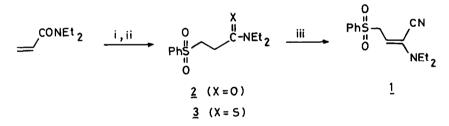
SYNTHESIS AND PHASE-TRANSFER MEDIATED ALKYLATIONS OF 2-DIETHYLAMINO-4- PHENYLSULFONYL-2- BUTENENITRILE AN EFFICIENT HOMOENOLATE EQUIVALENT

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<u>Summary</u> : The title compound is readily prepared from N-diethylacrylamide in three steps. Alkylation of <u>1</u> under phase-transfer conditions yields α -cyanoenamines <u>4</u> which can be transformed into saturated or unsaturated (α , β or β , γ) esters.

In conjunction with our interest in activated forms of carboxamides, we have developed a practical and general synthesis of α -cyanoenamines¹. These, on treatment with strong non-nucleophilic bases, were converted into allylic anions which behave as synthetic equivalents of homoenolate or α -carboxyl vinyl anions². Here we introduce a new homoenolate synthon <u>1</u> which is readily prepared in large amounts and can be alkylated under phase-transfer catalysis conditions. The synthesis of 1 is outlined in Scheme 1.



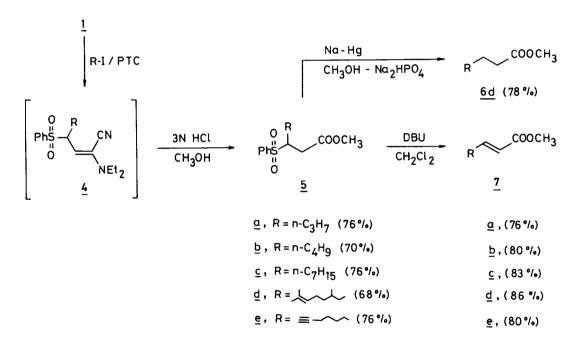
i, $PhSO_2Na$, $AcOH-H_2O$, reflux 8h, 100% ii, P_4S_{10} (1.2 equiv), $NaHCO_3$ (cat.), DME, 15h, 20°C, 96% iii, $(CH_3)_2 SO_4$ (1.2 équiv.), CH_3CN , 12H, 50°C then KCN (1.1 equiv. dry) 15h, 20°C.

Scheme 1

Addition of sodium benzenesulfinate to N-diethylacrylamide yields $\underline{2}$ which is directly treated with P_4S_{10} to give the thioamide-sulfone $\underline{3}$ in 96% overall yield. Successive treatment of $\underline{3}$ with dimethyl sulfate and potassium cyanide followed by filtration through silica gel gave a yellow oil which is recrystallised (ether-petr.ether) to give 60% of pure α -cyanoenamine $\underline{1}$ as the (E) isomer³. Compound $\underline{1}$ can be stored for months without significant change.

As a result of the enhanced acidity of the allylic proton in <u>1</u>, γ -alkylation can be performed in the presence of a wide variety of bases (BuLi or LDA in THF, NaH in THF or DME, tAmOK in tAmOH/THF).

The most practical procedure involves catalytic solid-liquid phase-transfer conditions using solid potassium hydroxyde as the base in THF⁴ (Scheme 2). Typically, a solution of <u>1</u> (7.4 mmoles) and alkyl halide (7.4 mmoles) in THF (6ml) containing a few drops of tricaprylmethylammonium chloride (Aliquat 336[®]) was added to a suspension of finely ground KOH (lg) in THF (4 ml) under vigorous stirring. The reaction time is about 2 hours. The white solid (potassium salt) is removed by filtration through alumina to give the practically pure α -cyanoenamine <u>4</u> as the single (E) isomer. Methanolysis (l.l equiv. of 3N HCl, CH₃OH, 20°C, 3-15h) gave the sulfone-ester <u>5</u> which was purified by chromatography on silica gel (ethyl acetate-petroleum ether, l:4).

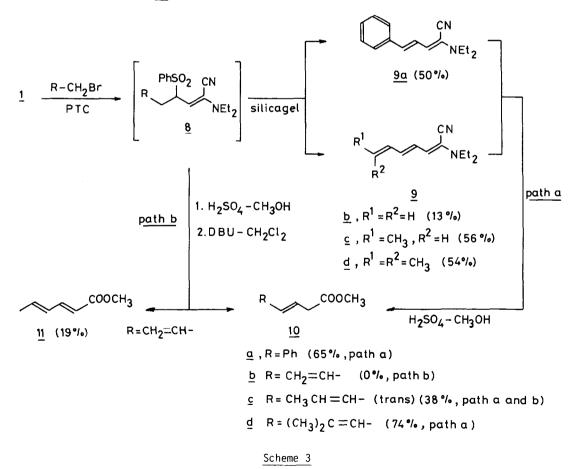


Scheme 2

The sequence proceeds with good yields when the alkylating agent is a primary alkyl iodide. The resulting ester can be readily desulfonylated with sodium-amalgam to give $\underline{6}^5$. Furthermore, base-catalyzed elimination of sulfinic acid smoothly converts $\underline{5}$ into the corresponding α,β ethylenic esters 7. Sequence $1 \rightarrow 6$ and $1 \rightarrow 7$ demonstrate the capacity of α -cyanoenamines 1 to act as a synthetic equivalent of both homoenolate or β -carboxyl vinyl anions 6,7.

It must be mentionned here that the dianion derived from 3-phenylsulfonylpropanoic acid could in principle, serve for the same purpose. However its formation requires fairly drastic conditions and its alkylation proceeds in modest yields⁸. Moreover, our attempts to deuterate or directly alkylate the anion derived from 2 only led to tars.

Secondary alkyl iodides and primary alkyl bromides react only sluggishly with <u>1</u> under the standard phase transfer conditions. The use of more basic systems (NaH or tBuOK in DMF or DMSO) leads to decomposition of <u>1</u>. However, with more reactive bromides, the alkylation proceeds quantitatively under the standard conditions (Scheme 3) but the methanolysis gives low yields of sulfone ester as a result of a competing elimination of benzene sulfinic acid. The lability of the benzenesulfonyl group in α -cyanoenamines <u>8</u> bearing benzylic or allylic substituents at C-4 is further demonstrated by their facile conversion into the new "capto-dative"⁹ trienes <u>9</u> on heating at 50°C in a slurry of silicagel in benzene. Compounds <u>9</u> were obtained as mixtures of configurational isomers in which the all (E) isomers predominate (e.g. 70% for <u>9d</u>). Methanolysis of <u>9</u> selectively yields the β , γ trans-unsaturated ester 10.



As shown for <u>10c</u>, these esters can be even more conveniently prepared in a one pot sequence : alkylation of <u>1</u>, acidic methanolysis and base-catalyzed elimination of benzenesulfinic acid. However, under these conditions, compound <u>10b</u> (R=CH₂=CH-) is isomerized into the fully conjugated methyl sorbate 11.

In conclusion, we have shown that the readily available synthon 1 can be very conviently used for the preparation of saturated or unsaturated (α,β or α,γ) esters as well as of new "capto-dative" polyenes.

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- 3. m.p.: 77-78°C; ¹H NMR (200 MHz) 1.03 (t, J=7.1 Hz, 6H), 3.14 (q, J=7.1 Hz, 4H), 4.03 (d, J=8.5 Hz, 2H), 4.75 (t, J=8.5 Hz, 1H), 7.51-7.71 (m, 3H), 7.86-7.90 (m, 2H).
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