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ALKYLATION AND HYDROLYSIS OF PHENYLACETONITRILES UNDER MICROWAVE IRRADIATION

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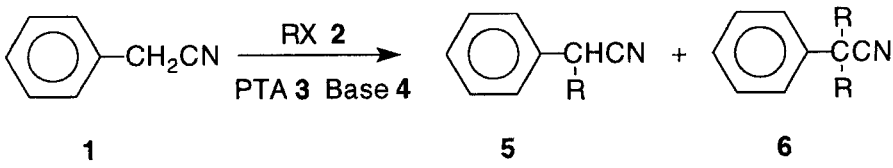
ABSTRACT : Alkylation of phenylacetonitriles is performed by solid-liquid phase transfer catalysis in 1-3 minutes under microwave irradiation (one hour with a two-phase system). These nitriles can be quickly hydrolysed in a microwave oven to yield the corresponding amides or acids according to the reaction time.

Alkylation of phenylacetonitriles with phase transfer agent (PTA) has been the subject of many investigations[1] since the works of Jarrousse[2] and the work-up is described in Organic Syntheses[3] : the reaction requires a few hours at 30°C. We here report the phase transfer catalysed (PTC) alkylation of these nitriles under microwave irradiation in a few minutes.



1 **5** **6**

a : R = benzyl ; **b** : R = n-hexyl ; **c** : R = allyl

3 : TEBACl=triethylbenzylammonium chloride ; TBABr=tetrabutylammonium bromide ; TBACl=tetrabutylammonium chloride.

We have first optimised with three alkyl bromides the conditions of the conventional reaction using the two-phase system. Table 1 summarises the results : the alkylation with **2a** is not very influenced by the nature of the phase transfer agent whereas a large excess of nitrile favours the formation of **5a** ; **6b** is not produced by reaction of **1** with **2b**, which is less reactive than **2a** and **2c** ; raising the temperature has no result on the distribution of the products but allows a better transformation of the starting compounds.

Table 1 - Alkylation of phenylacetonitriles (conventional method)

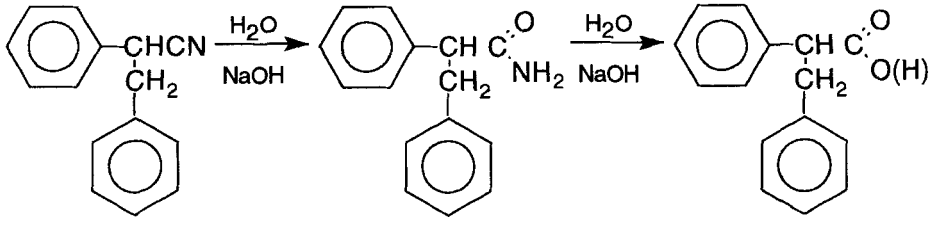
Starting Compounds				Time	Yields		
RX	**1** %	**3** %	**4**%	Temperature	Transf. %	**5**%	**6**%
2a	150	NaOH 610	TEBACl 2	1h, 25°C	100	60	25
2a	150	NaOH 610	TBABr 2	1h, 25°C	100	64	27
2a	150	NaOH 610	TBACl 2	1h, 25°C	100	66	31
2a	500	NaOH 610	TEBACl 2	1h, 25°C	100	80	7
2b	150	NaOH 610	TEBACl 2	1h, 25°C	77	100	0
2b	150	NaOH 610	TEBACl 2	1h, 45°C	93	97	0
2c	150	NaOH 610	TEBACl 2	1h, 25°C	100	77	20
2c	200	NaOH 610	TEBACl 2	1h, 25°C	100	81	16
2c	200	NaOH 610	TEBACl 2	1h, 45°C	100	81	16

The best results (see Table 2) of the alkylation in a microwave oven are obtained by a 350 W irradiation during one minute joining small amounts of potassium carbonate with sodium hydroxide[4] to prevent sparks in the oven. In the case of alkylation with **2c**, working with an excess of alkyl bromide is more advisable because of the partial evaporation of **2c** during irradiation.

Table 2 - Alkylation of phenylacetonitriles (microwave irradiation)

Starting Compounds				Time	Yields		
RX	**1** %	**3** %	**4**%	Power MW	Transf. %	**5**%	**6**%
2a	150	NaOH 610	TEBACl 15	1min, 350W	100	62	32
2a	150	NaOH 610	TEBACl 15	3min, 160W	100	58	35
2a	150	NaOH 540 K_2CO_3 60	TEBACl 15	1min, 350W	100	60	40
2b	150	NaOH 610	TEBACl 15	1min, 350W	79	70	0
2b	150	NaOH 540 K_2CO_3 60	TEBACl 15	3min, 160W	100	74	0
2c	150	NaOH 550	TEBACl 15	3min, 160W	100	48	10
2c	150	NaOH 540 K_2CO_3 60	TEBACl 15	3min, 160W	100	44	12
2c	50	NaOH 580	TEBACl 2	2min, 160W	57	96	2

One recent paper[5] reports the hydrolysis of benzonitrile under a microwave irradiation of fifteen minutes, to the corresponding amide as the major product, using a sealed Teflon container (90 psi). The hydrolysis of **5a** to the corresponding carboxylic acid is complete by a conventional heating with aqueous sodium hydroxide during 2,5 h. We here report that selective hydrolysis in carboxylic acid or amide is possible under microwave irradiation with open vessel.



5a **7a** **8a**

Table 3 - Hydrolysis of **5a**

Method	NaOH %	Time	Power MW	Transf. %	**7a** %	**8a** %
conventional	300	2,5 h		100	0	100
microwave	250	2 min	160W	71	81	1
microwave	250	8 min	160W	100	16	80

EXPERIMENTAL

Yields are expressed against the converted starting compounds and the less abundant one. NMR spectra are recorded on a Bruker AC 300 spectrometer in deuterochloroform.

*Alkylation of phenylacetonitrile by **2a** (typical procedure)*

Conventional : Phenylacetonitrile (7g, 60 mmol) and then benzyl bromide (7g, 40 mmol) are added dropwise at 18°C to an homogeneous mixture of sodium hydroxide (10 g, 250 mmol), TEBACl (0.2g, 0.9 mmol) and water (10 ml) ; the mixture is stirred at room temperature for one hour, diluted with 20 ml of water and extracted thrice with 20 ml of ether. The organic layers are washed with a solution of hydrochloric acid and water until neutrality ; after drying over magnesium sulfate and removal of the solvent, the residue is distilled under reduced pressure.

Microwave : A mixture of sodium hydroxide (1.44 g, 36 mmol), TEBACl (0.2, 0.9 mmol), phenylacetonitrile (1.07g, 9 mmol), benzyl bromide (1.05g, 6 mmol) and water (1.5 ml) is stirred in a conical flask at room temperature for two minutes. The flask is placed in the oven and the mixture is subjected to microwaves for one minute at 350W. The mixture is then treated as above.

Hydrolysis of diphenylpropionitrile ***5a*** *(typical procedure)*

Conventional : A mixture of diphenylpropionitrile (5g, 24 mmol), sodium hydroxide (2.88g, 72 mmol), 20 ml of 1,2-propanediol and 5 ml of water is refluxed for one hour. The mixture is diluted with 20 ml of water and acidified with 30 ml of a 0.2 N solution of hydrochloric acid. The precipitate is filtrated and washed with water.

Microwave : A mixture of diphenylpropionitrile (1g, 4.8 mmol), sodium hydroxide (0.48g, 12 mmol), 4 ml of 1,2-propanediol and 1 ml of water is stirred in a conical flask at room temperature for two minutes. The flask is placed in the oven and the mixture is subjected to microwaves for two minutes at 160W. The propionamide precipitates by addition of 8 ml of water. The filtrate is acidified with 10 ml of a 0.2 N solution of hydrochloric acid : the propionic acid is then filtered.

Compound **5a**[2] **:** mp = 54°C ; bp = 147°C / 0.7 ; ^{1}H RMN : 3.14 (dd, 1H, H-3, $J_{3,3'}$ = -13.5, $J_{2,3}$ = 6.7), 3.21 (dd, 1H, H-3', $J_{2,3'}$ = 8,1), 4.02 (dd, 1H, H-2), 7.12-7.36 (m, 10H, aromatic) ; ^{13}C RMN : 39.8 (C-2), 42.2 (C-3), 120.4 (C-1), 127.4 and 128.2 (C-7 and C-11), 127.5-129.3 (C-5, C-6, C-9, C-10), 135.2 and 136.3 (C-4 and C-8).

Compound **5b**[6] **:** bp = 135°C / 2 ; ^{1}H RMN : 0.87 (t, 3H, H-8), 1.20-1.36 (m, 6H, H-5, H-6, H-7), 1.40-1.51 (m, 2H, H-4), 1.80-1.96 (m, 2H, H-3), 3.76 (dd, 1H, H-2, J = 6.4 and 8.4), 7.28-7.41(m, 5H, aromatic) ; ^{13}C RMN : 14.0 (C-8), 22.5 (C-7), 27.0 (C-6), 28.6 (C-5), 31.5 (C-4), 35.9 (C-3), 37.4 (C-2), 127.2-129.9 (aromatic), 136.1 (C-1).

Compound **5c**[7] : bp = 87°C / 1.5 ; ^{1}H RMN : 2.60-2.71 (m, 2H, H-3), 3.85 (t, 1H, H-2, J = 7.24), 5.11-5.22 (m, 2H, H-5), 5.73-5.87 (m, 1H, H-4), 7.28-7.41 (m, 5H, aromatic) ; ^{13}C RMN : 37.5 (C-2), 44.2 (C-3), 120.2 (C-1), 127.3-129.1 (unsaturated).

Compound **6a**[8]: bp = 185°C / 0.7 ; ^{1}H RMN : 3.34 (s, 4H, H-3), 7.12-7.36 (m, 10H, aromatic) ; ^{13}C RMN : 46.5 (C-2), 51.2 (C-3), 121.2 (C-1), 126.9-130.4 (C-5, C-6, C-7, C-9, C-10, C-11), 135.0 and 137.2 (C-4 and C-8).

Compound **6c**[9] : bp = 99°C / 1.6 ; ^{1}H RMN : 2.60-2.71 (m, 4H, H-3), 5.11-5.22 (m, 4H, H-5), 5.60-5.73 (m, 2H, H-4), 7.28-7.41 (m, 5H, aromatic) ; ^{13}C RMN : 39.8 (C-3),120.3 (C-1), 127.3-129.1 (unsaturated).

Compound **7a**[10] : mp = 134°C ; ^{1}H RMN : 2.98 (dd, 1H, H-3, $J_{3,3'}$ = -13.4, $J_{2,3}$=7.2), 3.52 (dd, 1H, H-3', $J_{2,3'}$ = 7,6), 3.63 (dd, 1H, H-2), 5.31-5.43 (s, 2H, NH_2), 7.02-7.31 (m, 10H, aromatic) ; ^{13}C RMN : 39.4 (C-3), 54.8 (C-2), 126.2 and 127.5 (C-7 and C-11), 128.0-129.0 (C-5, C-6, C-9, C-10), 139.4 and 139.5 (C-4 and C-8), 175.1 (C-1).

Compound **8a**[11] : mp = 86°C ; ^{1}H RMN : 3.02 (dd, 1H, H-3, $J_{3,3'}$ = -13.8, $J_{2,3}$ = 7.1), 3.39 (dd, 1H, H-3', $J_{2,3'}$ = 7,4), 3.84 (dd, 1H, H-2), 7.08-7.31 (m, 10H, aromatic) ; ^{13}C RMN : 39.3 (C-3), 53.4 (C-2), 126.5 and 127.6 (C-7 and C-11), 128.1-128.9 (C-5, C-6, C-9, C-10), 138.0 and 138.7 (C-4 and C-8), 179.5 (C-1).

REFERENCES

1 - Dehmlow, E. ; Dehmlow, S. *Phase Transfer Catalysis,* 3rd Editon, VCH Publishers, Weinheim, 1993, p. 149 .

2 - Jarrousse, J. *C. R. Acad. Sci.* , 1951, 232 , 1424.

3 - Makozka, M. ; Jonczyk, A. *Org. Synth.,* 1976, 55, 91 .

4 - Deng, R. ; Wang, Y. ; Jiang, Y. *Synth. Commun.* , 1994, 24 , 111.
5 - Majetich, G. ; Hicks , R. *Res. Chem. Intermed.,* 1994, 20, 61 .
6 - Abe, N . *J. Org. Chem.* , 1972, 37, 526.
7 - Smissman, E . *J. Org. Chem.* , 1975, 40, 281.
8 - Asami, R. *Kogyo Kagaku Zasshi* , 1958, 61, 1238 .
9 - Brain, E . *J. Chem. Soc.* , 1962, 1445.
10 - Pfeisser, P. ; Engelhardt, I. ; Alfuss, W. *Liebig Ann. Chem.*, , 467, 190.
11 - Hauser, C. ; Chambers, W. *J. Am. Chem. Soc.*, 1956, 78, 4946.

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