Furan derivatives. IC. Role of acetic anhydride in nitration of 3-(2-furyl)acrylic acid

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An exothermic reaction, leading to 3-(2-furyl)acrylic anhydride and a little amount of furfurylideneacetone is taking place when reacting 3-(2-furyl)acrylic acid in acetic anhydride above 120°C. The 3-(5-acetyl-2-furyl)acrylic acid was formed under the afore-mentioned conditions only in the presence of H_3PO_4. The 3-(2-furyl)acrylic anhydride is more stable towards HNO_3 at temperatures under −5°C than the free acid and therefore, it was possible to nitrate it in acetic anhydride to 3-(5-nitro-2-furyl)acrylic acid with an HNO_3—CH_3COOH mixture, which means a simplification of the nitration process.

При нагревании 3-(2-фурил)акриловой кислоты в уксусном ангидриде проходила при температурах выше 120°C экзотермическая реакция, при которой образовался ангидрид 3-(2-фурил)акриловой кислоты и небольшое количество фурфурилиденацетона. 3-(5-Ацетил-2-фурил)акриловая кислота образовалась в этих условиях только в присутствии H_3PO_4. Ангидрид 3-(2-фурил)акриловой кислоты при температурах под −5°C более устойчивый по отношению к HNO_3 чем свободная кислота, что позволило его нитрование в ацетангидридном растворе на 3-(5-нитро-2-фурил)акрыловую кислоту смесью HNO_3 и CH_3COOH и упростило нитрационный способ.

Papers dealing with nitration of 3-(2-furyl)acrylic acid (*I*) with a mixture of acetic anhydride and nitric acid in relation to the molar ratio of reacting components and reaction conditions have reported yields of crude 3-(5-nitro-2-furyl)acrylic acid (*II*), contamined with a considerable amount of side products, up to 75% [1—12].

We ascertained that nitration proceeds through an unidentified nitration intermediate decomposing with water to product *II* [13]. So far, we investigated the influence of both HNO_3 concentration [12] and nitrogen oxides formed in the reaction mixture [14] on the reaction course. This paper aimed to examine the role of acetic anhydride in the total nitration process of *I*. To obtain yields above 70% of crude *II* with fuming HNO_3 it was necessary to use a considerable excess of

acetic anhydride. According to the nitration mode the general molar ratio of *I*:HNO_3:acetic anhydride varies from 1:4:7 to 1:6:10.

Provided, on the basis of hitherto known facts concerning the reaction of acetic anhydride with HNO_3, the main process at −25 to −5°C is the reaction

$$(CH_3CO)_2O + HNO_3 \rightleftarrows CH_3COONO_2 + CH_3COOH$$

then an equivalent amount of acetic acid corresponding to the consumed HNO_3 is formed in the nitration mixture.

Kinetic data of this reaction show the almost quantitative reaction between HNO_3 and acetic anhydride during 60 min [15] and the nitration mixture prepared from equivalent amounts of these components is thus acetyl nitrate in acetic acid. It is assumed [16] that acetyl nitrate undergoes protonization in the presence of acid catalysts (H_2SO_4, H_3PO_4, P_4O_{10}) and is, therefore, a more efficient nitration reagent than its nonprotonized form.

The situation is, of course, more complex, and as evidenced, acetyl nitrate is further decomposed into N_2O_4 and N_2O_5 [17] which could be the source of side reactions.

Another equivalent of acetic acid is generated from acetyl nitrate upon reaction with *I* and therefore, the minimal amount of acetic anhydride needed for a successful nitration and also the inhibition of acetic acid on the nitration of *I* have been examined.

The most convenient model reaction chosen was the so-called two-step nitration of *I* for which a solution of *I* in the solvent and the nitration mixture prepared separately were allowed to react at −5 to −15°C. The amount of acetic anhydride varied whilst those of *I* and HNO_3 were constant, so that the ratios of acetic anhydride:HNO_3 were 2:1, 1:1, and 1:2, *i.e.* the nitration of *I* proceeded with an excess of acetic anhydride or free HNO_3 in the nitration mixture. The decreasing amount of acetic anhydride was substituted by acetic acid. The nitration still proceeded at a molar ratio *I*:HNO_3:acetic anhydride 1:4:2 (44% yield) in the presence of 12 moles of acetic acid. Substitution of acetic anhydride by acetic acid under the condition of this experiment resulted in no reaction. Acetic acid inhibited, however, oxidation and the unreacted *I* has recovered in 87%. Catalyst of this reaction was H_3PO_4 (5% w/w).

Acetic anhydride and acetic acid were employed for dissolution of *I* and for preparation of nitration mixture. Yields of this nitration are listed in Table 1.

The dissolution of *I* in acetic anhydride at 120—140°C was accompanied with a strong exothermic reaction resulting in the formation of anhydride of *I* [18]. Besides this, *I* could be acylated in the furan ring and in the side ring and therefore, experiments aiming to obtain the latter products were made: the compound obtained after the exothermic reaction was hydrolyzed both in acid and alkaline medium, acids were removed from the solution from which 4-(2-fu-

Table 1

Preparation of 3-(5-nitro-2-furyl)acrylic acid by a two-step nitration of 3-(2-furyl)acrylic acid (0.5 mole) catalyzed by H_3PO_4 (5% w/w)

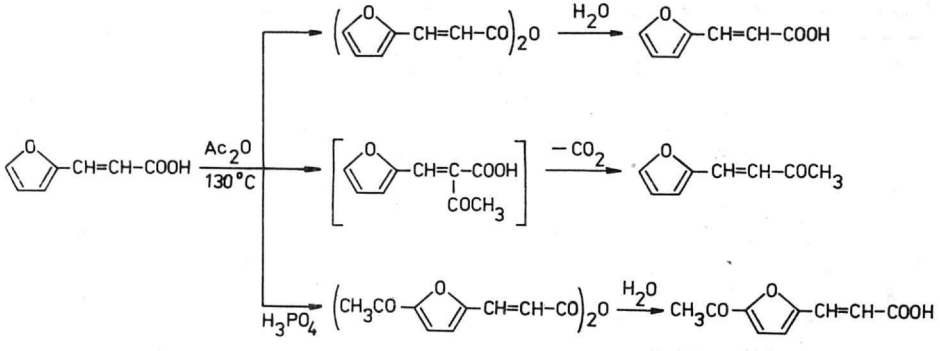
Experiment	Nitration mixture moles $HNO_3 : Ac_2O : AcOH$	Solution of *I* moles *I* : Ac_2O : AcOH	Yield %	
			crude	pure
1	4 : 5 : 0	1 : 3 : 0	73.2	61.7
2	4 : 4 : 0	1 : 0 : 8[b]	52.4	49.7
3	4 : 3 : 0	1 : 5 : 0	76.5	66.3
4	4 : 2 : 4	1 : 2 : 4	57.9	50.2
5	4 : 1 : 8[a]	1 : 3 : 0	69.4	56.4
6	4 : 0 : 8[a]	1 : 0 : 8[b]	—	—
7	4 : 0 : 8[a]	1 : 1 : 6[b]	30.6	2.3
8	4 : 0 : 8	1 : 2 : 4	44.2	28.9
9	4 : 0 : 8[a]	1 : 3 : 2	64.5	52.1
10	4 : 0 : 8	1 : 4 : 0	71.6	60.1
11	4 : 0 : 10[a]	1 : 3 : 0	67.7	55.2

a) The content of the flask becomes solid at 0°C and therefore about 1/3 of HNO_3 was added before cooling at −20°C.

b) The solution of *I* partly crystallizes in he dropping funnel and herefore a part of *I* comes in the nitration mixture as solid.

ryl)-3-(buten-2-one)furfurylideneacetone was obtained as a result of acetylation and decarboxylation of *I* (Scheme 1).

It has been found [19] that acetylation of the furan ring in the presence of strong acids (H_2SO_4, $HClO_4$) takes place already at room temperature. The possibility to run this reaction with H_3PO_4 was also investigated. At temperatures around 0°C



Scheme 1

(H_3PO_4 catalyst) no 3-(5-acetyl-2-furyl)acrylic acid was observed to be formed, whereas above 100°C the acetylation of the ring took place. The acetylation of *I* proceeded in very good yields when H_3PO_4 (50% w/w on *I*) was used. The addition of H_3PO_4 to the reaction mixture and maintaining the temperature below 0°C lowered at minimum the possibility of this reaction to occur.

The mixture obtained upon dissolution of *I* in acetic anhydride at elevated temperature contained *I*, anhydride of *I*, and a small amount of furfurylideneacetone; the dissolution in acetic acid remained *I* unchanged. Tables 1 and 2 show that *I* is more sensitive to the presence of free HNO_3 than its anhydride and affords more side products when nitrated. On the other hand, the anhydride *I* endures the contact with free HNO_3 in the nitration mixture at low temperatures and its nitration gives good yields.

The findings were utilized in the nitration of the anhydride *I*. At a molar ratio *I* : HNO_3 : acetic anhydride 0.5 : 6 : 10 (Table 2) the influence of temperature on the formation of a maximum amount of *II* was studied and nitrations also at other molar ratios were tried at −15 to −5°C. Almost 90% yields of *II* were achieved at a molar ratio 0.5 : 3 : 7.

Lower sensitivity of the anhydride *I* towards free HNO_3 was utilized in the one-step nitration: the anhydride *I* was dissolved in acetic anhydride at room temperature, cooled to −15°C at which temperature fuming HNO_3 was added. Yields (Table 3) were found to be a little less than from the two-step process. Five-fold excess of HNO_3 markedly lowers the yields in this case when compared

Table 2

Preparation of 3-(5-nitro-2-furyl)acrylic acid by a two-step nitration of 3-(2-furyl)acrylic anhydride (0.05 mole)

Experiment	Reaction mixture moles *IA* : HNO_3 : Ac_2O[a]	Nitration interval °C	Catalyst	Yield %
1	0.5 : 6 : 10	−25 to −15	—	77.1
2	0.5 : 8 : 10	−15 to − 5	—	83.1
3	0.5 : 6 : 10	−15 to − 5	—	54.6[b]
4	0.5 : 6 : 10	− 5 to + 5	—	71.0
5	0.5 : 3 : 7	−15 to − 5	—	89.1
6	0.5 : 3 : 5	— —	—	84.2
7	0.5 : 3 : 5	— —	H_2SO_4 (1% w/w)	86.3
8	0.5 : 2 : 5	— —	—	82.5

a) 3-(2-Furyl)acrylic anhydride was dissolved in acetic anhydride (41 g) in all cases.

b) Product *I* was isolated from the nitration mixture by pouring it into ethanol cooled at −20°C.

Table 3

Preparation of 3-(5-nitro-2-furyl)acrylic acid by a one-step nitration of 3-(2-furyl)acrylic anhydride (0.05 mole) at −5 to −15°C

Experiment	Reaction mixture moles *IA* : HNO_3 : Ac_2O	Yield %
1	0.5 : 6 : 10	76.5
2	0.5 : 6 : 6	71.0
3	0.5 : 4 : 4	83.6
4	0.5 : 3 : 3	82.5
5	0.5 : 3 : 2	74.9

with the first procedure. Lower yields were obtained upon nitration with two moles of acetic anhydride; this reaction proceeds partly in a heterogeneous phase.

The results presented enabled a modification of the one-step nitration of *I*: in the first step the anhydride *I*, prepared from *I* and acetic anhydride at elevated temperature, was cooled at working temperature and nitrated with fuming nitric acid. In this procedure the amount of acetic acid in reaction mixture is limited by the solidification of acetic acid at lower temperatures.

This modification of the one-step nitration of *I* gave a little lower yields of *II* than those obtained in the two-step nitration, the advantage being the simplification of the process (Table 4).

Yields of the raw products obtained in the two-step nitration were evaluated in a usual manner as in other papers. Since the obtained products evidently differed from each other and the quantitative analytical determination of *II* in the mixture was so far unsuccessful, the amount of the main product *II* was estimated by

Table 4

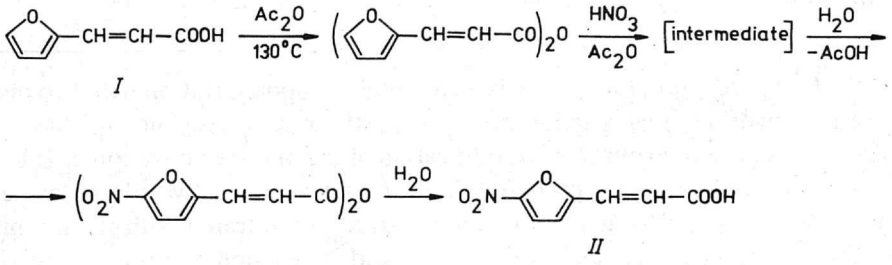
Preparation of 3-(5-nitro-2-furyl)acrylic acid by a one-step nitration of 3-(2-furyl)acrylic acid (1 mole) catalyzed by H_3PO_4 (5% w/w) at −5 to −15°C

Experiment	Reaction mixture moles *I* : HNO_3 : Ac_2O : AcOH	Yield %
1	1 : 5 : 7 : 0	65.6
2	1 : 4 : 6 : 0	68.8
3	1 : 4 : 5 : 0	69.1
4	1 : 3 : 4 : 0	64.8
5	1 : 4 : 4 : 2	67.2
6	1 : 4 : 3 : 4	67.2
7	1 : 4 : 2 : 6	47.8

crystallization of the raw product from ethanol under standard conditions (the 24 h-crystallization of *II* at 20°C from a boiling saturated ethanolic solution).

The mixture of *I* dispersed in acetic anhydride at room temperature gave upon nitration low yields only (*ca* 30%). The increased amount of acetic anhydride needed for total dissolution of *I* at room temperature resulted in yields of *II* under the level of those obtained from dissolution of *I* in a less amount of acetic anhydride at elevated temperature (40%).

Basing upon observations with nitration of *I* and experience reported in [13] one is entitled to presume the reaction sequence seen in Scheme 2



Scheme 2

In the two-step nitration acetic acid is employed to dissolve *I* and the nitration mixture consists of equimolar amounts of acetic anhydride and HNO_3. Is the amount of acetic anhydride less, then yields of *II* decrease and the amount of side products increases. If minimum three equivalents of acetic anhydride are used for dissolution of *I* at elevated temperature then the nitration takes place with HNO_3 in acetic acid with a strong mineral acid as catalyst. The decrease of the amount of acetic anhydride for dissolution of *I* under three moles per one mole of *I* resulted in an increased occurrence of side products.

As it follows from findings presented the successful nitration of *I* involves the use of acetyl nitrate; the nitration of anhydride of *I* is also possible with a mixture of HNO_3 and CH_3COOH, this constituting a new approach to the preparation of *II*. The optimum results of the just reported two-step nitration were obtained using a molar ratio acetic anhydride : acetic acid 1 : 1, when acetic anhydride was the solvent for *I* and acetic acid was used for preparation of nitration mixture.

Experimental

Melting points were determined on a Kofler micro hot-stage. The i.r. spectra of 10^{-2} M solutions in $CHCl_3$ or CCl_4 were measured with a UR-20 spectrophotometer (Zeiss, Jena) calibrated against a polystyrene foil, in 1.02 mm cells.

3-(2-Furyl)acrylic acid twice crystallized from water, dried in a vacuum drier at 100°C for 6 h had m.p. 142°C. 3-(2-Furyl)acrylic anhydride prepared according to [18] crystallized from benzene had m.p. 76.5°C. Acetic anhydride, acetic acid, HNO_3 (s.g. = 1.52), and H_3PO_4 were of anal. grade. Furfurylideneacetone prepared according to [20] had m.p. 39—40°C.

Action of acetic anhydride on 3-(2-furyl)acrylic acid at elevated temperature

Method A

The 3-(2-furyl)acrylic acid (138 g; 1 mole) and acetic anhydride (306 g; 3 moles) in a 500 ml distillation flask provided with a descending water-cooled condenser were heated at 130°C. The strongly exothermic reaction, lasting 10 min, was accompanied with distillation of acetic acid (42 ml). The solution, obtained after this spontaneous reaction, was evaporated on a vacuum rotary evaporator and the solid residue extracted with water-free hot benzene (3 × 100 ml), to which charcoal was added, filtered, and allowed to crystallize. The crude 3-(2-furyl)acrylic anhydride (108 g), m.p. 73—75°C, crystallized from CCl_4 had m.p. 76.5°C.

Method B

The components were allowed to react as before, the hot solution of 3-(2-furyl)acrylic anhydride was poured into water (250 ml) and boiled for 1 h in a flask provided with a reflux condenser. After hydrolysis the solution was heated with charcoal, filtered through a heated filter funnel and the filtrate was allowed to cool spontaneously. The separated 3-(2-furyl)acrylic acid was filtered off at 40°C, the filtrate neutralized with Na_2CO_3 and cooled. The solution exhibiting a positive ketone test, was extracted with ether (3 × 100 ml), acidified with conc HCl, and the separated 3-(2-furyl)acrylic acid was filtered off with suction. The ethereal extracts were evaporated under diminished pressure and the obtained viscous liquid was subjected to a vacuum distillation; the fraction collected at 120—126°C/1.6 kPa was identified as furfurylideneacetone. Yield 2.1 g (1.5%). The solution of 3-(2-furyl)acrylic acid was ketone-free.

Method *C*

A mixture of 3-(2-furyl)acrylic acid (69 g; 0.5 mole), H_3PO_4 (35 g), and acetic anhydride (250 g) heated under a reflux condenser for 30 min, was poured into Na_2CO_3 solution (500 ml) and heated for 1 h. Charcoal added to the solution was filtered off, the filtrate was acidified with HCl, and the separated yellow-brown 3-(5-acetyl-2-furyl)acrylic acid (63 g; 66.3%), m.p. 178—190°C, was crystallized from ethanol to give white crystalline product, m.p. 192°C.

Nitration of 3-(2-furyl)acrylic acid

Two-step procedure

The 3-(2-furyl)acrylic acid (69 g; 0.5 mole) and acetic anhydride (204 g; 2 moles) were heated at 130°C; after the exothermic reaction was through the solution was cooled to room temperature. Nitric acid (126 g; 2 moles) was gradually added to acetic acid (240 g; 4 moles) in a cooled three-necked flask provided with a stirrer, dropping funnel, and thermometer at a temperature allowing still a vigorous stirring and not exceeding −15°C. The nitration mixture was stirred for additional 1 h and then H_3PO_4 (3.5 g) and dropwise the solution of 3-(2-furyl)acrylic acid in acetic anhydride were added at −15 to −5°C. The mixture was stirred for 1 h, slowly poured onto crushed ice (1 kg) and stirring was continued till the orange-red oily substance was fully decomposed. The temperature of water during decomposition was kept at 0°C by addition of ice. The aqueous solution was allowed to stand overnight, the yellow precipitated solid was filtered by suction, washed with water, air- and vacuum-dried at 80°C for 6 h. Yield of crude 3-(5-nitro-2-furyl)acrylic acid was 65.5 g (71.6%), m.p. 238—239°C. Crystallization from ethanol afforded 55 g (60.1%) of pure acid, m.p. 240—241°C.

The original process was kept constant, the molar ratio varied; when a mixture of solvents was used 3-(2-furyl)acrylic acid was dissolved in acetic anhydride and boiling acetic acid was added to this solution. Results are listed in Table 1.

One-step procedure

3-(2-Furyl)acrylic acid (138 g; 1 mole) and acetic anhydride (408 g; 4 moles) were heated at 130°C and, after the exothermic reaction, acetic acid (120 g; 2 moles) was added; the mixture was cooled to −15°C, conc H_3PO_4 (7 g) was added and HNO_3 (252 g; 4 moles) dropped under vigorous stirring so that the temperature did not exceed −5°C. Stirring at −15°C was then continued for 1 h, the mixture was poured onto crushed ice (2 kg) and the decomposition and isolation of the main product was proceeded as before. Yield of 3-(5-nitro-2-furyl)acrylic acid was 123 g (67.2%), m.p. 238—239°C. This procedure was used also with other molar ratios. Results are listed in Table 4.

Nitration of 3-(2-furyl)acrylic anhydride

Two-step procedure

3-(2-Furyl)acrylic anhydride (12.9 g; 0.05 mole) was dissolved in acetic anhydride (41 g; 0.4 mole) at room temperature and this solution was dropwise added into a nitration mixture, prepared in a usual way from HNO_3 (19 g; 0.3 mole) and acetic anhydride (30 g; 0.3 mole) at −15 to −5°C. Stirring was continued at −15°C for 1 h and then the mixture was poured onto scrushed ice (200 g) and stirred for 2 h. The aqueous solution was allowed to stand at room temperature for 24 h, the precipitated yellow solid was vacuum filtered, washed with water and diethyl ether on the filter and dried. Yield of 3-(5-nitro-2-furyl)-acrylic acid was 16.3 g (89.1%), m.p. 238—240°C.

This procedure was constant in all experiments where the molar ratios were varied; results are given in Table 2. To estimate the amount of 3-(5-nitro-2-furyl)acrylic acid separated directly in the nitration mixture, one nitration mixture was poured into ethanol (200 ml) cooled at −20°C and the separated yellow product was suction-filtered and washed with cooled ethanol on the filter (*cf.* Table 2, experiment *3*).

One-step procedure

3-(2-Furyl)acrylic anhydride (12.9 g; 0.05 mole) was dissolved in acetic anhydride (41 g; 0.4 mole) and HNO_3 (25 g; 0.4 mole) was added at −15 to −5°C. The reaction mixture was then stirred for 1 h and the solid was isolated as before. Yield of 3-(5-nitro-2-furyl)-acrylic acid was 15.3 g (83.6%), m.p. 237—239°C.

Results obtained with varying molar ratios of constituents under constant procedure are listed in Table 3.

References

1. Gilman, H. and Wright, G. F., *J. Amer. Chem. Soc.* ***52,*** 4165 (1930).
2. Inoue, H. and Ueno, R., *Japan* 4371 (1951); *Chem. Abstr.* ***47,*** 12757 (1953).
3. Saikachi, H., Kimura, R., and Hoshida, H., *Yakugaku Zasshi* ***73,*** 1132 (1953); *Chem. Abstr.* ***48,*** 12072*f* (1954).
4. Sasaki, T., *Bull. Chem. Soc. Jap.* ***27,*** 398 (1954).
5. Kováč, J., *Thesis.* Slovak Technical University, Bratislava, 1956.
6. Arata, Y., Oohashi, T., Aoki, M., and Sakai, K., *Yakugaku Zasshi* ***76,*** 211 (1956); *Chem. Abstr.* ***50,*** 1469*h* (1956).
7. Kováč, J., *Zborník prác Chemickotechnologickej fakulty SVŠT.* (Collection of Communications, Section Chemistry, Slovak Technical University.) P. 309, Bratislava, 1960.
8. Venters, K., Hillers, S., and Cirule, V., *Latv. PSR Zinat. Akad. Vestis* ***1962,*** 131.
9. Inoue, H. and Ueno, R., *Japan* 10688 (1962); *Chem. Abstr.* ***59,*** 3895*g* (1963).
10. Ueno, R., *US* 3013023 (1962); *Chem. Abstr.* ***57,*** 784*g* (1961).
11. Venters, K., Hillers, S., and Cirule, V., *Metody Poluch. Khim. Reaktivov Prep.* ***14,*** 80 (1966).
12. Kováč, J., Komanová, E., and Považanec, F., *Chem. Zvesti* ***25,*** 63 (1971).
13. Kováč, J., Frimm, R., and Jurášek, A., *Zborník prác Chemickotechnologickej fakulty SVŠT.* (Collection of Communications, Section Chemistry, Slovak Technical University.) P. 65, Bratislava, 1969—1970.
14. Kováč, J., *Zborník prác Chemickotechnologickej fakulty SVŠT.* (Collection of Communications, Section Chemistry, Slovak Technical University.) P. 45, Bratislava, 1971.
15. Mantsch, O., Bodor, N., and Hodorsan, F., *Rev. Chim.* (Bucharest) ***13,*** 1435 (1968).
16. Venters, K. and Hillers, S., *Nitrocompounds,* p. 71. Wydawnictwo Naukowo-Techniczne, Warszawa, 1963.
17. Bordwell, F. G. and Garbisch, E. W., Jr., *J. Org. Chem.* ***28,*** 1765 (1963).
18. Ikeda, M., *Yakugaku Zasshi* ***75,*** 60 (1955); *Chem. Abstr.* ***50,*** 929*c* (1956).
19. Dorofeenko, G. N., Karbon, V. Y., Dulenko, L. V., and Novikov, V. N., *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.* ***1964,*** 432.
20. Ponomarev, A. A., *Sintezy i reaktsii furanovykh veshchestv,* p. 55. Izd. Saratov. Univ., Saratov, 1960.

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