PREPARATION OF DINITRILES OF AMINOMALONIC ACIDS*

Z. ARNOLD and M. SVOBODA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 116 10 Prague 6

Received July 13th, 1976

The novel preparation of the type *I* aminomalonodinitriles consists in the reaction of a tertiary carboxamide with phosgene and the subsequent treatment with cuprous cyanide. A simple preparation of the chloroform solution of N,N-dimethyl-N-chloromethyleneammonium chloride (*IIa*) from dimethylformamide and phosgene is reported in detail.

Some time ago, the preparation of N,N-dimethylaminomalonodinitrile (*Ia*) on a larger scale was required. Compound *Ia* was prepared for the first time in this Laboratory by reaction of N,N-dimethyl-N-chloromethyleneammonium chloride (*IIa*) with hydrogen cyanide in the presence of sodium cyanide[1]. Later on, compound *Ia* was obtained by Gold and Bayer[2] by the reaction of hydrogen cyanide with tetramethylformamidinium salts. In order to circumvent handling of anhydrous hydrogen cyanide, a modification of the original method[1] has been now developed consisting in introduction of the nitrile groups by means of cuprous cyanide. When the exothermic reaction in acetonitrile is over, the product remains bound in the form of a complex with cuprous salts and must be liberated prior to the isolation by the action of a reagent which forms stronger complexes with cuprous salts then the aminodinitrile. In the case of compound *Ia*, introduction of gaseous ammonia into the reaction mixture proved to be the most advantageous procedure for decomposition of the complex. The aminodinitrile *Ia* is obtained in about 70% yields, the procedure being simple, non-hazardous, and suitable for preparations on a larger scale. The starting N,N-dimethyl-N-chloromethyleneammonium chloride (*IIa*) is conveniently[3,4] obtained from dimethylformamide and phosgene in an almost quantitative yield; the application of a concentrated chloroform solution of the reagent *IIa* is particularly advantageous (for its preparation see the experimental part).

$(CH_3)_2N{-}CR(CN)_2$ (*I*) $\qquad$ $[(CH_3)_2N{=}CR{-}Cl]^{(+)}Cl^{(-)}$ (*II*)

a, R = H; *b*, R = CH_3; *c*, R = C_6H_5; *d*, R = SCH_3; *e*, R = $N(CH_3)_2$

* Part XXXV in the series Synthetic Reactions of Dimethylformamide; Part XXXIV: This Journal *42*, 1027 (1977).

The aminomalonodinitriles *I* belong to poorly examined substances. In addition to compound *Ia*, the methyl homologue *Ib* was prepared by a two-step procedure[5] from N,N-dimethylacetamide (yield 55·8%) by the O-alkylation with triethyloxonium fluoroborate and refluxing of the thus-obtained quaternary salt with alkali metal cyanide in acetonitrile for 50 h. In the attempted application of this procedure to the synthesis of the dinitrile *Ia*, the yield was 2·7% only[5]. The method starting from thioamides[6] seems to be more general. The S-alkylation with an alkyl iodide in step one is followed by the reaction with mercuric cyanide in step two. In addition to the above mentioned compounds *Ia* and *Ib*, the derivatives *Ic* and *Id* were prepared by the thioamide method.

When compared with the above two methods[5,6], the present synthesis of compound *Ia* appears more advantageous in view of the accessibility of the starting material and simple reaction conditions. It was therefore of interest to examine a wider applicability of the present procedure with the use of three additional dimethylamino compounds differring in their reactivity, namely, N,N-dimethylacetamide, N,N-dimethylbenzamide, and tetramethylurea. All the corresponding products *I* were obtained in satisfactory yields but some reaction conditions had to be modified. Since the stability of cuprous complexes was higher than in the case of compound *Ia*, some agents more active than ammonia were looked after. An aqueous solution of alkali metal cyanide proved to be the most efficient reagent for this purpose. Depending on the substituent R, the above tertiary amides may be expected to display a different reactivity towards phosgene from an instantaneous reaction to a reaction requiring many hours. A great variability can also be expected in the stability of the intermediates *II* that in some cases may undergo further transformations such as autocondensations[8], elimination of hydrogen chloride[9] and the like. For dimethylacetamide a procedure was developed which should be to our opinion of general applicability in cases of a high reactivity of the starting amide and decreased stability of the intermediary imonium chloride *II*: a suspension of cuprous cyanide in the acetonitrile solution of dimethylacetamide is treated at a low temperature with a solution of phosgene in chloroform. The product *Ib* was finally isolated in 57% yield. On the other hand, preparation of the phenyl derivative *Ic* from N,N-dimethylbenzamide exemplifies a procedure for the case of a stable imonium chloride *II*. An interesting application is represented by the preparation of compound *Ie* which is simultaneously a geminal dinitrile and a geminal bis(dimethylamino) derivative. On the basis of observations reported in the present paper, suitable conditions could be found to our opinion for the conversion of further tertiary amides and related compounds to the corresponding aminodinitriles of type *I*.

The present dimethylaminomalonodinitriles were characterised by IR spectra exhibiting as a common feature a region of $\nu(CH_3)$ vibrations containing six bands at about 2800–3000 cm^{-1}. On the other hand, the $\nu(CN)$ vibrations are extremely

weak, probably due to the presence of the dimethylamino group[1]. Contrary to the earlier reported[1] IR spectrum of compound *Ia*, the present spectrum taken with a sample purified by repeated chromatography and cautious distillation does not contain any band in the carbonyl region.

EXPERIMENTAL

The IR spectra were taken on a Zeiss UR-20 apparatus. The ^{1}H-NMR spectra were recorded on a Varian HA-100 apparatus.

Preparation of 2M N,N-Dimethyl-N-chloromethyleneammonium Chloride (*IIa*) in Chloroform

At about 15°C, phosgene is introduced into a solution of dimethylformamide (146·2 g; 2 mol) in chloroform (600 ml); two sulfuric-acid-containing wash-bottles are placed before the reaction flask and behind the reflux condenser. As soon as the reaction sets in (evolution of carbon dioxide), the mixture is maintained at a temperature below 10°C by external ice-cooling. During the reaction, the streams of phosgene and escaping carbon dioxide are of an equal intensity. As soon as the stream of carbon dioxide is markedly slower, the introduction of phosgene is interrupted and the mixture is allowed to react spontaneously to the cessation of carbon dioxide evolution. In order to remove excess phosgene, small portions (about 1 ml each) of dimethylformamide are gradually added as long as carbon dioxide is evolved. The mixture is finally made up to the volume of 1 000 ml with chloroform to afford a 2M solution of the required reagent.

N,N-Dimethylaminomalonodinitrile (*Ia*)

In a nitrogen atmosphere at −10°C, a suspension of cuprous cyanide (112·5 g; 1·25 mol) in acetonitrile (450 ml) was treated dropwise with a 2·2M chloroform solution of N,N-dimethyl-N--chloromethyleneammonium chloride (*IIa*; 227 ml; 0·5 mol). The mixture was stirred for 4 h under cooling with ice and water, the flask surrounded with ice and sodium chloride, and the content saturated with gaseous ammonia at a temperature up to +10°C. The precipitate was filtered off and washed with four 250 ml portions of ether. The filtrate and washings were combined, filtered with active charcoal, and the filtrate evaporated under diminished pressure. The residue was dissolved in ether (500 ml), the ethereal solution filtered with active charcoal, the filtrate evaporated, and the residue rectified under diminished pressure. Yield, 38·2 g (70%) of compound *Ia*, b.p. 32−33°C/0·2 Torr, n_D^{20} 1·4302 (reported[6], n_D^{25} 1·4331). The purified sample (n_D^{20} 1·4282) for spectral measurements was obtained by chromatography on silica gel in 1 : 1 light petroleum–--ether solvent mixture. ^{1}H-NMR spectrum (CCl_4): δ 2·45 s (6 H), δ 4·60 s (1 H). IR spectrum (CCl_4): $\nu(CH_3)$ 2802, 2843, 2881, 2920, 2961, 2992 cm^{-1}; ν(CN) 2233 (vw) cm^{-1}.

(N,N-Dimethylamino)methylmalonodinitrile (*Ib*)

At −40°C, a stirred suspension of cuprous cyanide (3·0 g) in a solution of dimethylacetamide (0·87 g; 0·01 mol) in acetonitrile (25 ml) was treated with 20% solution of phosgene in chloroform (6 ml). The stirring was continued at −30°C for 30 min and then at 0°C for 1 h. The mixture was diluted with ether (80 ml), the precipitate collected with suction, and washed with ether. The precipitate in ether (50 ml) was then under ice-cooling treated dropwise with a solution of sodium cyanide (10·0 g) in water (20 ml) and the layers were separated. The aqueous layer was extracted with ether (50 ml). The ethereal layers were combined, washed with water (4 times

10 ml), dried over anhydrous magnesium sulfate, evaporated, and the residue rectified under diminished pressure. Yield, 0·71 g (57%) of compound *Ib* boiling at 65—75°C (bath temperature) and 11 Torr; n_D^{20} 1·4251 (reported[5], n_D^{21} 1·4228 and[6] n_D^{25} 1·4287). For $C_6H_9N_3$ (132·2) calculated: 58·52% C, 7·37% H, 34·12% N; found: 58·83% C, 7·66% H, 34·29% N. IR spectrum (CCl_4): $\nu(CH_3)$ 2805, 2847, 2884, 2910, 2975, 3006 cm^{-1}; ν(CN) 2234, 2260 (vw) cm^{-1}.

(N,N-Dimethylamino)phenylmalonodinitrile (*Ic*)

N,N-Dimethylbenzamide (1·5 g; 0·01 mol) was added with ice-cooling into a 20% solution of phosgene in chloroform (10 ml), the mixture stirred with ice-cooling for 2 h, kept at room temperature overnight, and evaporated under diminished pressure. The crystalline hygroscopic residue was dissolved under nitrogen in acetonitrile (40 ml), the solution cooled down with ice, and treated with a mixture of cuprous cyanide (3·0 g) and sodium cyanide (1·5 g). The whole mixture was stirred at 0°C for 2 h and then at room temperature overnight. The next day, the mixture was saturated with gaseous ammonia, diluted with ether, and filtered. The filtrate was evaporated under diminished pressure and the residue chromatographed on silica gel (50 g) in ethyl acetate. Yield, 0·65 g (35%) of compound *Ic* boiling at 65°C (bath temperature) and 0·2 Torr; n_D^{20} 1·5078 (reported[6], n_D^{25} 1·5102). IR spectrum (CCl_4): $\nu(CH_3)$ 2804, 2845, 2884, 2912, 2972, 3004 cm^{-1}; ν(CN) 2236, 2255 (vw) cm^{-1}.

Bis(dimethylamino)malonodinitrile (*Ie*)

Phosgene in chloroform (20 ml of a 20% solution) was added to tetramethylurea (1·16 g; 0·01 mol), the mixture kept overnight, and evaporated under diminished pressure to remove excess phosgene and the solvent. Acetonitrile (25 ml), cuprous cyanide (3·0 g), and sodium cyanide (1·5 g) was then added at −40°C to the residue. The mixture was stirred until the temperature was 0°C (the precipitate changed its consistence) and then for additional 3 h. The precipitate was collected with suction and processed analogously to the preparation of compound *Ib*. Yield, 0·65 g (43%) of compound *Ie*, b.p. 75°C/12 Torr, n_D^{20} 1·4360. For $C_7H_{12}N_4$ (152·2) calculated: 55·24% C, 7·95% H, 36·81% N; found: 55·11% C, 8·25% H, 36·53% N. IR spectrum (CCl_4): $\nu(CH_3)$ 2807, 2844, 2883, 2914, 2973, 3002 cm^{-1}; ν(CN) 2235 (w) cm^{-1}.

REFERENCES

1. Arnold Z.: This Journal *26*, 1113 (1961).
2. Gold H., Bayer O.: Chem. Ber. *94*, 2594 (1961).
3. Arnold Z.: This Journal *24*, 4048 (1959).
4. Bosshard H. H., Zollinger H.: Helv. Chim. Acta *42*, 1659 (1959).
5. Plieninger H., El-Berins R., Mah H.: Chem. Ber. *104*, 3983 (1971).
6. Yamaguchi T., Inomata K., Mukayiama T.: Bull. Chem. Soc. Jap. *41*, 673 (1968); Chem. Abstr. *69*, 43589 (1968).

Translated by J. Pliml.