

POTASSIUM-GRAPHITE (C_8K) AS A METALLATION REAGENT. ALKYLATION OF NITRILES
AND ESTERS WITH ALKYL HALIDES UNDER HETEROGENEOUS CONDITIONS

Diego Savoia, Claudio Trombini and Achille Umani-Ronchi
Istituto Chimico "G.Ciamician", Università di Bologna
Via Selmi 2, 40126 Bologna, Italy

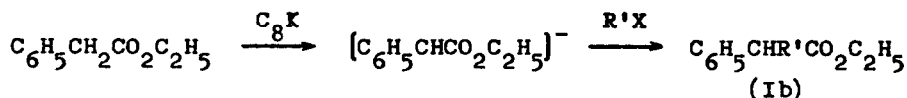
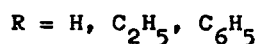
(Received in UK 4 January 1977; accepted for publication 13 January 1977)

Potassium-graphite¹ (C_8K) has still now found only few applications in the synthesis of organic compounds, essentially as a catalyst in polymerization reactions² and in the nuclear and side-chain alkylation of aromatic compounds with ethylene³. Furthermore it acts as a reducing agent, by an electron transfer process, towards carbonyl compounds⁴ and metal carbonyls⁵.

We recently described a new simple method of reductive cleavage of the carbon-sulphur bond in α,β - and β,γ -unsaturated sulphones with C_8K , which affords the corresponding alkenes in good yields⁶.

We now put in evidence the metallating properties of potassium-graphite towards weakly acidic substrates.

Thus we found that C_8K , a bronze coloured powder easily obtained by melting potassium over graphite under argon⁴, reacts with aliphatic nitriles and esters in dry tetrahydrofuran at -60° to abstract an active hydrogen⁷. In fact when a solution of alkyl halide in tetrahydrofuran is added, the alkylated product (Ia) or (Ib) is obtained upon quenching with water and working up.

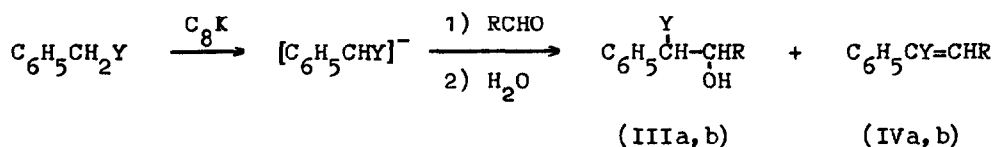


The Table summarizes the results obtained in the alkylation of acetonitrile, butyronitrile, phenylacetonitrile and ethyl phenylacetate with alkyl halides in a variety of experimental conditions. Optimal results are obtained when the molar ratio substrate : C_8K : alkyl halide is 1 : 2 : 2. The products are identified either by comparison with authentic samples or by spectroscopic and mass spectral data.

The Wurtz coupling reaction of the alkyl halides in presence of C_8K ⁸ always accompanies the alkylation reaction, especially if C_8K is used in large excess; therefore a corresponding amount of alkyl halide is required.

A remarkable advantage of our new alkylation reaction, compared to others⁹, lies in the fact that practically pure monoalkylated derivatives are obtained; only small amounts of the dialkylated products are isolated.

Carbanions are intermediates in this reaction. In order to test this assumption we carried out the metallation of phenylacetonitrile and ethyl phenylacetate with C_8K in an usual manner, then the solution was filtered by means of a bench-top apparatus under argon. Upon addition of an aldehyde to the solution, followed by working up, the β -hydroxy nitrile (IIIa) or ester (IIIb) and the corresponding α,β -unsaturated derivative (IVa) or (IVb), with a total yield of 35 % were isolated.



a : Y = CN ; R = C_3H_7 or C_6H_5

b : Y = $CO_2C_2H_5$; R = C_3H_7 or C_6H_5

The condensation of acetonitrile with benzaldehyde in the same conditions failed, probably owing to the insolubility of cyanomethyl potassium salt in tetrahydrofuran at low temperature.

We want again to emphasize that the good yield obtained of monoalkylated nitriles and esters, the simplicity of work-up and the unexpensiveness of the reagent make the described method highly competitive.

TABLE

Alkylation of nitriles and esters

Substrate	Alkyl halide	Molar ratio subst:C ₈ K:hal	Yield ^a (%) of alkylated products	
			mono-	di-
CH ₃ CN	1-C ₈ H ₁₇ Br	1 : 2 : 2	50 ^{b,c}	3
CH ₃ CN	1-C ₈ H ₁₇ Br	1 : 4 : 4	65 ^c	7
CH ₃ CN	2-C ₈ H ₁₇ Br	1 : 2 : 2	25 ^c	-
CH ₃ CN	C ₆ H ₅ CH ₂ Cl	1 : 2 : 2	42 ^c	-
C ₃ H ₇ CN	1-C ₄ H ₉ Br	1 : 2 : 2	52 ^c	-
C ₆ H ₅ CH ₂ CN	CH ₃ J	1 : 2 : 2	60 ^d	6
C ₆ H ₅ CH ₂ CN	1-C ₄ H ₉ Br	1 : 2 : 2	67 ^d	3
C ₆ H ₅ CH ₂ CN	2-C ₃ H ₇ Br	1 : 4 : 4	58 ^d	6
C ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅	CH ₃ J	1 : 2 : 2	70 ^d	4
C ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅	CH ₃ J	1 : 4 : 4	71 ^d	5
C ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅	1-C ₄ H ₉ Br	1 : 2 : 2	70 ^d	5
C ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅	2-C ₃ H ₇ Br	1 : 2 : 2	45 ^d	4

^a The yields indicated refer to pure isolated products

^b With the molar ratio 1 : 1 : 1 the yield of monoalkylated product is 30%

^c See general procedure

^d Metallation reaction is performed at -60° for 2 hr

General procedure for the alkylation of aliphatic nitriles and esters.

Caprinitrile. To a suspension of potassium-graphite (C₈K) (2.70 g, 20 mmol) in 30 ml of dry THF, prepared accordingly to a reported procedure⁴, was added a solution of acetonitrile (0.41 g, 10 mmol) in 10 ml of dry THF at -60° under argon. After stirring the mixture for 4 hr at -60°, a solution of 1-bromo-octane (3.86 g, 20 mmol) in 10 ml of dry THF was added dropwise and the temperature was allowed to raise at 25°. The mixture was quenched after 1 hr with 0.5 ml of water, graphite was removed by filtration and the solution was dried (Na₂SO₄) and evaporated. The residue was chromatographed on silica gel column, using hexane-ether (99 : 1) as solvent, to obtain caprinitrile (0.77 g, 50%) and 2-octylcaprinitrile (0.08 g, 3%).

References

1. M.C.Robert, M.Oberlin and J.Mering, Chem.Phys.Carbon, 10, 141 (1973).
2. M.A.M.Boersma, Catalysis Rev., 10, 243 (1974).
3. H.Podall and W.E.Foster, J.Org.Chem., 23, 401 (1958).
4. J.M.Lalancette, G.Rollin and P.Dumas, Canad.J.Chem., 50, 3058 (1972).
5. C.Ungurenasu and M.Palie, J.C.S.Chem.Comm., 1975, 388.
6. D.Savoia, C.Trombini and A.Umani-Ronchi, J.C.S.Perkin I, in press.
7. It is known that C_8K reacts with weak protic acids as water and alcohols to give a partially reduced graphite, as shown by E.S.C.A. spectroscopy: D.E.Bergbreiter and J.M.Killough, J.C.S.Chem.Comm., 1976, 913.
8. F.Glockling and D.Kingstone, Chem.Ind., 8, 1037 (1961).
9. F.W.Bergstrom and R.Agostinho, J.Amer.Chem.Soc., 67, 2152 (1945); L.Horner and H.Guesten, Ann., 652, 99 (1962); D.S.Watt, Tetrahedron Letters, 1974, 707.