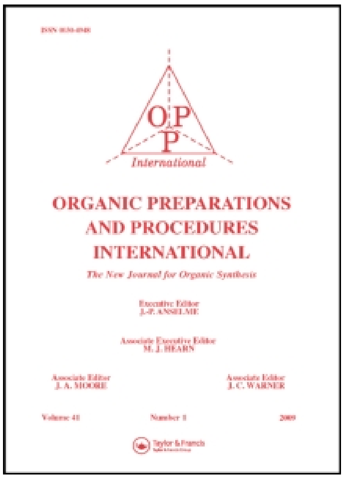

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ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS. NOVEL SYNTHESIS OF PYRAZOLES, PYRIDONES AND PYRROLO[2.3-b]PYRIDONES

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TABLE 2. Spectral Data

Cpd.	IR (KBr)	^{1}H-NMR, 60 MHz ($CDCl_3$/TMS)
IIa	3235, 1692 cm^{-1}	δ 2.13 (s, 3 H), 2.32 (s, 3H), 7.56 (b, 1H), 7.82-8.15 (m, 2 H)
IIb	3236, 1686 cm^{-1}	δ 2.15 (s, 3 H), 2.33 (s, 3 H), 7.52-8.15 (m, 3 H)
IIc	3263, 1653 cm^{-1}	δ 2.13 (s, 3 H), 2.25 (s, 3 H), 7.57 (b, 1 H), 7.90 (b s, 1 H), 8.51 (b s, 1 H)
IId	3250, 1652 cm^{-1}	δ 2.20 (s, 3 H), 2.31 (s, 3 H), 7.50 (b, 1 H), 7.80 (b s, 1 H), 8.34 (b s, 1 H)
IIIa	3300, 1650 cm^{-1}	δ 2.30 (s, 3 H), 7.20-8.35 (m, 8 H)
IIIb	3290, 1653 cm^{-1}	δ 2.28 (s, 3 H), 7.18-8.39 (m, 8 H)
IIIc	3311, 1650 cm^{-1}	δ 2.30 (s, 3 H), 7.20-8.70 (m, 8 H)
IIId	1675, 1709 cm^{-1} (sh)	δ 2.20 (s, 3 H), 7.15-8.10 (m, 12 H)

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ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS. NOVEL SYNTHESIS OF PYRAZOLES, PYRIDONES AND PYRROLO[2,3-b]PYRIDONES

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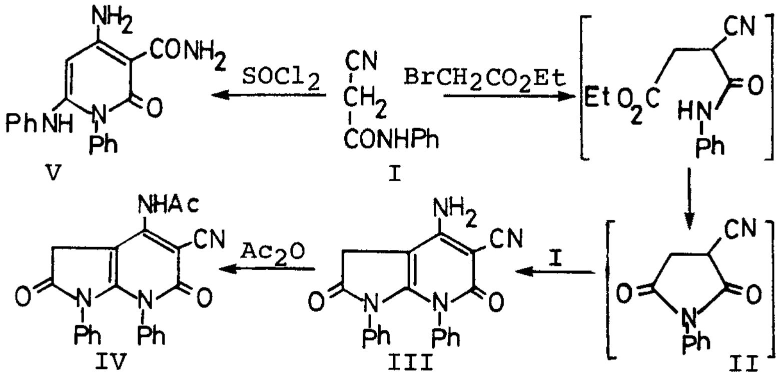
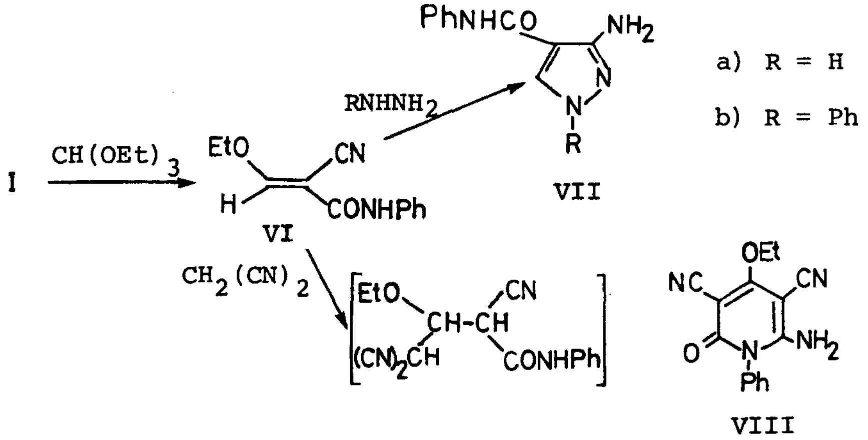
Functionallized nitriles are versatile reagents which are extensively utilized in heterocyclic synthesis.[1-3] Recently the cyanoacetanilide I has been utilized as starting material for the synthesis of azoles[4] and azines.[5] This paper reports the use of I to obtain pyridones and pyrazoles.

Treatment of I with ethyl bromoacetate gave a product of molecular formula $C_{20}H_{14}N_4O_2$; better yields could be obtained on using 2:1 molar ratio of I to ethyl bromoacetate. Structure III was suggested for this product based on the spectral and elemental data. The formation of III may be assumed to proceed via condensation of ethyl bromoacetate with the active methylene group of I followed by cyclization via loss of ethanol to form the intermediate II; reaction of II with I to form the pyrrolopyridine derivative III; when III was refluxed with acetic anhydride the acetamido derivative IV was obtained. Upon being heated at reflux in thionyl chloride, I gave the pyridine derivative V, which may be formed via the addition of active methylene from one mole to the cyano function of another mole then cyclization with loss of water.



On the other hand, compound I reacts with ethyl orthoformate to yield ethoxymethylenecyanoacetanilide VI. The reaction of I with ethyl orthoformate is analogous to the reaction of malononitrile with the same reagent.[6] The pyrazole derivatives VIIa and VIIb were obtained on treatment of VI with hydrazine hydrate and phenylhydrazine respectively. This reaction finds precedent in the reaction of ethoxymethylenemalononitrile with hydrazine hydrate.[7] Compound VI reacted with malononitrile presumably *via* the 2,3-dihydropyridone derivative, which readily underwent air oxidation to afford VIII; ready oxidation of hydropyridones has been previously observed.[8]



EXPERIMENTAL SECTION

Mps. are uncorrected. ^{1}H NMR spectra were determined in DMSO on a Varian 60 MHz Spectrometer with TMS as internal standard and chemical shifts are expressed as δ (ppm). IR spectra were obtained in a Pye Unicam SP-1100 spectrophotometer (KBr). Analytical data were performed by the Microanalytical Centre, Cairo University

Pyrrolo[2,3-b]pyridine Derivative III.- A solution of I (0.02 mol) in 50 ml of ethanol and a few drops of triethylamine was treated with ethyl bromoacetate (0.01 mol). The reaction mixture was heated under reflux for 5 hrs and then evaporated *in vacuo*. The remaining solid product was collected and crystallized from ethanol to give a 65% yield of III as yellow crystals, mp. 135°.

^{1}H NMR: δ 3.3 (m, 2H, CH_2), 4.17 (q, 2H, NH_2), 7.4 (m, 10H, $2C_6H_5$); IR: 1660 cm^{-1} (CO), 2218 cm^{-1} (CN)

Anal. Calcd for $C_{20}H_{14}N_4O_2$: C, 70.2; H, 4.1; N, 16.4

Found: C, 69.9; H, 4.4; N, 16.7

Reaction of III with Acetic Anhydride.- A suspension of III (2 g) in acetic anhydride (30 ml) was refluxed for 4 hrs. The excess acetic anhydride was evaporated *in vacuo* and the reaction mixture was cooled. The resulting solid was collected and crystallized from ethanol to give a 67% yield of IV as yellow crystals, mp. 183°.

IR: 1725 cm^{-1} (CO), 2220 cm^{-1}(CN)

Anal. Calcd for $C_{22}H_{16}N_4O_3$: C, 68.8; H, 4.2; N, 14.6

Found: C, 68.6; H, 4.0; N, 14.6

Pyridone Derivative V.- A mixture of compound I (0.1 mol) and thionyl chloride (50 ml) was heated on a water bath for 1 hr. The excess thionyl chloride was removed under vacuum and the solid was collected and crystallized from ethanol to give a 73% yield of V as brown crystals, mp. 235°.

^{1}H NMR: δ 5.66 (s, 4H, $2NH_2$), 7.5 (m, 10H, $2C_6H_5$), 7.9 (s, 1H, CH), 12.3 (s, br, 1H, NH); IR: 1715 cm^{-1} (CO), 3200-3300 cm^{-1} (NH_2).

Anal. Calcd for $C_{18}H_{16}N_4O_2$: C, 67.5; H, 5.0; N, 17.5

Found: C, 67.2; H, 4.8; N, 17.2

Ethoxymethylenecyanoacetanilide VI.- To a mixture of compound I (0.01 mol) in acetic anhydride (30 ml) was added ethyl orthoformate (0.01 mol). The reaction mixture was heated under reflux for 3 hrs. and then evaporated *in vacuo*. The remaining solid was collected and crystallized from ethanol to give a 65% yield of VI as yellow crystals, mp. 155°.

^{1}H NMR: δ 1.3 (t, 3H, CH_3), 4.38 (q, 2H, CH_2), 6.3 (s, 1H, CH), 7.5 (m, 5H, C_6H_5), 8.3 (s, br, 1H, NH); IR: 1720 cm^{-1} (CO), 2220 cm^{-1} (CN).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.7; H, 5.6; N, 13.0

Found: C, 67.1; H, 5.3; N, 13.1

Pyrazole Derivatives VIIa and VIIb.- A solution of VI (0.01 mol) in ethanol (50 ml) was treated with 0.01 mol of hydrazine hydrate (or phenylhydrazine). The reaction mixture was refluxed for 2 hrs. and then evaporated *in vacuo*. The solid was collected and crystallized from ethanol.

Compound VIIa, 63% yield, yellow crystals, mp. 170°.

^{1}H NMR: δ 7.5 (m, 5H, C_6H_5), 8.3 (s, br, 1H, NH), 5.7 (s, 2H, NH_2); IR: 1710 cm^{-1} (CO), 3330 cm^{-1} (NH_2).

Anal. Calcd for $C_{10}H_{10}N_4O$: C, 59.4; H, 5.0; N, 27.2

Found: C, 59.2; H, 5.1; N, 27.6

Compound VIIb, 70% yield, brown crystals, mp. 190°.

^{1}H NMR: δ 7.4 (m, 5H, C_6H_5), 8.3 (s, br, 1H, NH), 5.66 (s, 2H, NH_2); IR: 1710 cm^{-1} (CO), 3330 cm^{-1} (NH_2).

Anal. Calcd for $C_{16}H_{14}N_4O$: C, 69.1; H, 5.0; N, 20.1

Found: C, 68.9; H, 5.2; N, 20.3

3,5-Dicyanopyridin-6-one Derivative VIII.- To a solution of VI (0.01 mol) in ethanol (50 ml) was added malononitrile (0.01 mol) and a few drops of triethylamine. The reaction mixture was refluxed for 6 hrs. and then evaporated *in vacuo*. The remaining solid was collected and crystallized from ethanol to give a 70% yield of VIII as brown crystals, mp. 240°.

IR: 1710 cm^{-1} (CO), 2215 cm^{-1} (CN), 3320 cm^{-1} (NH_2).

Anal. Calcd for $C_{15}H_{12}N_4O_2$: C, 64.3; H, 4.3; N, 20.0

Found: C, 64.0; H, 4.5; N, 19.8

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SYNTHESIS OF 2-ALKOXY-5-NITROBENZAMIDES BY PHASE-TRANSFER CATALYZED NUCLEOPHILIC SUBSTITUTION OF 2-CHLORO-5-NITROBENZAMIDES

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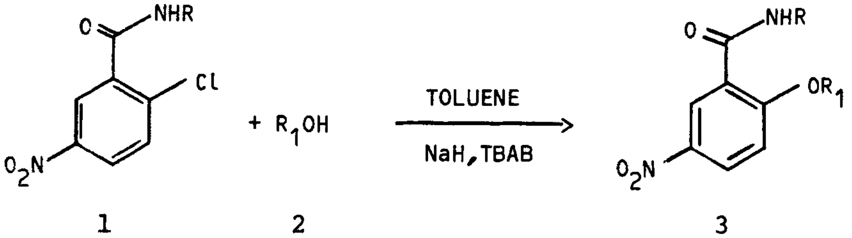
A new application of liquid-liquid PTC (LL-PTC) for the synthesis of ethers of primary alcohols by nucleophilic substitution of 2-chloro-5-nitrobenzamides was previously reported;[1] we also demonstrated that all other alcohols and phenols failed to give any product with acceptable yields even under forcing conditions. This could be explained in terms of steric hindrance of the ion-pair extracted together with water of solvation into the organic phase.[2] In order to test this hypothesis and to provide a generalized application of the proposed reaction for ether preparation, we decided to investigate a heterogeneous solid-liquid (SL) system where the nucleophilicity of the ion pair is strongly enhanced.[3,4]



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We report our results of the conversion of 2-chloro-5-nitrobenzamides 1