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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

New Procedures for Preparing 2,2,3,3-Tetracyanocyclopropyl Ketones

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Abstract—New procedures were developed for preparing 2,2,3,3-tetracyanocyclopropyl ketones, based on reactions of substituted glyoxals with bromomalononitrile.

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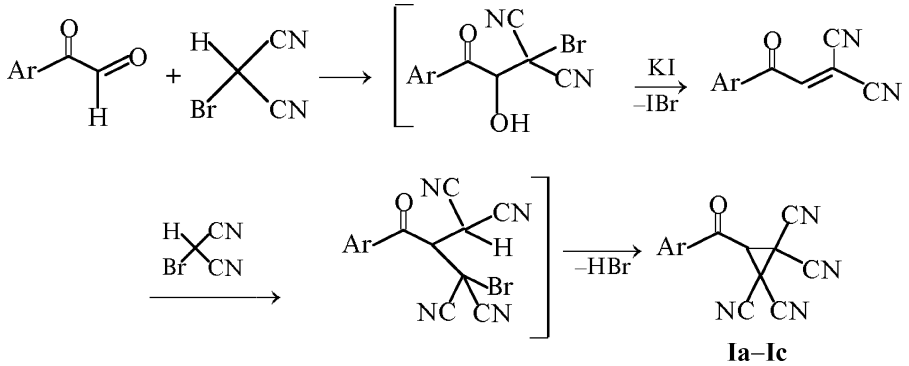
Tetracyanocyclopropyl ketones are highly reactive and can be used in syntheses of various framework and fused heterocyclic systems [1, 2]. However, the known procedures for their preparation are labor-consuming and involve the use of expensive chemicals such as tetracyanoethylene [1], which largely restricts studies of their properties. It is known that alkyltetracyanocyclopropanes can be prepared by the Wideqvist reaction consisting in treatment of carbonyl compounds with bromomalononitrile and KI in aqueous ethanol at room temperature for 0.5–12 h [3–6]. Application of this procedure to synthesis of cyclopropanes substituted with five and six electron-withdrawing groups is inefficient, because, as noted previously, such cyclopropanes actively react with iodides to form propenides [1]. Indeed, by the Wideqvist reaction with substituted glyoxals as carbonyl compounds, the expected 2,2,3,3-tetracyanocyclopropyl ketones **Ia–Ic** were prepared in low yields (21–26%) and only with a few aryl substituents (Scheme 1).

Therefore, our goal was to find procedures for preparing compounds **I** without using iodides as reductants. As we showed previously [7], in some cases cyclopropanation of carbonyl compounds with bromomalononitrile can occur without participation of KI [7]. Using this approach, by treatment of substituted glyoxals with excess bromomalononitrile in isopropyl alcohol, we prepared cyclopropanes **Ia–If** in 37–57% yield based on glyoxal. The drawback of this procedure is that bromomalononitrile should be taken in a threefold excess (Scheme 2).

It is known that bromomalononitrile is capable

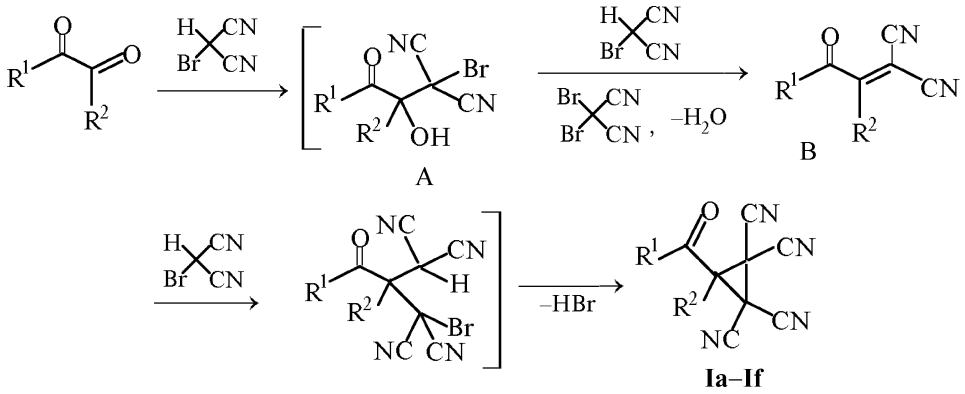
Scheme 1.



Ia–Ic

Ar = Ph (**a**), 4-BrPh (**b**), or 4-MeOPh (**c**).

Scheme 2.

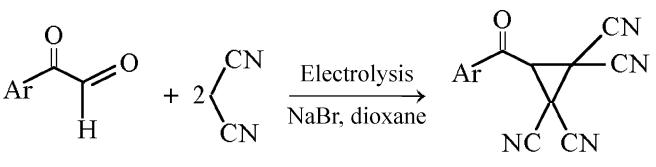


Ia–If

R^1 = Ph, R^2 = H (**a**); R^1 = 4-Br-Ph, R^2 = H (**b**); R^1 = 4-MeOPh, R^2 = H (**c**); R^1 = Me, R^2 = H (**d**); R^1 = *tert*-Bu, R^2 = H (**e**); R^1 = Ph, R^2 = CH^3 (**f**).

of reversible disproportionation to malononitrile and dibromomalononitrile. Apparently, such transformations also accompany reactions of bromomalononitrile with glyoxals. In the first step, bromomalononitrile undergoes addition to the aldehyde group with the formation of intermediate A, which is followed by bromine exchange leading to the formation of dibromomalononitrile and intermediate B, i.e., bromomalononitrile acts as a debrominating agent instead of KI used in the classical Wideqvist method. Presumably, malononitrile can also act as a debrominating agent in this process. Based on this hypothesis, we developed a new procedure for preparing cyclopropanes **I**. In this procedure, malononitrile is used as dehydrobrominating agent. After transformation into bromomalononitrile, it can participate in the reaction with glyoxal. Using this procedure, we isolated cyclopropanes **Ia–If** in 48–82% yields based on glyoxal.

To optimize the synthesis and save solvents and reactants, various one-pot or domino processes are developed. Using this approach, we modified the above-described procedure for preparing cyclopropanes **I**. The modified process involved bromination of a mixture of malononitrile and appropriate glyoxal. With this method, the yield of **Ia–If** was 46–65% based on glyoxal. The advantage of this procedure is that it is unnecessary to synthesize bromomalononitrile, and thus its loss in the course of isolation and purification is avoided.



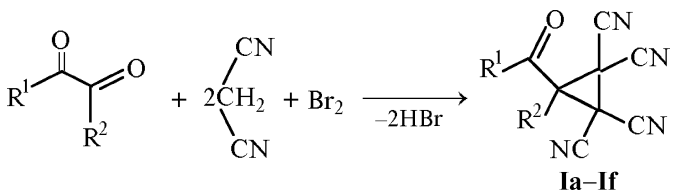
Ia–Ic

The second components of the reaction system, glyoxals, are synthesized by oxidation of the corresponding ketones with selenium dioxide [8]. To further develop the synthetic procedure, we attempted to use the reaction mixture after the synthesis of glyoxals without their preliminary isolation. This approach allows saving of solvents and eliminates losses in the step of glyoxal isolation. In this case, the yield was 42–69% (based on the starting ketone).

Among advanced methods of organic synthesis, electrochemical procedures acquire increasing importance. The use of electric current allows development of efficient, convenient, and environmentally safe processes. Some of tetracyanocyclopropane derivatives were prepared by joint electrolysis of methylene-active compounds with carbonyl compounds [9, 10]. The procedure is based on anodic generation of bromine whose subsequent transformations are similar to those in a common chemical process. By this procedure we prepared cyclopropanes **Ia–Ie** in 23–34% yield:

$$\text{Anode: } 2Br^- - 2e \rightarrow Br_2,$$

$$\text{Cathode: } 2H_2O + 2e \rightarrow 2OH^- + H_2,$$



Ia–If

where Ar = Ph (**a**), 4-BrPh (**b**), 4-MeOPh (**c**).

The drawback of this procedure is the formation of OH^- at the cathode. Hydroxide ion is reactive toward the

formed cyclopropane. This fact may be responsible for the relatively low yield.

EXPERIMENTAL

The reaction progress and product purity were monitored by TLC on Silufol UV-254 plates (development by UV irradiation, treatment with iodine vapor, or heat treatment). The IR spectra were recorded with an FSM-1202 Fourier IR spectrometer from thin films of samples prepared as mulls in mineral oil. The ^{1}H NMR spectra were taken on a Bruker DRX-500 spectrometer, working frequency 500.13 MHz, solvent DMSO-d_6, internal reference TMS. The mass spectra were measured with a Shimadzu GCMS-QP2010S DI device (electron impact, 70 eV).

3-Benzoylcyclopropane-1,1,2,2-tetracarbonitrile Ia. (1) 1.52 g (0.01 mol) of phenylglyoxal was dissolved in 20 ml of ethanol, after which 2.9 g (0.02 mol) of bromomalononitrile and 3.32 g (0.02 mol) of KI in 10 ml of water were added. The mixture was stirred for 15 min. The precipitate that formed was filtered off and washed with ethanol. If necessary, the precipitate can be recrystallized from dioxane. Yield 0.52 g (21%), T_{dec} = 211–212°C. The IR and ^{1}H NMR data coincide with those reported previously [11].

(2) 1.52 g (0.01 mol) of phenylglyoxal was dissolved in 20 ml of isopropyl alcohol, after which 4.35 g (0.03 mol) of bromomalononitrile was added, and the mixture was stirred for 15 min. The precipitate that formed was filtered off and washed with isopropyl alcohol. Yield 1.03 g (42%).

(3) To a solution of 1.52 g (0.01 mol) of phenylglyoxal in 20 ml of isopropyl alcohol, we added 0.66 g (0.01 mol) of malononitrile and then 1.45 g (0.01 mol) of bromomalononitrile. The mixture was stirred for 15 min. The precipitate that formed was filtered off and washed with isopropyl alcohol. Yield 1.60 g (65%).

(4) 1.52 g (0.01 mol) of phenylglyoxal and 1.32 g (0.02 mol) of malononitrile were dissolved in 10 ml of isopropyl alcohol. To the resulting solution, a solution of 1.6 g (0.02 mol) of bromine in 10 ml of 1 : 1 isopropyl alcohol–water mixture was added dropwise with vigorous stirring with a magnetic stirrer. The precipitate that formed was filtered off and washed with isopropyl alcohol. Yield 1.28 g (52%).

(5) 1.11 g (0.01 mol) of SeO_2 and 1.2 g (0.01 mol) of acetophenone were dissolved in a mixture of 10 ml of isopropyl alcohol and 5 ml of water. The solution was refluxed until the precipitation of metallic selenium was complete. The precipitate was separated by decantation. To the resulting solution, after cooling, we successively added with stirring 0.66 g (0.01 mol) of malononitrile and 1.45 g (0.01 mol) of bromomalononitrile. The mixture was stirred for 15 min. The precipitate that formed was filtered off and washed with isopropyl alcohol. Yield 1.25 g (51%).

(6) A solution of 1.52 g (0.01 mol) of phenylglyoxal, 1.32 g (0.02 mol) of malononitrile, and 2.06 g (0.02 mol) of NaBr in a mixture of 30 ml of dioxane and 30 ml of water was subjected to electrolysis in a diaphragmless cell equipped with a C anode and a Fe cathode (area of each electrode 2 cm^2) at 20°C and a constant current density of 100 mA cm^{-2}, with continuous stirring. After the reaction completion (TLC monitoring), the solvent was separated by decantation from a tarry liquid which was triturated with isopropyl alcohol. The precipitate that formed was filtered off and washed with several portions of isopropyl alcohol and water. Yield 0.57 g (23%).

CONCLUSIONS

(1) The use of bromomalononitrile or malononitrile as debrominating agent instead of KI in the Wideqvist reaction allows the yield of 2,2,3,3-tetracyanocyclopropyl ketones to be increased and the range of glyoxals that can be involved in the reaction to be expanded.

(2) The procedure allows multicomponent or one-pot implementation.

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