Preparation of Some Highly Polarised Ethenes by the Addition of Amines to Suitable Carbonitriles

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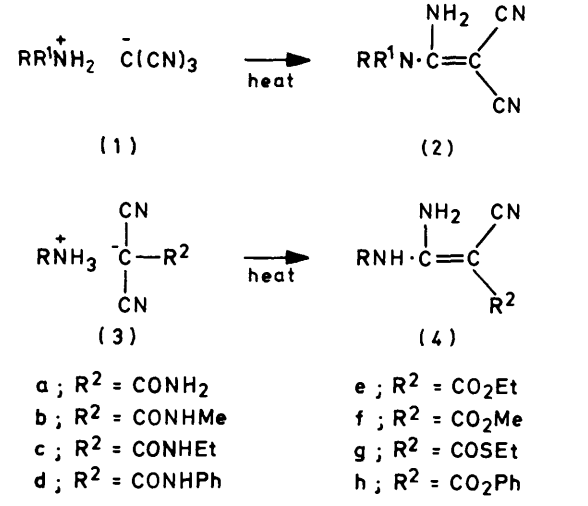
Substituted diaminomethylene derivatives of malononitrile (2) and of cyanoacetamides, cyanoacetates, and cyanothiolacetates (4)—(6) have been prepared from amine salts of tricyanomethane (1) and of related anions (3) having one ester or amide function in place of a cyano group.

Allenstein [1] found that arylammonium tricyanomethanides (1; R = Aryl) were converted into substituted diaminomethylenemalononitriles (2) on heating; Trofimenko, Little, and Mower [2] carried out the same reaction with piperidinium and pyrrolidinium tricyanomethanides indicating that secondary amine salts might be used. The scope of the reaction has now been expanded to provide a route to a wide variety of substituted diaminoethylene derivatives (2) and also (4) of cyanoacetamides, cyanoacetates, and cyanothiolacetates (Scheme 1). A convenient procedure for preparing the required potassium salts of the anions in the intermediates (3) has also been developed.

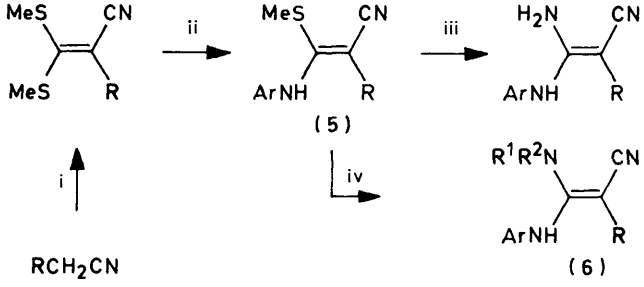
The route to the diaminomethylene compounds (2) and (4) (Scheme 1) is complementary to that described by Gompper and Toepfl [3] (Scheme 2). They found it necessary to use pressure in the reaction of intermediates (5) with ammonia, and their route involved displacement of methanethiol, with the obvious attendant problems. The route in Scheme 1 is thus often more convenient. On the other hand, we found the method of Scheme 2 worked very well at normal pressure when aliphatic amines were used instead of ammonia, to give products (6) not obtainable from the salts (1) and (3), since nitrile-derived amino functions are inevitably primary.

Middleton and Engelhardt [4] also prepared some diaminomethylenemalononitriles from dialkoxymethylenemalononitriles, and obtained a cyanopropenamide (4a) from one of them by hydrolysis. A few diaminocyanopropenoates (4e, f) have been reported before, prepared from 3-amino-3-aryloxy-2-cyanopropenoates [5] or from 3-amino-2-cyano-4,4,4-trichlorobutenoates.[6,7]

Allenstein [1] had prepared his salts (1) from anilines and aminochloromethylenemalononitrile, and so they were mixed with arylammonium chlorides. He heated the dry mixtures to obtain the methylenemalononitriles (2). Trofimenko, Little, and Mower [2] used no solvent when they prepared the piperidine and pyrrolidine derivatives. We tried heating the salts (1) in xylene, pyridine, 2-methoxyethanol, water, and the amine from which the particular salt had been prepared. Some aliphatic salts reacted well in xylene, but water proved to be the most convenient medium for the conversion of arylammonium and *N*-alkylarylammonium salts. It was not necessary to isolate the required salts, being sufficient to heat a mixture of the arylamine, potassium tricyanomethanide (which we prepared by a modification of the published method [2] from dibromomalononitrile–potassium bromide complex [8]), and an equivalent amount of hydrochloric acid in water. Hydrochloric acid was chosen because the by-product, potassium chloride, had a high water-solubility and was thus easily removed. The route was also suitable for conversion of the related arylammonium salts (3) into the diaminomethylene derivatives (4). As far as could be ascertained qualitatively, the reaction rate depended inversely on the basicity of the amine



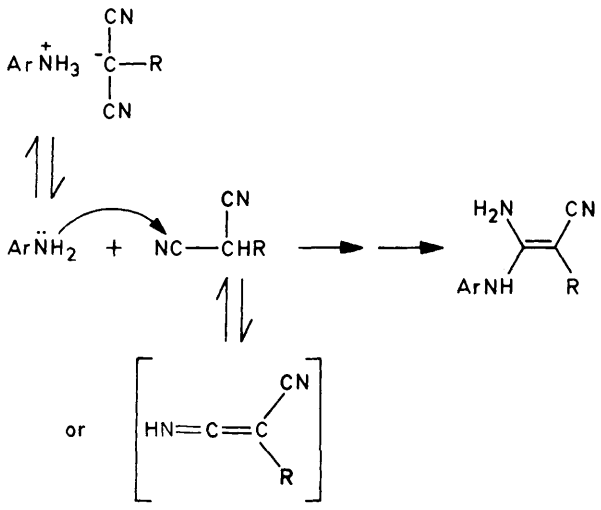
Scheme 1.



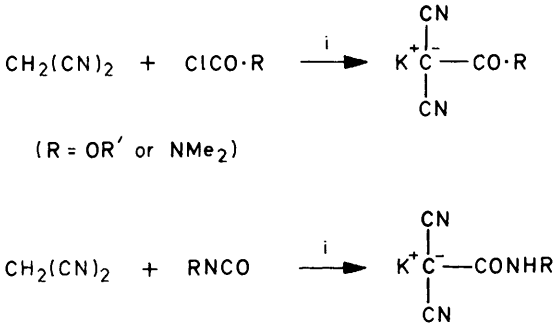
Scheme 2. *Reagents:* i, CS_2; ii, $ArNH_2$; iii, NH_3; iv, R^1R^2NH

used. This is understandable if it is supposed that the reaction requires dissociation of the salt to allow attack by the free amine on the nitrile, or related ketenimine (Scheme 3). The acids related to the salts (1) and (3) are all strong, so at best the concentration of free acid in the reaction mixture will be low. With the salts of more basic amines, such as aliphatic amines, the concentration of free amine would also be very low, and the reaction was indeed unacceptably slow in these cases. Some of these salts were converted quickly when heated in the related amine instead of water. Only a few examples were tried, and only one using an acid other than tricyanomethane; the piperidine salt of ethyl dicyanoacetate reacted well in piperidine.

We have seen no evidence of geometrical isomerism amongst the foregoing compounds (4)—(6), an observation consistent



Scheme 3.



Scheme 4. *Reagents.* i, aq.KOH

with previous reports [9] that similar, polarised ethylenes have very low energy barriers to rotation about the formal double bond. The very high polarity of the double bond in these 3-aminoprop-enenitriles, -enamides and -enoate esters (4)—(6), predictable from the electronic characters of the substituents which make carbon-3 positive and carbon-2 negative, is confirmed by ^{1}H n.m.r. data. Thus the ^{1}H chemical shifts of the 2-carboxyamide protons are at an unusually high field, around δ 6.5—7.5, whilst the shifts of the 3-amino group protons, around δ 7.8—10.8 (in the compounds examined), are at unusually low field. This respective shielding and deshielding is consonant with the expected directions of the extreme polarisation of the π-electron system.

The potassium salts of dicyanoacetates and dicyanothiolacetates needed in this work were prepared by a convenient new procedure, using the addition of malononitrile and a chloroformate in tetrahydrofuran to aqueous potassium hydroxide. Potassium salts of *N*-monoalkyldicyanoacetamides and of *N*,*N*-dimethyldicyanoacetamide were prepared similarly using alkyl isocyanates and dimethylcarbamoyl chloride, respectively (Scheme 4).

Experimental

Potassium and Alkylammonium Salts of Tricyanomethanide (cf. *Ref.* 2).—Dibromomalononitrile–potassium bromide complex [8] (1 kg) was added to a suspension of potassium cyanide (500 g) in acetone (2.3 l), with stirring during 30 min, and with cooling, when needed, to keep the temperature at 35—40 °C. The mixture was then stirred at 35—40 °C for 1.5 h and then heated to 50 °C and filtered hot. The filtrate was allowed to cool and diluted with xylene (2.5 l) to precipitate potassium tricyanomethanide (290 g, 58% based on KCN), which was washed with ethanol to remove brown impurities. The product was free from cyanide (Prussian blue test), contained less than 2% potassium bromide (measurement of material insoluble in dry acetone), and had a purity of >95% as shown by conductiometric titration against silver nitrate.

From potassium tricyanomethanide, by metathesis in water with amine hydrochloride, the following ammonium tricyanomethanides were prepared: *N*-decyl- (94%), m.p. 125—127 °C (water), *N*-butyl-*N*-ethyl- (95%) as an oil, and *N*-ethyl-*N*-phenyl- (80%), m.p. 60 °C (decomp.).

Potassium Salt of 2,2-*Dicyano*-N-*methylacetamide*.—A solution of malononitrile (6 g, 0.09 mol) and methyl isocyanate (6 ml, 5.8 g, 0.1 mol) in tetrahydrofuran (10 ml) was added, with stirring, to one of potassium hydroxide (5.1 g, 0.09 mol) in water (40 ml) during 10 min at 25—30 °C (water cooling). After 1 h the red solution was evaporated to dryness and the residue recrystallised from propan-2-ol–water (1 : 1) to give the *product* (2 g, 14%), m.p. 294—295 °C (decomp.) (Found: C, 37.05; H, 2.3; N, 26.0. $C_5H_4KN_3O$ requires C, 37.25; H, 2.5; N, 26.1%). Concentration of the mother-liquors gave more product (6.4 g, 43%), m.p. 283—285 °C (decomp.), but with identical i.r. spectrum.

Potassium Salt of 2,2-*Dicyano*-N-*ethylacetamide*.—This *salt* was prepared similarly, and precipitated (17%) from the reaction solution at 0 °C, m.p. 270 °C (decomp.) (Found: C, 41.15; H, 3.55; N, 23.6. $C_6H_6KN_3O$ requires C, 41.15; H, 3.45; N, 24.0%). Concentration of the filtrate gave a further crop (34%) with identical i.r. spectrum.

Potassium Salt of Ethyl Dicyanoacetate.—A solution of ethyl chloroformate (570 g, 5.25 mol) and malononitrile (330 g, 5 mol) in tetrahydrofuran (500 ml) was added, with stirring, to one of potassium hydroxide (560 g, 10 mol) in water (2 : 1) during 40 min, keeping the temperature below 40 °C. The mixture was stirred at room temperature for 1 h and then cooled to 0 °C. The precipitate was washed (ice-cold water and with ethanol) to give the *product* (416 g, 47%), m.p. 297—298 °C (decomp.) (Found: C, 40.75; H, 3.15; N, 15.7. $C_6H_5KN_2O_2$ requires C, 40.9; H, 2.85; N, 15.9%).

Potassium Salt of S-*Ethyl Dicyanoethanethioate*.—This *salt* (47%) was prepared analogously, m.p. 285 °C (decomp.) (Found: C, 37.25; H, 2.3; N, 14.55. $C_6H_5KN_2OS$ requires C, 37.5; H, 2.6; N, 14.6%).

2,2-*Dicyano*-N-*phenylacetamide* (cf. *Ref.* 11).—Triethylamine (70 ml, 51 g, 0.505 mol) was added slowly to propane-1,3-dinitrile (33 g, 0.5 mol) and phenyl isocyanate (59.6 g, 0.5 mol) in tetrahydrofuran (200 ml), keeping the temperature below 40 °C. At 3 °C the triethylammonium salt of 2,2-dicyano-*N*-phenylacetamide (116 g, 81%) separated, m.p. 93—94 °C (from tetrahydrofuran). This salt was stirred in water, strongly acidified (conc. HCl) to give dicyano-*N*-phenylacetamide, contaminated with 20% of its triethylamine salt (as shown by titration): this mixture was used for preparing compound (4d; R = ClC_6H_4) and analogues.

The following illustrate general procedures used to prepare many new substituted diaminomethylenemalononitriles.[10]

(*a*) 3-*Amino*-2-*cyano*-3-*decylaminopropenenitrile*. Decylammonium tricyanomethanide (8 g) was heated under reflux in xylene (50 ml) for 4 h. Recrystallisation (ethanol) gave the

waxy *product* (2; R = $C_{10}H_{21}$, R^1 = H) (4.4 g, 55%), m.p. 98—100 °C (Found: C, 67.7; H, 9.75; N, 22.55. $C_{14}H_{24}N_4$ requires C, 67.7; H, 9.7; N, 22.6%).

(*b*) 3-*Amino*-3-(N-*butyl*-N-*ethylamino*)-2-*cyanopropenenitrile*. *N*-Butyl-*N*-ethylammonium tricyanomethanide (18.6 g) was heated in *N*-ethylbutylamine (100 ml) for 8 h. Cooling the solution to 0 °C precipitated the *product* (2; R = Bu, R^1 = Me) (8.6 g, 46%), m.p. 107—110 °C (Found: C, 62.4; H, 8.35; N, 29.45. $C_{10}H_{16}N_4$ requires C, 62.45; H, 8.4; N, 29.15%). Acidification of the reaction liquors with 2M-hydrochloric acid (600 ml) gave a further crop (5 g, 27%), m.p. 106—110 °C.

(*c*) 3-*Amino*-2-*cyano*-3-(N-*ethyl*-N-*phenylamino*)*propenenitrile*. *N*-Ethyl-*N*-phenylammonium tricyanomethanide (10.6 g, 0.05 mol) was heated under reflux in water (100 ml) for 4 h. Recrystallisation of the precipitate from ethanol gave the *product* (2; R = Ph, R^1 = Et) (6.4 g, 60%), m.p. 151—153 °C (Found: C, 68.0; H, 5.8; N, 26.45. $C_{12}H_{12}N_4$ requires C, 67.9; H, 5.7; N, 26.4%).

(*d*) 3-*Amino*-3-(2-*chlorophenylamino*)-2-*cyanopropenenitrile*. 2-Chloroaniline (6.4 g, 0.05 mol), potassium tricyanomethanide (7 g, 0.055 mol), concentrated hydrochloric acid (4.5 ml, *ca.* 0.05 mol), and water (50 ml) were heated under reflux for 8 h. Recrystallisation of the precipitate from 2-methoxyethanol gave the *product* (2; R = 2-ClC_6H_4, R^1 = H) (6.2 g, 57%), m.p. 203—205 °C (Found: C, 54.7; H, 3.5; N, 25.8. $C_{10}H_7ClN_4$ requires C, 54.9; H, 3.25; N, 25.65%). 3-*Amino*-2-*cyano*-3-*piperazinopropenenitrile*, prepared similarly (14 h), had m.p. 180—184 °C (yield, 70% after 4 days) (Found: C, 54.2; H, 6.3; N, 39.8. $C_8H_{11}N_5$ requires C, 54.2; H, 6.25; N, 39.5%).

In many other similar preparations, required reaction times ranged from a few minutes to 40 h.

Compounds (4)—(6) listed below were prepared similarly from other carbonitrile salts by heating them with amines and hydrochloric acid in water. 3-*Amino*-2-*cyano*-3-(3-*nitrophenylamino*)*propenamide* (4a; R = 3-NO_2·C_6H_4). This *compound* (73%) was prepared from the potassium salt of 2,2-dicyanoacetamide (0.11 mol), concentrated hydrochloric acid (9 ml, 0.1 mol), water (100 ml), and 3-nitroaniline (0.1 mol) under reflux for 12 h, m.p. 233—235 °C (from 2-methoxyethanol) (Found: C, 48.35; H, 3.65; N, 28.2. $C_{10}H_9N_5O_3$ requires C, 48.6; H, 3.65; N, 28.35%). Similarly prepared (using appropriate amines and dicyano compounds) were 3-*amino*-2-*cyano*-3-(3-*methylphenylamino*)-N-*methylpropenamide* (4b; R = 3-MeC_6H_4) (38 h) (52%), m.p. 75—77 °C (after being washed with ethanol) (Found: C, 62.5; H, 6.45; N, 24.4. $C_{12}H_{14}N_4O$ requires C, 62.6; H, 6.15; N, 24.35%), 3-*amino*-3-(3-*chlorophenylamino*)-2-*cyano*-N-*ethylpropenamide* (4c; R = 3-ClC_6H_4) (24%), m.p. 131—133 °C (from ethanol) (Found: C, 54.3; 4.75; N, 21.45. $C_{12}H_{13}ClN_4O$ requires C, 54.45; H, 4.9; N, 21.15%), and 3-*amino*-3-(4-*chlorophenylamino*)-2-*cyano*-N-*phenylpropenamide* (4d; R = 4-ClC_6H_4) (20 h; 80% yield), m.p. 194 °C (from 2-methoxyethanol) Found: C, 61.65; H, 4.3; N, 17.7. $C_{16}H_{13}ClN_4O$ requires, C, 61.45; H, 4.2; N, 17.9%).

Ethyl 3-*amino*-2-*cyano*-3-(4-*methoxyphenylamino*)*propenoate* (4e; R = 4-$MeOC_6H_4$). This *compound* (31%) was prepared from the potassium salt of ethyl dicyanoacetate (0.11 mol), 4-methoxyaniline (0.1 mol), concentrated hydrochloric acid (9 ml, 0.1 mol), and water (100 ml) under reflux for 24 h, m.p. 174—176 °C (Found: C, 59.7; H, 5.9; N, 16.1. $C_{13}H_{15}N_3O_3$ requires C, 59.75; H, 5.8; N, 16.1%). Analogously from potassium *S*-ethyl dicyanoethanethioate, S-*ethyl* 3-*amino*-2-*cyano*-3-(3,4-*dichlorophenylamino*)*propenethioate* (4g; R = 3,4-$Cl_2C_6H_3$) was obtained as an oil, which on trituration with propan-2-ol gave the product (63%), m.p. 142—145 °C (Found: 45.8; H, 3.4; N, 13.25. $C_{12}H_{11}Cl_2N_3OS$ requires C, 45.6; H, 3.5; N, 13.3%).

Ethyl 3-*amino*-2-*cyano*-3-*piperidinopropenoate* (4e; RNH = $[CH_2]_5N$). The piperidine salt of ethyl dicyanoacetate (7.5 g, 0.033 mol) was heated under reflux in piperidine (20 ml) for 24 h. The solution was poured into a mixture of ice (70 g) and concentrated hydrochloric acid (25 ml) and the precipitate was recrystallised (ethanol) to give the *product* (1.8 g, 25%), m.p. 104—106 °C (Found: C, 59.0; H, 8.0; N, 19.1. $C_{11}H_{17}N_3O_2$ requires C, 59.15; H, 7.8; N, 18.8%).

Potassium 4-(1-*amino*-2-*cyano*-2-*ethoxycarbonylethenylamino*)*benzenesulphonate hemihydrate* (4e; R = $KO_3SC_6H_4$). 4-Aminobenzenesulphonic acid (8.7 g, 0.05 mol), the potassium salt of ethyl dicyanoacetate (9 g, 0.051 mol), and water (50 ml) were heated under reflux for 36 h. The solution was evaporated to dryness and the residue was recrystallised from a minimum of water to give the *product* (6 g, 34%), m.p. 260 °C (decomp.) (Found: C, 40.1; H, 3.45; N, 11.8. $C_{12}H_{12}KN_3O_5S·\frac{1}{2}H_2O$ requires C, 40.2; H, 3.7; N, 11.7%. The water content was confirmed by thermogravimetric analysis).

Phenyl 3-*amino*-2-*cyano*-3-*phenylaminopropenoate* (4h; R = Ph). A solution of malononitrile (6.6 g, 0.1 mol) in phenyl chloroformate (13 ml, *ca.* 0.103 mol) was added slowly, with stirring, to one of potassium hydroxide (11.2 g, 0.2 mol) in water (25 ml), with ice-cooling to keep the temperature below 40 °C. The mixture was stirred at 30—40 °C for a further 15 min and then cooled to 0 °C. A small amount of diphenyl carbonate which was precipitated was rejected. The filtrate was evaporated to dryness and the residue washed (ether) and dried. The crude potassium salt of phenyl dicyanoacetate (10.5 g, 0.047 mol, 47%) was heated under reflux with aniline hydrochloride (6.1 g, 0.047 mol) in water (58 ml) for 24 h and the sticky precipitate triturated with ethanol to give a blue-grey powder. Recrystallisation from dimethylformamide gave the *product* (2 g, 14%) (total yield, 24% of purified product), m.p. 214—215 °C (Found: C, 68.5; H, 4.7; N, 15.1. $C_{16}H_{13}N_3O_2$ requires C, 68.8; H, 4.7; N, 15.05%).

Methylthio(phenylamino)methylenemalononitrile (5; R = CN, Ar = Ph) was prepared by the method of Gompper and Toepfl.[3c] Similarly obtained were 2-*cyano*-3-*methylthio*-3-(*phenylamino*)*propenamide* (5; R = $CONH_2$, Ar = Ph) (4 h) (87%), m.p. 151—153 °C (Found: C, 57.0; H, 5.0; N, 18.15. $C_{11}H_{11}N_3OS$ requires C, 56.65; H, 4.75; N, 18.0%). δ [$(CD_3)_2SO$] 2.16 (3 H, s, SMe), 7.3 (2 H, br, $CONH_2$; removed by D_2O), 7.6 (5 H, s, Ph), and 10.6 (1 H, s, NH; removed by D_2O), and *methyl* 3-(4-*bromophenylamino*)-2-*cyano*-3-*methylthiopropenoate* (5; R = CO_2Me, Ar = 4-BrC_6H_4) (4 h) (39%), m.p. 140—142 °C (Found: C, 43.7; H, 3.0; N, 8.55. $C_{12}H_{11}BrN_2O_2S$ requires C, 44.05; H, 3.4; N, 8.55%), δ [$(CD_3)SO$] 2.28 (3 H, s, SMe), 3.67 (3 H, s, OMe), 7.2—7.7 (4 H, Ar H), and 10.8 (1 H, s, NH; removed by D_2O).

2-*Cyano*-3-*methylamino*-3-*phenylaminopropenenitrile* (6; R = CN, R^1 = Me, R^2 = H, Ar = Ph). Methylthio(phenylamino)methylenemalononitrile (6.4 g, 0.03 mol), methylamine (4.8 ml of a 27.5% w/v solution in ethanol ≡ 1.3 g, 0.042 mol), and ethanol (25 ml) were heated under reflux for 7 h, and the solution was then cooled. Recrystallisation of the precipitate from ethanol gave the *product* (2.5 g, 42%), m.p. 168—170 °C (Found: C, 66.75; H, 5.2; N, 27.95. $C_{11}H_{10}N_4$ requires C, 66.65; H, 5.1; N, 28.25%), δ [$(CD_3)_2SO$] 2.8 (3 H, d, Me), 7.0—7.5 (5 H, m, Ph), 7.85 (1 H, br, N*H*Me; removed by D_2O), and 9.3 (1 H, s, N*H*Ph; removed by D_2O).

Similarly prepared were 2-*cyano*-3-*dimethylamino*-3-(*phenylamino*)*propenamide* (6; R = $CONH_2$, R^1 = R^2 = Me, Ar = Ph) (54%), m.p. 164—166 °C (Found: C, 62.8; H, 6.45; N, 24.45. $C_{12}H_{14}N_4O$ requires C, 62.6; H, 6.15; N, 24.35%); δ [$(CD_3)_2SO$] 2.82 (6 H, s, NMe_2), 6.55 (2 H, s, $CONH_2$; removed by D_2O), 6.9—7.4 (5 H, m, Ph), and 10.2 (1 H, s, NH; removed by D_2O), and *methyl* 3-(4-*bromophenylamino*)-2-*cyano*-3-(*ethylamino*)*propenoate* (6; R = CO_2Me, R^1 =

Et, R^2 = H, Ar = 4-BrC_6H_4) (20 h) (51%), m.p. 144—145 °C (from ethanol) (Found: C, 48.2; H, 4.25; N, 13.15. $C_{13}H_{14}BrN_3O_2$ requires C, 48.15; H, 4.35; N, 12.95%).

3-*Amino*-2-*cyano*-3-*phenylamino*-N,N-*dimethylpropenamide*. A solution of malononitrile (6.6 g, 0.1 mol) and *N*,*N*-dimethylcarbamoyl chloride (11 g, 0.102 mol) in tetrahydrofuran (10 ml) was added with stirring to potassium hydroxide (11.2 g, 0.2 mol) in water (30 ml) at <30 °C during 15 min. After 2 h the solution was evaporated, and the residue was washed with ethanol, dried, and dissolved in water. This solution of the potassium salt of dicyano-*N*,*N*-dimethylacetamide was refluxed with aniline hydrochloride (10.4 g, 0.08 mol) for 14 h. At room temperature the *product* (6; R = $CONMe_2$, R^1 = R^2 = H, Ar = Ph) (1.4 g) separated, m.p. 134—135 °C (from ethanol) (Found: C, 62.85; H, 6.3; N, 24.0. $C_{12}H_{14}N_4O$ requires C, 62.6; H, 6.15; N, 24.35%).

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