethyl 3-(2-furyl)-2-cyanoacrylate was prepared by Beckert's method[14].

Method 1: The nitrated product appeared in the form of a suspension in the reaction mixture after being dissolved once completely. The precipitate was filtered to give a crude product, decomposition point 145–50°, which was identified with the specimen prepared by method 2.

Method 2: Heuck[3] reported concerning this nitration, but did not describe the yield. The nitrated product was obtained in the form of a suspension in the reaction mixture. By pouring it on cracked ice a crude product, m.p. 130–45°, was obtained which was recrystallized from ethanol to give the same m.p. 153° as described by Heuck[3]. In this case, the addition of one drop of conc. sulfuric acid to the reaction mixture was useful to prevent the mixing of a small amount of the unreacted material.

(10) Nitration of Diacetylvinylfuran.—Diacetylvinylfuran was prepared as follows: 5 g. of freshly distilled furfural, b.p.$_{19}$ 62°, and 5 g. of acetylacetone, b.p. 136–137°, were dissolved in 15 cc. of ethanol. To this solution was added 3 cc. of piperidine in pyridine solution (1%) and the resulting mixture was heated in a water bath of 70° for four hours. The solvent was removed under reduced pressure and the residual oil was extracted with ether. The ether layer was washed twice with 15 cc. of water and dried with anhydrous sodium sulfate. After removing ether, the residual dark red oil was distilled under reduced pressure. The greater part distilled at 138–140°/3 mm. Hg., amounting to 6 g., and the yield was 65%.

Found: C, 67.26; H, 5.45, Calcd. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.61%.

Method 1: When the starting material was

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9) H. Saikachi et al; *Japan J. Pharm. & Chem.*, **22**, 258 (1950); **23**, 188, 270 (1951).

10) Org. Syn. Col. Vol II, 956.

11) J. Thiele and H. Landers, *Ann.*, **269**, 303 (1909).

12) E. Knoevenagel, *Ber.*, **31**, 2595 (1895).

13) H. Claisen and F. E. Mathews, *Ann.*, **218**, 175 (1883).

14) C. Beckert, *J. prakt. Chem.*, (2), **50**, 17 (1894).

added in the form of a solution in a small amount of acetic anhydride, a clear yellow solution was obtained. After pouring the reaction mixture on cracked ice, the resulting oil was cooled by ice water to give a yellow crystal with a low melting point, 28°.

Found: N, 6.50, Calcd. for $C_{10}H_9O_5N$: N, 6.28%.

Method 2: The nitration product was obtained instantly after the addition of the starting material to stirred fuming nitric acid. After pouring the reaction mixture on cracked ice, the same procedure as that used in the above method 1 was applied for isolating the nitrated product to give a product of m.p. 28°, which was identified with the specimen of method 1.

(11) Nitration of Furfuralmalonitrile.—Furfuralmalonitrile was prepared by Heuck's method[15].

Method 1: A small amount of the nitrated product precipitated from the yellow clear solution. The reaction mixture was poured on cracked ice and the precitate was filtered to give a crude product of m.p. 173° (decomp.), which was identified with the specimen of method 2 after recrystallization from ethanol by a mixed melting point.

Method 2: Heuck[3] reported on this nitration, but did not describe the yield. A clear solution was obtained in the course of the nitration. Following the same procedure as method 1, a crude product of m.p. 173–5° was obtained, which was recrystallized from ethanol to result in raising its melting point to 179°, which was in good accordance with the description of Heuck[3].

(12) Nitration of 2-Cyano-3-(2-furyl) acrylic Acid.—2-Cyano-3-(2-furyl)acrylic acid was prepared by Heuck's method[16].

Method 1: The color of the reaction mixture changed to blue and the nitrated product precipitated gradually. After pouring the reaction mixture on cracked ice, a dark red precipitate was filtered and washed with water to give a crude product of m.p. 241–5° (decomp.), which was recrystallized from ethanol and was identical with the specimen of method 2.

Method 2: The same procedure as method 1 was applied on the dark red reaction mixture. A crude product of m.p. 246–9° (decomp.) was recrystallized from ethanol to give a compound of m.p. 250° (decomp.), the same as that of Heuck[3].

(13) Nitration of Furfuralmalonic Acid.—Furfuralmalonic acid was prepared by Knoevenagel's condensation[17]. Method 1 and 2 were applied to this compound. The evolution of carbon dioxide was observed and the nitrated product could not be isolated. This nitrated product was prepared by another method[10].

The results of the above experiments are summarized in Table II.

TABLE I

NITRATION OF FURYLACRYLIC ACID (F.A.A.)

F.A.A.	Nitration Mixture		Temp. of Nitration	Yield	(decomp. of the Product
	HNO_3	Ac_2O			
mol.	mol.	mol.	°C	%	°C
0.25	0.25	1.40	−7	10.77	228°
”	0.50	1.40	”	23.73	223°
”	0.65	1.40	”	28.02	”
”	1.00	1.40	”	32.32	”
”	1.15	1.40	”	38.88	”
”	1.40	1.40	”	43.09	”
”	1.55	1.40	”	38.88	”
0.25*	0.75	0.75	”	43.60	”
”	1.40	1.40	”	48.50	”
”	1.75	1.75	”	43.00	”
”	1.40	1.40	−15	55.00**	”
”	1.40	1.40	−15	49.00***	”

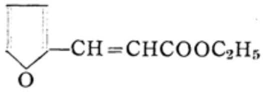
* Furylacrylic acid was added directly into the nitration mixture. In other experiments without asterisk the same acid was added in the form of a solution in acetic anhydride.

** The maximum yield ever known.

*** One drop of conc. sulfuric acid was added to the reaction mixture.

TABLE II

NITRATION OF FURFURYLIDENE COMPOUNDS

Ex. No.	Compound to be nitrated	Method 1		Method 2	
		Yield %	m.p. of the product °C	Yield %	m.p. of the product °C
(1)		49.5	123°	*	

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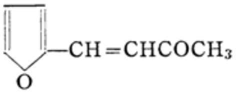
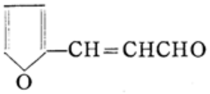
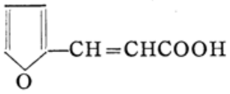
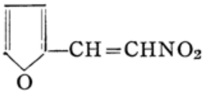
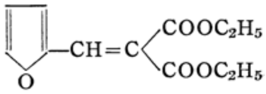
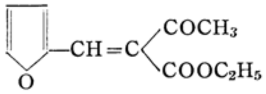
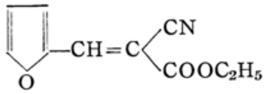
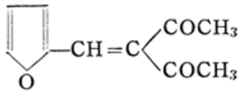
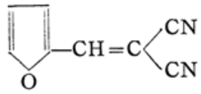
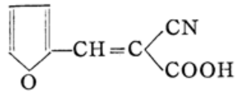
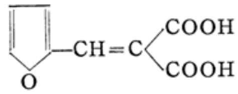
15) R. Heuck, *Ber.*, **28**, 2253 (1895).

16) R. Heuck, Ibid., **27**, 2625 (1894).

17) E. Knoevenagel, *Ber.*, **31**, 2612 (1898).

(2)		0.1	224 (dec.)**	*	
(3)		5.0	200 (dec.)	*	
(4)		0.4	114 (dec.)	*	
(5)		48.5	223 (dec.)	*	
(6)		23.0	134–9	35.8	128–32
(7)		96.5	75–83	92.5	84–89
(8)		10.3	127–9	11.8	128–9
(9)		26.8	145–50 (dec.)	61.0	130–45 (dec.)
(10)		60.0	28	20.0	28
(11)		30.0	173	52.5	173–74
(12)		35.3	241–5 (dec.)	54.9	246–49 (dec.)
(13)		*		*	

* Decomposition occurred and no crystalline product was obtained.

** The m.p. (dec.) is that of its semicarbazone of the produced nitro-furfurylideneacetone.

Summary

The nitration, by using both fuming nitric acid mixed with acetic anhydride and fuming nitric acid alone, was carried out on 13 kinds of furfurylidene compounds,

$C_4H_3O–CH=CR_1R_2$.

(1) These furfurylidene-type compounds in which R_1 and R_2 are electro-groups are stable against both acidic reagents and can be nitrated without formation of the nitration intermediate.

(2) In the case of a group being –CHO or $–COCH_3$, the nitration temperature must be

kept low enough to avoid decomposition.

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Institute of Scientific Research for
Practical Life, Medical Faculty of
Kyoto University, Kyoto