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Potassium Fluoride on Alumina. An Efficient Solid Base for Elimination, Addition, and Condensation

Junko YAMAWAKI, Takehiko KAWATE, Takashi ANDO,* and Terukiyo HANAFUSA
The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki, Osaka 567

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Synopsis. Alumina coated with potassium fluoride proved to be a versatile solid base for olefin- and acetylene-forming elimination, the Michael addition, aldol condensation, and the Darzens condensation.

The utility of fluoride salts as potential bases in a variety of synthetic reactions has been recognized in recent years.[1,2] However, low solubilities of fluoride salts in ordinary solvents hamper their wide applications in organic synthesis. On the other hand, there has been increasing use of inorganic solid supports as reagents or reaction media in recent years.[3,4] In our previous papers,[5–7] we reported that alumina coated with potassium fluoride (KF-alumina) is a versatile solid-supported reagent for promoting *C*-, *N*-, *O*-, and *S*-alkylations with alkyl halides. In the present paper, we describe the application of KF-alumina as a solid base for elimination, addition, and condensation.

β-Elimination reaction of alkyl bromides was carried out with KF-alumina (*ca.* 2.5 equiv. KF) in acetonitrile or diglyme with stirring at room temperature or with heating below 100 °C. Typical examples are summarized in Table 1. Elimination of phenethyl, 2-phenoxyethyl, and secondary alkyl bromides proceeded smoothly to give the corresponding olefins. For example, an 86% yield of styrene was obtained from phenethyl bromide at room temperature after 24 h; the elimination did not proceed when KF powder or alumina was used separately. These results show the high reactivity of KF-alumina for β-elimination. When a simple primary alkyl bromide was used as a substrate, hydrolysis became the main reaction in preference to elimination to form substantial amounts of an alcohol and an ether together with an olefin.

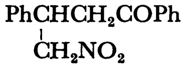
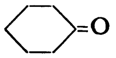
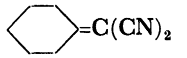
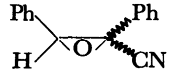
KF-Alumina was also applicable to the synthesis of acetylenes. Phenylacetylene and diphenylacetylene were obtained in good yields from the corresponding vicinal bromides under milder reaction conditions than those of

TABLE 1. β-ELIMINATION WITH KF-ALUMINA[a)]

Substrate	Solvent	T/°C	Time/h	Product	Yield/%[b)]
$PhCH_2CH_2Br$	CH_3CN	25	24	$PhCH{=}CH_2$	86
$PhCH_2CH_2Br$	—[c)]	25	20	$PhCH{=}CH_2$	75[d)]
$PhOCH_2CH_2Br$	Tetraglyme	45	45	$PhOCH{=}CH_2$	73[d)]
$CH_3(CH_2)_6CH_2Br$	Diglyme	100	24	$C_6H_{13}CH{=}CH_2$	14[e)]
$CH_3(CH_2)_5CHBrCH_3$	Diglyme	100	15	$C_6H_{13}CH{=}CH_2$	36[f)]
				trans-$C_5H_{11}CH{=}CHCH_3$	29
				cis-$C_5H_{11}CH{=}CHCH_3$	13
Cyclohexyl bromide	Diglyme	100	15	Cyclohexene	88
$PhCHBrCH_2Br$	CH_3CN	25	27	$PhC(Br){=}CH_2$	80
$PhCHBrCH_2Br$	Penta ether[g)]	100	6	$PhC{\equiv}CH$	70[d)]
trans-$PhCH{=}CHBr$	Diglyme	100	24	$PhC{\equiv}CH$	70
meso-$PhCHBrCHBrPh$	Diglyme	100	3	$PhC{\equiv}CPh$	74
meso-$PhCHBrCHBrPh$	DME	85	48	$PhC{\equiv}CPh$	89[d)]

a) KF-Alumina containing *ca.* 2.5 equiv. KF was used. b) Unless otherwise mentioned, yields were determined by GLPC using internal standards. c) Without solvent. d) Isolated yields after purification. e) Starting material (8%), 1-octanol (34%), and dioctyl ether (25%) were obtained. f) Starting material (10%) was also detected. g) Tetraethylene glycol dibutyl ether.

TABLE 2. ADDITION AND CONDENSATION WITH KF-ALUMINA[a)]

Run	Starting materials		Solvent	Time/h	Product	Yield/%[b)]
	A	B				
1	$PhCH{=}CHCOPh$	CH_3NO_2	CH_3CN	3.5	 $PhCH(CH_2NO_2)CH_2COPh$	74
2	PhCHO	$CH_2(CN)_2$	CH_3CN	3	$PhCH{=}C(CN)_2$	86
3	PhCHO	$PhCH_2CN$	DME	21	$PhCH{=}C(CN)Ph$	82
4		$CH_2(CN)_2$	DME	15		55
5	PhCHO	PhCHClCN	Benzene	4		82[c)]

a) At room temperature. Molar ratio of A:B:KF-alumina was 1:20:0.2 for run 1, 1:1:0.25 for run 2 and 4, 1:1:0.5 for run 3, and 1 : 1 : 5 for run 5. b) Unless otherwise mentioned, isolated yields after purification are shown. c) Yield determined by ^{1}H-NMR using an internal standard. The ratio of *cis* to *trans* was 56 : 44. When 1,2-dimethoxyethane was used as solvent, the ratio decreased to 28 : 72, while the addition of 0.5 and 1.0 equiv. water to KF in benzene increased the ratio to 61 : 39 and 71 : 29, respectively.

conventional methods using strong bases (Table 1). Interestingly, in the elimination of *meso*-stilbene dibromide there was difference in composition of products by the solvent used. After 44 h at 50 °C in 1,2-dimethoxyethane diphenylacetylene and (*E*)-*α*-bromostilbene were formed in 24 and 66% yields, respectively. On the other hand, the reaction in acetonitrile gave a 30% yield of *trans*-stilbene, the debromination product, in addition to the above two products in 52 and 12% yields, respectively. This is the first observation of debromination by KF, although the debromination by NaI or LiBr in *N,N*-dimethylformamide has been reported already.8)

KF-Alumina was found to promote the generation of dichlorocarbene from chloroform, which was trapped with cyclohexene to give a 31% yield of 7,7-dichlorobicyclo[4.1.0]heptane after 48 h at 25 °C. This *α*-elimination by KF-alumina, however, is not so efficient as the well-known method using phase transfer catalysts.

A catalytic amount of KF-alumina promoted the Michael addition and aldol condensation under mild conditions in satisfactory yields as shown in Table 2. No reaction took place when alumina without KF was added to the mixture of benzaldehyde and benzyl cyanide (run 3). The Darzens condensation of benzaldehyde and *α*-chlorophenylacetonitrile proceeded smoothly with KF-alumina in benzene to give 2,3-diphenyloxirane-2-carbonitrile (Table 2, run 5). Interestingly, the ratio of *cis*- to *trans*-isomer varied from 3 : 7 to 7 : 3 depending not only on the solvent used but also on the added water to the reaction system (Table 2, footnote c).9) This phenomenon may give a valuable clue to suggest the characteristics of inorganic solid-organic liquid interfacial reaction, and a further mechanistic study along this line is under way.

In all cases studied, work-up was simple and nonaqueous. Reaction products were isolated by filtration of the solid and evaporation of the solvent; purification by distillation, recrystallization or column chromatography was done when necessary. In conclusion, these results confirmed the utility of KF-alumina as a solid base for a variety of synthetic reactions.

Experimental

General. Unless otherwise mentioned, reagents were obtained commercially and used without further purification. *α*-Chlorophenylacetonitrile was prepared from *α*-hydroxyphenylacetonitrile and thionyl chloride.10) Solvents were dried with molecular sieves 3A or 4A. Neutral alumina was purchased from Merck Japan Ltd. (type 90 for column chromatography, activity I, 70—230 mesh) and used as obtained.

KF-Alumina Reagent. Alumina (30 g) was mixed with KF (20 g) in 200 cm^3 of water, and the water was removed at 50—60 °C in a rotary evaporator. This impregnated alumina was then dried in a vacuum drying oven at 75 °C for several hours.

Typical experimental procedures are described in the following three examples.

Styrene: A mixture of phenethyl bromide (3.70 g, 20 mmol) and KF-alumina (15 g, *ca.* 100 mmol KF) without solvent was agitated mechanically by a Mini Vapour S-3 vibrating apparatus (Tokyo Rikakikai Co., Ltd.) at room temperature for 20 h. Purification by distillation gave 1.55 g of the product (74.5%): bp 26—27 °C/2.67 kPa (lit,11) bp 54 °C/4.00 kPa); purity by GLPC 99.4%.

Phenylacetylene: A mixture of styrene dibromide (12.0 g, 45 mmol) and KF-alumina (74.8 g, *ca.* 450 mmol KF) in 30 cm^3 of Penta Ether (tetraethylene glycol dibutyl ether) was mechanically stirred at 100 °C for 6 h. The solid material was filtered off and washed with ether, and the ether was evaporated. Purification by distillation gave 3.13 g of the product (70.4%): bp 62—72 °C/8.00—9.33 kPa (lit,12) bp 39—40 °C/1.87 kPa); purity by GLPC 97%.

Benzylidenemalononitrile: Condensation of malononitrile (1.32 g, 20 mmol) and benzaldehyde (2.12 g, 20 mmol) in 15 cm^3 of acetonitrile in the presence of KF-alumina (0.78 g, *ca.* 5 mmol KF) was carried out at room temperature for 3 h. The alumina was filtered off, and the solvent was evaporated. Purification by column chromatography (silica gel, benzene) gave 2.64 g of the product (85.7%): mp 83.5—84.0 °C (lit,13) mp 83.5—84.0 °C).

Identification of the Products. All the products are the known compounds, and all the isolated products in Tables 1 and 2 were identified by the spectroscopic (IR, ^{1}H NMR, and UV) and other physical data (mp, bp, and elemental analysis), which were compared with those of the authentic samples or the following literatures: phenoxyethylene,14) 1,3-diphenyl-4-nitrobutanone,15) *α*-phenylcinnamonitrile,16) cyclohexylidenemalononitrile,17) and diphenyloxirane-2-carbonitrile.18)

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