

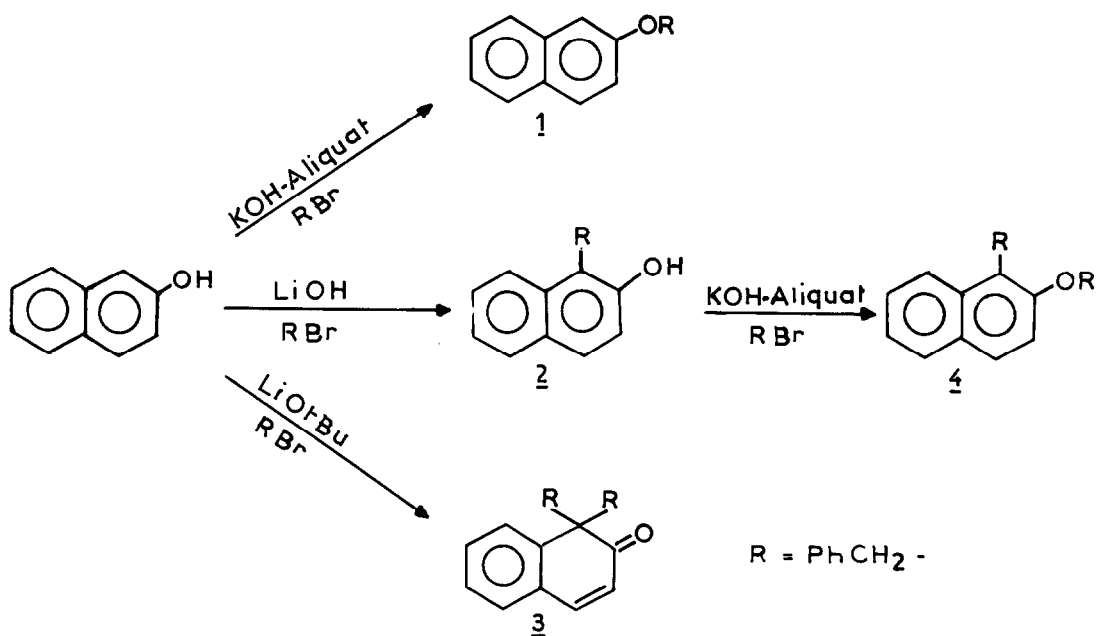
HIGHLY SELECTIVE BENZYLATIONS OF  $\beta$ -NAPHTHOXIDE ANION IN HETEROGENEOUS MEDIA

G. Bram, A. Loupy, J. Sansoulet and F. Vaziri-Zand

Laboratoire des Réactions Sélectives sur Supports, UA (CNRS) 478, Batiment 410  
Université de Paris-Sud, 91405 ORSAY CEDEX, France

**Abstract.** Each of the four products resulting from the benzylation of the ambident  $\beta$ -naphthoxide anion can be efficiently and selectively obtained in mild and economical conditions by a judicious choice of the solid base: LiOH, LiOtBu or KOH-Aliquat.

Preparative selective alkylation (O-versus C-, mono- versus di-) of an ambident anion<sup>1,2</sup> such as the  $\beta$ -naphthoxide ion is still an unsolved challenge. By alkylation with PhCH<sub>2</sub>Br, four products can be formed, and usually all are formed competitively.



Since the pioneering and fundamental works of N. KORNBLUM et al.,<sup>3</sup> it is known that the nature of the medium is a very important factor in the orientation of the alkylation: O-alkylation is favoured in polar aprotic solvents and C-alkylation in protic ones<sup>3-6</sup>. An increase of the O-alkylation is obtained when reactions are performed in homogeneous medium in the presence of crown-ethers<sup>4,6</sup> or cryptands<sup>4</sup>. A similar trend is observed either in liquid-liquid<sup>7</sup> or in solid-liquid<sup>4,8</sup> phase transfer catalysis conditions. Alkylation on alumina in "dry media" conditions<sup>9</sup> leads to significant C-alkylation. Heterogeneous reactions performed in hydrocarbon solvents give rise to good percentages of C-alkylation of  $\beta$ -naphthoxide<sup>10,11</sup> and other phenoxide anions<sup>11,12</sup> especially with reactive halides (benzylic or allylic types).

Actually, most of the described results deal mainly with the O-versus C-competition and a strict differentiation between the different products of C-alkylation 2, 3 and 4 is rarely effected; if many syntheses of O-benzylated 1 are described<sup>3,8</sup>, there is, to our knowledge, no preparative method giving selectively each of the four different alkylation products.

We describe here such selective syntheses which are heterogeneous solid-liquid reactions performed in the absence of any organic solvent. The observed selectivities depend on the nature of the solid base used.

Table. Benzylation of  $\beta$ -naphthoxyde anion

a	Base	t(h)	Temp.	<u>1</u> "O" %	<u>2</u> "C" %	<u>3</u> "di-C" %	<u>4</u> "C-O" %
1:1:1	KOH-Aliquat (40%)	3	60°C	85 <sup>b</sup> (75) <sup>c</sup>			
1:2:2	LiOH	2	85°C		96 <sup>b</sup> (90) <sup>c</sup>		
1:3:3	LiOtBu	2	85°C			88 <sup>b</sup> (80) <sup>c</sup>	10 <sup>b</sup>
1:1.5:1	<u>2</u> + KOH-Aliquat (40%)	2	85°C				85 <sup>b</sup> (74) <sup>c</sup>

a : Ratio naphthol : base : PhCH<sub>2</sub>Br. b : Yield by VPC. c : Yield in isolated product

- The O-alkylation to give 1 is due to solid-liquid phase transfer catalysis alkylation without added organic solvent<sup>13</sup>, solid KOH being the anion-generating base and Aliquat the phase transfer catalyst.

- Mono C-alkylated  $\beta$ -naphthol 2 is obtained in the absence of catalyst, with solid LiOH as base<sup>14</sup>.

- Di C-alkylated compound 3 is directly and selectively obtained when the stronger solid base LiOtBu is used, in the absence of catalyst<sup>15</sup>.

- C- and O- dialkylated product 4 is easily obtained when 2 is O-alkylated in the presence of solid KOH and Aliquat.

In every case, good yields are obtained under mild and economical experimental conditions (2 - 3 h, 85°C) and with a very easy work up. Furthermore, there is no need for previous formation of naphthoxide anion as sodium or potassium salt.

These results achieved with catalysed and non-catalysed solid-liquid reactions constitute a new illustration of the potential, for preparative organic synthesis, of heterogeneous reactions performed without solvent.

#### NOTES AND REFERENCES

- 1) N. Kornblum, R.A. Smiley, R.K. Blackwood and D.C. Iffland, J. Am. Chem. Soc., 1955, 77, 6269.
- 2) O.A. Reutov, I.P. Beletskaya and A.L. Kurts, "Ambident Anions" Consultants Bureau, New-York, 1983.
- 3) N. Kornblum, R. Seltzer and P. Haberfield, J. Am. Chem. Soc., 1963, 85, 1148.
- 4) S. Akabori and H. Tuji, Bull. Soc. chim. Jpn, 1978, 51, 1197
- 5) A. Aljazaa, J.H. Clark and J.M. Miller, Chem. Lett., 1983, 89
- 6) S. Shinkai, T. Fukunaga and O. Manabe, J. Org. Chem., 1979, 44, 4990
- 7) E. d'Incan and P. Viout, Tetrahedron, 1975, 31, 159.
- 8) For O-alkylation of  $\beta$ -naphthol with polymer-supported phase transfer catalyst see for example : D. Balasubramanian, P. Sukumar and B. Chandani, Tetrahedron Lett., 1979, 3543. Y. Hamada, N. Kato, Y. Kakamu and T. Shiori, Chem. Pharm. Bull., 1981, 29, 2246. N. Ohtani, C.A. Wilkie, A. Nigam and J.L. Regen, Macromolecules, 1981, 14, 516. W.M. McKenzie and D.C. Sherrington. Polymer, 1981, 22, 431. F. Montanari, S. Quici and P. Tundo, J. Org. Chem., 1983, 48, 199.
- 9) G. Bram, N. Geraghty, G. Nee and J. Seyden-Penne, J.C.S. Chem. Comm., 1980, 325.
- 10) J. Carnduff and D.G. Leppard, J.C.S. Perkin I, 1976, 2570.
- 11) F. Bigi, G. Casiraghi and G. Sartori, Tetrahedron, 1983, 39, 169.
- 12) N. Kornblum and A.P. Lurie, J. Am. Chem. Soc., 1959, 81, 2705. In this paper, N. Kornblum emphasized that " full utilization in synthesis of the fact that heterogeneous reaction results in C-alkylation would provide quantitative yields of C-alkylated products .... (but) in practice this proves extremely difficult if not impossible ".

- (13) J. Barry, G. Bram, G. Decodts, A. Loupy, P. Pigeon and J. Sansoulet, *Tetrahedron*, 1983, 39, 2672. *Tetrahedron*, 1983, 39, 2673.
- (14) Synthesis of 2 :  $\beta$ -naphthol (360 mg, 2.5 mmol) and LiOH (120 mg, 5 mmol), were both finely ground, mixed and stirred for 15 minutes. PhCH<sub>2</sub>Br (852 mg, 5 mmol) was added and the mixture was heated at 85°C for 2 hours. 50 ml of diethyl ether was then added and after filtration on Florisil and evaporation, the residue was chromatographed on Florisil (pentane/diethyl ether) to give 2 (527 mg, 90%).
- (15) Synthesis of 3 :  $\beta$ -naphthol (360 mg), 2.5 mmol) and LiOtBu (600 mg, 7.5 mmol) were both finely ground, mixed and stirred for 15 minutes. PhCH<sub>2</sub>Br (1.28 g, 7.5 mmol) was added and the mixture was heated at 85°C for 2 hours. 50 ml of diethyl ether was then added and after filtration on Florisil and evaporation the residue was chromatographed on silicagel (pentane/diethyl ether) to give 4 (651 mg, 80%)

(Received in France 16 July 1984)