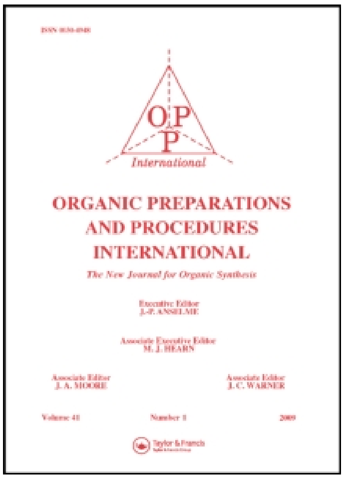
This article was downloaded by:
On: *26 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

ADDITION OF ACETONITRILE ANIONS TO UNSATURATED SYSTEMS UNDER ULTRASONICALLY DISPERSED POTASSIUM SYSTEM

Yang Gao[a]; Hui Wang[a]; Minghua Xu[a]; Hongzhen Lian[a]; Yi Pan[a]; Yaozeng Shi[a]
[a] Department of Chemistry, Nanjing University, Nanjing, PR CHINA

To cite this Article Gao, Yang , Wang, Hui , Xu, Minghua , Lian, Hongzhen , Pan, Yi and Shi, Yaozeng(2001) 'ADDITION OF ACETONITRILE ANIONS TO UNSATURATED SYSTEMS UNDER ULTRASONICALLY DISPERSED POTASSIUM SYSTEM', Organic Preparations and Procedures International, 33: 4, 351 — 356
To link to this Article: DOI: 10.1080/00304940109356599
URL: http://dx.doi.org/10.1080/00304940109356599

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

ORGANIC PREPARATIONS AND PROCEDURES INT., 33 (4), 351-356 (2001)

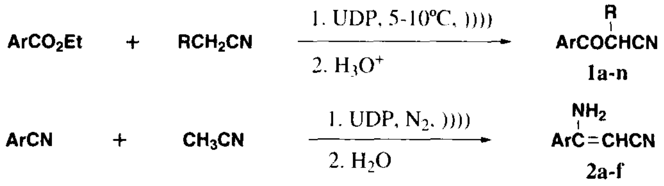
ADDITION OF ACETONITRILE ANIONS TO UNSATURATED SYSTEMS UNDER ULTRASONICALLY DISPERSED POTASSIUM SYSTEM

Yang Gao, Hui Wang[†], Minghua Xu, Hongzhen Lian[††],
Yi Pan*, and Yaozeng Shi

Department of Chemistry, Nanjing University, Nanjing, 210093, P. R. CHINA

Substituted benzoylnitriles[1-4] and β-amino-β-arylacrylonitriles[5,6] are important intermediates both in organic synthesis and pharmaceutical chemistry. The most commonly adopted method for the synthesis of benzoylnitriles is the addition-elimination reaction of phenylacetonitrile and acetonitrile with aromatic esters in the presence of sodium alkoxide.[7,8] It, however, gives poor yields and requires long reaction times. Hauser *et al*[9,10] reported an alternative synthetic route for benzoylnitriles by using sodium amide as base, which gave moderate yields and is relatively rapid, but required low temperature (-33°) and strict handling conditions. β-Amino-β-arylacrylonitriles are commonly prepared by the nucleophilic addition reaction of acetonitrile anion, prepared by in-situ deprotonation of acetonitrile, to aromatic nitriles. As acetonitrile is a very weak acid (pKa = 31.3)[11], strong bases such as *t*-BuOK[12] or $NaNH_2$ are required.[6,12-16] The nucleophilic reactions usually give poor yields and require long reaction times (at least 10 hrs). Application of Ultrasonically Dispersed Potassium (UDP) in organic synthesis has received much attention for many years,[17-24] mainly due to UDP's strong basicity, reducing power and easy availability. One of the important features of UDP is its ability of removing alkyl protons from various compounds to form corresponding carbanions. As part of our research in the application of UDP system, we report here the preparation of benzoylnitriles and β-amino-β-arylacrylonitriles by nucleophilic addition reaction of acetonitrile anions to aromatic esters and nitriles in the presence of UDP.

The UDP system in the present work was obtained readily by ultrasonic irradiation of a suspension of potassium in toluene in the presence of naphthalene. As a strong electron-acceptor, naphthalene is effective in facilitating the dispersion of potassium.[25] The reactions proceeded smoothly as expected (*Scheme 1*). The results are summarized in Tables 1 and 2.



Scheme 1

Table 1. Mps, Yields, Infrared and MS Spectra of the Products

Cmpd	R	Ar	mp. (°C)	Yield (%)	Time (h)	IR (cm^{-1})	MS (m/z)
1a	Ph	Phenyl	84-86[a]	75	1.0	2210, 1690	221 (M^+), 105 (100), 77, 51
1b	Ph	*m*-Chlorophenyl	91-92	72	1.0	2260, 1698	255 (M^+), 139 (100), 111, 75
1c	Ph	*p*-Bromophenyl	178-180	68	1.5	2210, 1695	301 (M^+), 299, 185, 183 (100), 157, 155
1d	Ph	*p*-Methylphenyl	106-107[b]	62	1.0	2220, 169	235 (M^+), 119 (100), 91, 65
1e	Ph	*p*-Anisyl	123-124	59	4.0	2210, 169	251 (M^+), 135 (100), 107, 92
1f	Ph	1-Naphthyl	103-104	76	2.0	2210, 1690	271 (M^+), 155 (100), 127, 101
1g	Ph	4-Pyridyl	87-88	61	1.5	2210, 1680	212 (M^+), 106 (100), 78
1h	H	Phenyl	77-78[c]	83	1.0	2250, 1695	145 (M^+), 105 (100), 77, 51
1i	H	*m*-Chlorophenyl	80-83	85	1.5	2290, 1700	179 (M^+), 139 (100), 111, 75
1j	H	*p*-Anisyl	106-108[d]	75	1.0	2250, 1695	159 (M^+), 119 (100), 91, 65
1k	H	*p*-Bromophenyl	135-136[e]	79	1.0	2270, 1695	175 (M^+), 135 (100), 107, 92
1l	H	*p*-Methylphenyl	175-176	81	1.0	2250, 1692	205 (M^+), 203, 185, 183 (100), 157, 155, 135
1m	H	2-Naphthyl	101-102	71	1.5	2250, 1690	195 (M^+), 155 (100), 127, 101
1n	H	2-Furyl	76-78	87	1.0	2250, 1685	135 (M^+), 95 (100), 67
2a	H	Phenyl	83-84[f]	71	30	3450, 3350, 2200, 1620	144 (M^+, 100), 117, 104, 90
2b	H	*m*-Methylphenyl	Oil.	73	30	3420, 3340, 2200, 1615	158 (M^+, 100), 131, 118, 103
2c	H	*p*-Chlorophenyl	142-145[g]	70	40	3450, 3350, 2170, 1640	178 (M^+, 100), 151, 138, 116
2d	H	*p*-Bromophenyl	147-148	59	50	3470, 3370, 2200, 1620	224 (M^+, 100), 222, 197, 195, 179, 155, 143
2e	H	2-Naphthyl	91-93	65	60	3430, 3330, 2200, 1620	194 (M^+), 193 ($M-1^+$, 100), 166, 154, 127
2f	H	*p*-Anisyl	115-116[h]	74	30	3420, 3340, 2200, 1630	174 (M^+, 100), 159, 147, 134, 104

a). *lit.*[8] 89-90°; b). *lit.*[26] 104-104.5°; c). *lit.*[7] 81°; d). *lit.*[27] 103-104°; e). *lit.*[28] 129-130°; f). *lit*[6]: 86-87°; g). *lit*[29]: 144°; h). *lit*[16]: 117°.

It was found that the solvent plays an important role in the reactions. Although toluene was used for the preparation of the UDP system, THF or diglyme were found to be essential for the reaction. THF was used for the reaction of phenylacetonitrile to the esters. Diglyme was required, however, for the reactions of acetonitrile, which may be due to the poor solubility of KCH_2CN formed in toluene or THF. The reactivity of acetonitrile is slightly better than that of phenylacetonitrile. Although there was not much difference in reactivity between phenyl and naphthyl or furyl for the

Table 2. Elemental Analyses and ^{1}H NMR Data

Cmpd	^{1}HNMR (δ)	Elemental Analyses (Found)		
		C	H	N
1a	5.61 (s, 1H, CH), 7.56-7.72 (m, 10H, ArH)	-	-	-
1b	5.70 (s, 1H, CH), 7.32-7.86 (m, 9H, ArH)	70.59(70.34)	3.92(3.87)	5.49(5.56)
1c	5.58 (s, 1H, CH), 7.66-7.89 (m, 9H, ArH)	60.00(59.79)	3.33(3.14)	4.67(4.38)
1d	2.42 (s, 3H, -CH_3), 5.64 (s, 1H, CH), 7.28-7.74 (m, 9H, ArH)	-	-	-
1e	3.96 (s, 3H, -OCH_3), 5.60 (s, 1H, CH), 7.52-8.10 (m, 9H, ArH)	76.49(76.08)	5.18(5.32)	5.58(5.29)
1f	5.70 (s, 1H, CH), 7.23-8.21 (m, 11H, ArH), 8.34-8.86 (m, 1H, ArH)	84.13(84.32)	4.80(4.69)	5.17(5.23)
1g	5.52 (s, 1H, CH), 7.42-7.86 (m, 5H, ArH), 8.40-8.52 (d, J=5.2Hz, 2H, ArH), 8.62-8.86 (d, J=5.2Hz, 2H, ArH)	79.25(79.38)	4.72(4.54)	13.21(13.07)
1h	4.00 (s, 2H, -CH_2-), 7.70-7.97 (m, 5H, ArH)	-	-	-
1i	4.10 (s, 2H, -CH_2-), 7.20-8.00 (m, 4H, ArH)	-	-	-
1j	2.43 (s, 3H, -CH_3), 4.07 (s, 2H, -CH_2-), 7.14-7.97 (t, J=8Hz, 4H, ArH).	75.45(75.14)	5.70(5.85)	8.79(8.37)
1k	3.92 (s, 3H, -OCH_3), 4.02 (s, 2H, -CH_2-), 8.07-8.17 (t, J=9Hz, 4H, ArH)	68.56(68.94)	5.18(5.57)	8.00(7.86)
1l	4.00 (s, 2H, -CH_2-), 7.53-8.00 (m, 4H, ArH)	-	-	
1m	4.15 (s, 2H, -CH_2-), 7.28-8.28 (m, 6H, ArH), 8.50-8.98 (m, 1H, ArH)	80.00(79.81)	4.65(4.85)	7.18(7.03)
1n	3.98 (s, 2H, -CH_2-), 6.53-6.73 (t, J_1=3.8Hz, J_2=1.8Hz, 1H, ArH), 7.30-7.47 (d, J=3.8Hz, 1H, ArH), 7.70 (d, J=1.8Hz, 1H, ArH)	62.23(62.19)	3.73(3.80)	10.37(10.47)
2a	4.18 (s, 1H, =CH-), 4.37-5.40 (br, 2H, -NH_2), 7.47 (s, 5H, ArH)	75.37(74.98)	5.62(5.59)	19.82(19.43)
2b	2.30 (s, 3H, -CH_3), 4.00 (s, 1H, =CH-), 4.73-5.63 (br, 2H, -NH_2), 7.10-7.27 (m, 4H, ArH)	75.54(75.92)	6.55(6.37)	17.91(17.71)
2c	4.15 (s, 1H, =CH-), 4.33-5.33 (br, 2H, -NH_2), 7.30 (s, 4H, ArH)	60.11(60.51)	4.05(3.95)	15.89(15.68)
2d	4.23 (s, 1H, =CH-), 4.47-5.40 (br, 2H, -NH_2), 7.15-7.83 (t, J=9.2Hz, 4H, ArH)	48.77(48.55)	3.29(3.16)	12.22(12.55)
2e	4.17 (s, 1H, =CH-), 4.53-5.65 (br, 2H, -NH_2), 7.13-8.33 (m, 7H, ArH)	80.34(80.38)	5.43(5.18)	14.23(14.42)
2f	3.83 (s, 3H, -OCH_3), 4.14 (s, 1H, =CH-), 4.60-5.27 (br, 2H, -NH_2), 6.77-7.70 (t, J=9Hz, 4H, ArH)	69.02(68.95)	5.83(5.79)	15.70(16.08)

esters, the nature of the substituents on the phenyl ring of the esters affected the reaction quite substantially. None of the expected products were obtained when the substituents were nitro, hydroxyl or carboxyl even when excess UDP was utilized. In contrast, it seems that the substituents on the phenyl ring have little influence on reactivity and yields in the reactions with nitriles. The reactions are much faster and the yields better than those reported both for the reactions of esters and of nitriles.

In conclusion, the present UDP promoted reactions of acetonitrile anions with esters or nitriles provide an efficient method for the preparation of benzoylnitriles and β-amino-β-arylacrylonitriles in good yields, short reaction times and under mild handling conditions.

EXPERIMENTAL SECTION

IR spectra were taken on a IDP-440 or 5DX-FT spectrometer. ^{1}H NMR data were recorded in $CDCl_3$ on a Jeol PMX-60SI spectrometer and chemical shifts (δ) were referred to TMS. Mass spectra were determined on a VG-ZAB-HS spectrometer. Ultrasonic wave was generated by a KQ-50 (250Watts) Ultrasonic Cleaner. Melting points are uncorrected. Toluene, tetrahydrofuran (THF) and 2-methoxyethyl ether (diglyme) were distilled from sodium-potassium alloy or sodium- potassium-benzophenone prior to use.

Preparation of Ultrasonically Dispersed Potassium-Naphthalene System.- A suspension of potassium (0.7 g, 18 mmol) in a solution of naphthalene (0.05 g, 0.4 mmol) in anhydrous toluene (25 mL) was subjected to ultrasonic irradiation at 5-10° under nitrogen atmosphere. A black colored homogeneous solution was obtained in 5-10 min.

General Procedure for the Preparation of Benzoylnitriles.- Phenylacetonitrile (1.87 g, 16 mmol) or acetonitrile (0.74 g, 18 mmol), dissolved in 3 mL anhydrous tetrahydrofuran (1a-g) or dimethylcarbitol (2h-2n), was added dropwise to the UDP system prepared as above. The mixture was irradiated by ultrasonic for 15 min at 5-10°. Then with stirring and ultrasonic irradiation, a solution of the corresponding aromatic ester (9 mmol) in 2 mL anhydrous tetrahydrofuran (1a-g) or dimethylcarbitol (1h-n) was added dropwise to the mixture. After the reaction was completed (TLC monitoring), about 15 mL iced water was added (**CAUTION!**). The mixture was extracted with ether (2x10 mL). The combined organic layer was washed with water and then dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the remaining residue was purified by column chromatograph on silica gel (eluent: petroleum (bp: 60-90°)/ethyl acetate:4.5/5 (V/V)) to give the pure product.

Reaction of Acetonitrile with Aromatic Nitriles, General Procedure.- A UDP-naphthalene system was obtained as above from 0.4 g potassium (10.3 mmol), 25 mL toluene and 0.05 g naphthalene (0.4 mmol). A solution of acetonitrile (0.42 g, 10.3 mmol) and diglyme (3 mL) was added to the UDP-naphthalene system in 10 min under ultrasonic irradiation. Then a solution of aromatic nitrile in diglyme was added dropwise. The mixture was irradiated under stirring by ultrasonic for another 10 min. After the reaction was completed (TLC monitoring), about 15 mL iced water (**CAUTION!**) and then the aqueous layer was extracted twice with 20 mL ether. The combined organic layer was washed with water and then dried over anhydrous Na_2SO_4. The volatiles were removed *in vacuo* and the remaining residue was purified by column chromatograph on silica gel (eluent: petroleum (bp: 60-

90°)/ethyl acetate:4/5 (V/V)) to give the products.

Acknowledgment.- We are grateful for the financial support from The National Natural Science Foundation of China and The Natural Science Foundation of Jiangsu Province.

REFERENCES

† Present address: College of Chemical Engineering, Nanjing University of Science and Technology, Nanjing 210094, P. R. China

†† Present address: Center of Materials Analysis, Nanjing University, Nanjing 210093, P. R. China

1. A. Takamizawa and Y. Hamashima, *Yakugaku Zasshi*, **84**, 1113 (1964).
2. Y. Tomioka, A. Mochiike, J. Himeno and M. Yamazaki, *Chem. Pharm. Bull.*, **29**, 1286 (1981).
3. Y. Shih and J. Wang and L. Liu, *Heterocycles*, **24**, 1599 (1986).
4. D. N. Ridge, J. W. Hanifin, L. A. Harten, B. D. Johnson, J. Menschik, G. Nicolau, A. E. Sloboda and D. E. Watts, *J. Med. Chem.*, **22**, 1385 (1979).
5. J. W. Hanifin, B. D. Johnson, J. Menschik, D. N. Ridge and A. E. Sloboda, *J. Pharm. Sci.*, **68**, 535 (1979).
6. J. Kuthan, V. Jehlicka and E. Hakr, *Collect. Czech. Chem. Commun.*, **32**, 4309 (1967).
7. J. B. Dorsch and S. M. McElvain, *J. Am. Chem. Soc.*, **54**, 2960 (1932).
8. B. W. Howk and S. M. McElvain, *ibid.*, **54**, 282 (1932).
9. C. J. Eby and C. R. Hauser, *ibid.*, **79**, 723 (1957).
10. R. Levine and C. R. Hauser, *ibid.*, **68**, 760 (1946).
11. F. G. Bordwell, *Acc. Chem. Res.*, **21**, 456 (1988).
12. K. Shibata, K. Urano and M. Matsui, *ibid.*, **61**, 2199 (1988).
13. K. Shibata, H. Kondo, K. Urano and M. Matsui, *Chem. Express*, **2**, 169 (1987); *Chem. Abs.*, **107**, 236174p (1987).
14. K. Shibata, Y. Saito, K. Urano and M. Matsui, *Bull. Chem. Soc. Jpn.*, **59**, 3323 (1986).
15. A. Dornow, I. Kuhlcke and F. Baxmann, *Chem. Ber.*, **82**, 254 (1949).
16. N. Palit, *J. Indian Chem. Soc.*, **10**, 529 (1933).

17. J. L. Luche, C. Petrier and C. Dupuy, *Tetrahedron Lett.*, **25**, 753 (1984).

18. T. Chou and M. You, *ibid.*, **26**, 4495 (1985).

19. T. Chou and M. Chen, *Heterocycles*, **26**, 2829 (1987).

20. T. Chou, S. Hung, M. Peng and S. Lee, *Tetrahedron Lett.*, **32**, 3551 (1991).

21. L. X. Wang, Y. Z. Shi, Y. M. Yao and H. W. Hu, *Chin. Chem. Lett.*, **5**, 825 (1994); *Chem. Abs.*, **122**, 132690x (1995).

22. L. X. Wang, Y. Z. Shi, M. H. Xu and H. W. Hu, *Org. Prep. Proced. Int.*, **28**, 226 (1996).

23. L. X. Wang, M. H. Xu, Y. Z. Shi and H. W. Hu, *Chin. Chem. Lett.*, **7**, 709 (1996); *Chem. Abs.*, **125**, 328230d (1996).

24. X. Chen, X. L. Wang, H. Z. Lian, J. J. Chen, Y. Pan and Y. Z. Shi, *Chin. J. Chem.*, **17**, 80 (1999); *Chem. Abs.*, **130**, 282010e (1999).

25. T. Azuma, S. Yanagida, H. Sakurai, S. Sasa and K. Yoshino, *Synth. Commun.*, **12**, 137 (1982).

26. R. N. McDonald and D. G. Hill, *J. Org. Chem.*, **35**, 2942 (1970).

27. A. Dornow, I. Kuhlcke and F. Baxmann, *Chem. Ber.*, **82**, 254 (1949).

28. A. Sonn, *Ber.*, **51**, 821 (1918).

29. E. von Meyer, *J. prakt. Chem.*, **92**, 174 (1915).

(Received September 5, 2000; in final form April 10, 2001)