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DIRECT SYNTHESIS OF α,β-UNSATURATED NITRILES FROM ACETONITRILE

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Since quaternary ion[1] and macrocycle mediated[2] phase transfer catalysis have become widely used techniques,[3] interest in hydroxide ion as both base and nucleophile has enjoyed a revival. Indeed, "anhydrous hydroxide" generated from water and t-butoxide ion has been utilized in several modifications of the Haller-Bauer reaction recently.[4]

Most phase transfer catalysis involving hydroxide ion has been conducted in a nonpolar cosolvent like benzene or dichloromethane.[3] Recently, a number of crown catalyzed nucleophilic substitution reactions have been conducted in acetonitrile solution and there was no apparent intervention of solvent in these processes.[5] We report here that potassium hydroxide in acetonitrile solution either in the presence or absence of 18-crown-6[6] undergoes smooth condensation followed by spontaneous dehydration, to yield, α,β-unsaturated nitriles directly from a variety of aldehydes and ketones. In the table are summarized the syntheses of several α,β-unsaturated nitriles

$$CH_3\text{-CN} + \text{R-CO-R'} \xrightarrow{KOH} \text{RR'C=CH-CN}$$

including those resulting from condensation of cyclohexanone and benzophenone.

Although numerous reports of α,β-unsaturated nitrile syntheses are extant in the literature,[7] the present method is the most consistent and convenient direct condensation/dehydration sequence which involves a carbon-carbon bond forming process, and yields product unadulterated with β-hydroxynitriles. Previously reported strong base catalyzed condensation reactions generally afforded such mixtures.[6,7] Moreover, condensation of acetonitrile with cyclohexanone yields 2,2-pentamethyleneacrylonitrile rather than the β,γ-isomer usually obtained after decarboxylation of the cyanoacetic acid adduct.[7] We note that the condensation is sensitive to minor changes in the structure of the electrophile but reserve details of this, the influence of crown, the effect of added water and the differences in the associated cation for the complete report.

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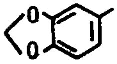
8. Preparation of E- and Z-4-Methoxycinnamonitrile: A 100 ml, three-necked, round-bottomed flask, equipped with addition funnel, reflux condenser and magnetic stirring bar, is charged with powdered KOH (85%, 3.30 g, 0.05 mole) and dry acetonitrile (40 ml). The mixture is brought to reflux and a solution of p-anisaldehyde (6.8 g, 0.05 mole) in acetonitrile (10 ml) is added in a stream. After addition, the reaction mixture is stirred for 10 min. and the hot solution is poured onto cracked (100 g). This mixture is extracted with three 75-ml portions of dichloromethane, dried over sodium sulfate, and evaporated in vacuo (bath temp., ca. 25°). There is obtained, after chromatography (alumina, ether/hexane, 3/7, v/v) a yellow oil [2.33 g, 29%, E:Z = 2:1 (nmr)] and an off-white solid [4.15 g, 52%, mp 62-63°, pure E isomer (nmr)]. Total yield of nitrile, 81%.

TABLE

$$R^1\text{-CO-}R^2 + CH_3CN^{a,b} \xrightarrow{KOH^c} R^1R^2C\text{=CH-CN}$$

R^1	R^2	glpc Yield[d]	Isol'd Yield[e]	Reaction Time	bp/pres or mp	Lit. mp or bp	Obs'd ir ν_{CN}
C_6H_5	H	88%	82%	3 min	60°/0.1	139°/30[f]	2180 cm^{-1}
4-Me-Ø	H	60%	61%	6 min	71-72°	60-70°[g]	2200 cm^{-1}
4-MeO-Ø	H	85%	81%	10 min	63-65°	61-64°[h]	2200 cm^{-1}
	H	---	86%	7 min	89.5-90.5°	94°[h]	2190 cm^{-1}
4-Cl-Ø	H	---	57%	20 sec	82-84°	84-87°[h]	2200 cm^{-1}
C_6H_5	C_6H_5	---	84%	4.5 h	128-131°/.2	160-200°/1.5 (47-48°[i])	2195 cm^{-1}
$-(CH_2)_5-$		---	50%	1 h	50°/0.15	82-84°/3-4[j]	2190 cm^{-1}

a. All solvents were dried, redistilled and stored under nitrogen, over 4A sieves. b. Solvent. c. 85% KOH (reagent) powdered under nitrogen prior to use. d. Determined by glpc on 5'x1/4" 10% SE-30 on 60/80 NAW Chrom. P, col. temp. 165°. e. Purif. by chrom. on alumina, 3/7 ether/hexane; substances pure to ir, nmr, tlc. f. Handbook of Chemistry and Physics, 51 ed. p. C-243. g. C. F. Koelsch, J. Am. Chem. Soc., 65, 57 (1943). h. G. P. Schiemenz & H. Engelhard, Chem. Ber., 95, 969 (1962). i. A. Uchida, S. Saito and S. Matsuda, Bull. Chem. Soc. Jap., 42, 2991 (1969); The subst. was obtained as a heavy oil whose spectroscopic properties were consistent with lit. values, but crystallization could not be induced. j. MS: m/e 120 (M-1), nmr: exocyclic vinyl H, 5.1 ppm, [lit.: G. Descotes and P. Laconche, Bull. Soc. Chim. Fr., 2149 (1968), 5.02 ppm and CN stretch 2200 cm^{-1}; isomerizes on heating to endocyclic olefin,