The Potassium Fluoride-Catalyzed Michael Addition of Nitroalkanes

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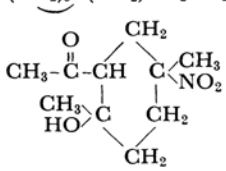
The recent publication by Kambe and Yasuda[1] on the potassium fluoride-catalyzed Michael reaction of nitroalkanes prompts us to report our results with this catalyst used routinely in similar reactions for the preparation of synthetic intermediates.

In addition to acrylonitrile and the various unsaturated esters reported by Kambe and Yasuda, we have found that potassium fluoride efficiently condenses acrylamide with nitroalkanes in an absolute ethanol solvent. It was previously observed[2] that phenylnitromethane reacted with only one mole of acrylamide using an aqueous potassium hydroxide catalyst or a Triton B catalyst; however, when the potassium fluoride catalyst was employed, moderate yields (45—50%) of the bis adduct could be obtained. The potassium fluoride catalyst usually gives better yields, simpler reaction conditions, and easier workup than potassium hydroxide[2] or liquid ammonia at room temperature.[3]

It was found that 0.25 to 1.0 molar equivalents

Table 1. Michael reaction of nitroalkanes with potassium fluoride catalyst

RNO_2 R	CH_2=CH-X X	Mole ratio RNO_2 : CH=CH-X	Product	Yield %	Mp or Bp °C
Methyl	$CONH_2$	1 : 2	$O_2NC(CH_2CH_2CONH_2)_3$	30	170—171[a,b]
Ethyl	$CONH_2$	1 : 2	$CH_3C(NO_2)(CH_2CH_2CONH_2)_2$	46	129—130[b,c]
Isopropyl	$CONH_2$	1 : 1	$(CH_3)_2C(NO_2)CH_2CH_2CONH_2$	75	77— 80[b,f]
Cyclohexyl	$CONH_2$	1 : 1	$(CH_2)_5C(NO_2)CH_2CH_2CONH_2$	50	67— 68[b,d]
Benzyl	$CONH_2$	1 : 2	$C_6H_5C(NO_2)(CH_2CH_2CONH_2)_2$	45	147—148[b,e]
Methyl	CN	1 : 3	$O_2NC(CH_2CH_2CN)_3$	69	112—113[g,h]
Ethyl	CN	1 : 2	$CH_3C(NO_2)(CH_2CH_2CN)_2$	64	203—206(0.8 mmHg)[i]
Propyl	CN	1 : 2	$C_2H_5C(NO_2)(CH_2CH_2CN)_2$	50	[j]
Benzyl	CN	1 : 2	$C_6H_5C(NO_2)(CH_2CH_2CN)_2$	67	99—100[g,k]
Cyclohexyl	CN	1 : 1	$(CH_2)_5C(NO_2)CH_2CH_2CN$	61	130—135(0.8 mmHg)[l]
Ethyl	$COCH_3$	1 : 2		64	72— 73[m,n]

a) J. M. Patterson, Ph. D. dissertation, Northwestern Univ., 1953 reports 168—169°C.
b) Recrystallized from water.
c) Ref. 3, mp 129.5—131°C.
d) Found: C, 53.89; H, 7.92; N, 14.08%. Calcd for $C_9H_{16}N_2O_3$: C, 53.99; H, 8.06; N, 13.99%.
e) Found: C, 56.15; H, 6.18; N, 14.79%. Calcd for $C_{13}H_{17}N_3O_4$: C, 55.90; H, 6.13; N, 15.05%.
f) Ref. 3, mp 77—81°C,
g) Recrystallized from absolute methanol.
h) Ref. 3, mp 112.5—114°C.
i) Ref. 3, bp 210—212°C/1 mmHg.
j) Yield based on amount of corresponding 1,7-heptanedioic acid obtained on hydrolysis of the crude dinitrile. *Cf.* Ref. 2.
k) Ref. 2, mp 99—100°C.
l) Lit. bp 98—108°C/0.15 mmHg: G. Buckley, F. Hunt, T. Elliott and A. Lowe, *J. Chem. Soc.*, **1947**, 1505.
m) Ref. 5, mp 77—79°C.
n) Recrystallized from hexane.

1) S. Kambe and H. Yasuda, This Bulletin, **39**, 2549 (1966).
2) J. M. Patterson, M. W. Barnes and R. L. Johnson, *J. Org. Chem.*, **31**, 3103 (1966).
3) S. Wakamatsu and K. Shimo, *ibid.*, **27**, 1069 (1962).

of potassium fluoride slightly increased the yield of the condensation product of acrylamide with 2-nitropropane. The following yields were obtained from 0.2 mol of each of the reactants on heating in 150 m*l* of ethanol for 96 hr.

Mole equivalents KF	Yield, %
0.25	58
0.50	63
1.00	69

While Kambe and Yasuda reported that nitroethane and 1-nitropropane reacted with only one mole of acrylonitrile using the potassium fluoride catalyst even in the presence of an excess of acrylonitrile, we have found that nitroethane and 1-nitropropane condense smoothly under these conditions with two moles of acrylonitrile when a 1 : 2 molar ratio of these compounds is used. Using this catalyst, phenylnitromethane also reacts with acrylonitrile to give an improved yield of the bis adduct over those methods reported previously.[2,4]

The reaction of nitroethane with methyl vinyl ketone was briefly examined with the hope of obtaining the disubstituted product. The product obtained, however, was the substituted nitrocyclohexane reported by Feuer and Harmetz[5] which arises from an intramolecular aldol condensation of the adduct resulting from the reaction of two moles of the ketone with nitroethane.

The results are tabulated in Table 1.

Experimental

Melting points were taken on a Fisher-Johns melting point block and are uncorrected. Boiling points are uncorrected.

The nitroalkanes (excepting phenylnitromethane), acrylonitrile, acrylamide, and potassium fluoride, are commercial samples and were used as received. Phenylnitromethane was synthesized by the method previously reported.[6]

The following experiments are representative of those used to produce the compounds listed in Table 1.

4-Nitro-4-methyl-1, 7-heptanedinitrile. A mixture of 7.5 g (0.1 mol) nitroethane, 10.6 g (0.2 mol) acrylonitrile and 5 g potassium fluoride in 75 m*l* of absolute ethanol was stirred for 24 hr at 40—50°C. The reaction mixture, which initially was green, became orange at the completion of the reaction. The solution was filtered, the filtrate added to ice water and the resulting mixture extracted with 100 m*l* of chloroform. After drying and removal of the solvent, the residue was distilled under nitrogen *in vacuo* to give 12.2 g of product, bp 203—206°C/0.8 mmHg. The product was further identified by hydrolysis with 18% hydrochloric acid to the corresponding 1, 7-heptanedioic acid, mp 111—112°C (lit[2] mp 113—114°C).

4-Nitro-4-phenyl-1, 7-heptanediamide. A mixture of 110 g (0.82 mol) phenylnitromethane, 115 g (1.62 mol) acrylamide and 25 g (0.42 mol) anhydrous potassium fluoride in 400 m*l* of absolute ethanol was stirred for five days at 65—70°C. The dark reaction mixture was filtered, the filtrate evaporated on a rotary evaporator to remove solvent and the residual dark green gum treated with 300 m*l* of water.[7] The crystalline mixture thus obtained was separated by filtration and the crystals treated with 100 m*l* of hot water, whereupon the insoluble material became gummy. The aqueous layer, after decantation and partial cooling, deposited a brown oil which was added to the gummy residue. Further cooling of the aqueous layer produced the product as tan crystals. The treatment with water of the combined oil and gummy residue was repeated until crystalline material was no longer obtained.

4) G. S. Misra and R. S. Asthana, *Ann.*, **609**, 240 (1957).

5) H. Feuer and R. Harmetz, *J. Org. Chem.*, **26**, 1061 (1961).

6) A. P. Black and F. H. Babers, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y. (1943), p. 512.

7) Adducts from other nitroalkanes and acrylamide were recrystallized from water to give pure products at this point.