Reaction of Alkylidenemalononitriles with Diazomethane

By

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At — 15° C isopropylidenemalononitrile (**5**) reacts with an *equimolar* amount of diazomethane to yield the pyrazoline **8**, which loses nitrogen upon heating, to give 2,2-dimethyl-1,1-cyclopropanedicarbonitrile (**9**), and 2-butylidenemalononitrile (**6**). At room temperature with an *excess* of diazomethane **5** gives a number of homologous 2-methyl-2-*n*-alkyl-1,1-cyclopropanedicarbonitriles **9**—**13** via the corresponding homologous alkylidenemalononitriles, as supported by the similarity of products obtained from the reaction of 2-pentylidenemalononitrile (**7**) and diazomethane.

Bei — 15° C reagiert Isopropylidenmalonitril (**5**) mit Diazomethan in mol. Verhältnis 1 : 1 zu dem Pyrazolin **8**, welches beim Erwärmen Stickstoff verliert und zu 2,2-Dimethyl-1,1-cyclopropandicarbonitril (**9**) und 2-Butylidenmalonnitril (**6**) umgesetzt wird.

Wird die Reaktion bei Zimmertemp. mit überschüss. CH_2N_2 ausgeführt, so erhält man ein Gemisch von homologen 2-Methyl-2-*n*-alkyl-1,1-cyclopropandicarbonitrilen **9**—**13**. Die Reaktion verläuft wahrscheinlich über die homologen Alkylidenmalonitrile, weil 2-Pentylidenmalonitril (**7**) und Diazomethan ein Gemisch von gleichartigen Produkten liefern.

Wessely[1] and co-workers described an elegant method for the preparation of several disubstituted 1,1-cyclopropanedicarboxylic acids (cf. Scheme 1).

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[*] Herrn Prof. Dr. *F. Wessely* zum 70. Geburtstag in Hochachtung gewidmet.

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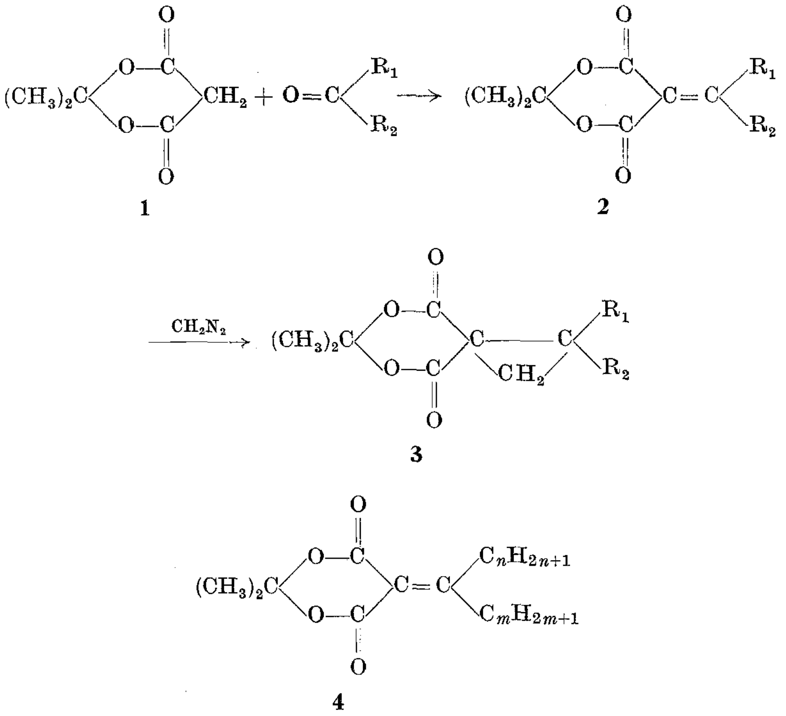
[1] *F. Wessely* and *A. Eitel*, Mh. Chem. **95**, 1577 (1964), and references cited there.

Scheme 1



In connection with our study on the mechanism of the isomerization of 1,1-cyclopropanedicarboxylic acids[2] *Wessely*'s convenient method was considered for the synthesis of 2,2-dimethyl-1,1-cyclopropanedicarboxylic acid (**14**). Thus starting from 2,2-dimethyl-4,6-dioxo-1,3-dioxan (**1**, *Meldrum* acid) and acetone, we obtained isopropylidene meldrum acid **2** ($R_1 = R_2 = CH_3$) in 64% yield. On adding an equimolar amount of diazomethane at — 20° C, it was found that no cyclopropane derivative was formed. Instead, a complex mixture of alkylidene meldrum acids **4**, with varied n and m was obtained. This mixture was ozonized and subsequently decomposed, thus giving a mixture of acetone, butanone, diethylketone and methyl propyl ketone.

The failure of this route prompted us to set up another approach for the synthesis of the acid **14**, which is represented by Scheme 2.

While this work was underway, *McGreer* et al.[3] and *Hamelin* et al.[4] reported that the pyrolysis of alkyl 3-cyano-4,4-dimethyl-1-pyrazoline-3-carboxylate gives among other products alkyl 1-cyano-2,2-dimethyl-1-cyclopropanecarboxylate in about 25% yield.

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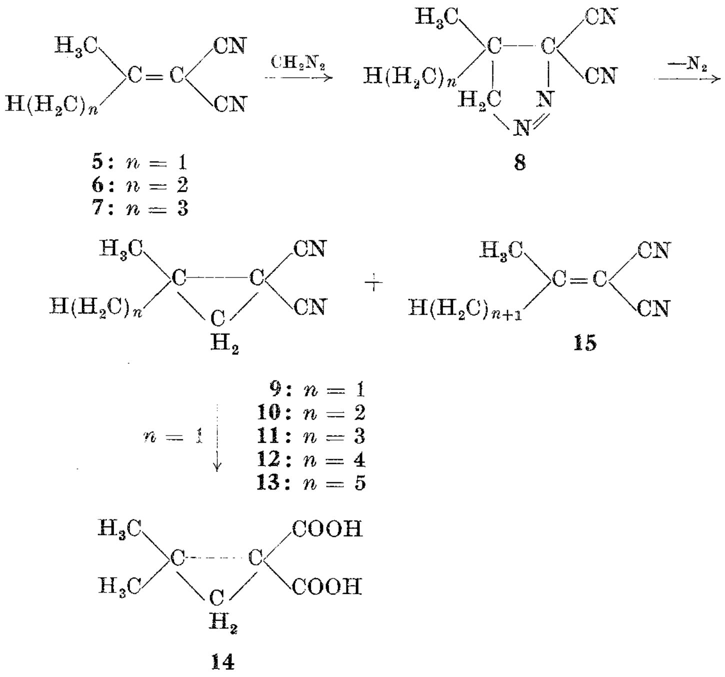
[2] *J. Bus*, Thesis, Amsterdam 1967.

Scheme 2



In carrying out the reaction with an equimolar amount of diazomethane and isopropylidenemalononitrile (**5**) at — 15° C, the pyrazoline derivative **8** ($n = 1$) can be isolated. Its structure is consistent with the NMR spectrum (vide experimental). Upon warming to room temperature **8** is rapidly converted into 2,2-dimethyl-1,1-cyclopropanedicarbonitrile (**9**) and 2-butylidenemalononitrile (**6**) by loss of nitrogen. When the reaction is started at room temperature, much more diazomethane is consumed by isopropylidenemalononitrile and it is evident (vide supra) that the excess of diazomethane is used for chain lengthening of the alkylidene group. Careful analysis by gaschromatography, NMR and mass spectrometry of a typical reaction mixture shows that it consists of a number of 2-methyl-2-*n*-alkyl-1,1-cyclopropanedicarbonitriles **9**—**13**. 2-Pentylidenemalononitrile (**7**) and diazomethane give under similar conditions the dicarbonitriles **11**—**13**. This result proves unequivocally that the 2-alkylidenemalononitriles (e.g. **6** and **7**) are intermediates. It must be emphasized that during the „addition" of diazomethane to isopropylidenecyanomalonic ester or

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[3] *D. E. McGreer, R. S. McDaniel,* and *M. G. Vinjé,* Canad. J. Chem. **43**, 1389 (1965).

[4] *H. Hamelin* and *R. Carrié,* C. r. hebdomad. Sé. Acad. Sci. **261**, 5545 (1965).

to isopropylidene meldrum acid (**2** → **4**), the methyl and the alkyl group *both* show a migratory aptitude, which is said to be normal in carbonium ion reactions[5]. However, on adding diazomethane to isopropylidenemalononitrile one methyl group is always retained in the intermediary homologues **15**, indicating an extraordinary preference of higher alkyl groups for migration. For the present we cannot offer a satisfactory explanation for this exceptional selectivity.

Experimental Part

With the collaboration of Miss *T. A. Langeveld.*

All melting and boiling points are uncorrected.

The mass spectra were taken on an A.E.I.M.S.-2H spectrometer at an ionizing potential of 70 eV, the NMR spectra on a Varian Associates A-60 spectrometer using tetramethylsilane ($\delta = 0$) as an internal standard. The infrared spectra were determined on a Unicam S.P. 200 infrared spectrometer.

2,2-Dimethyl-4,6-dioxo-1,3-dioxane (Meldrum acid) (**1**)

This product was prepared according to *Meldrum*[6]. The NMR spectrum ($CDCl_3$) shows two singlets at $\delta = 1.76$ ($-CH_3$) and at $\delta = 3.68$ ($-CH_2-$) with relative intensities of 3 : 1.

2,2-Dimethyl-5-isopropylidene-4,6-dioxo-1,3-dioxane (**2**) ($R_1 = R_2 = CH_3$)

Molecular sieves (20 g, type 4 A) and Meldrum acid (**1**) (0,12 mole) dissolved in a mixture of 15 ml of acetone and 30 ml of super dry pyridine were allowed to stand for 5 days at 20° C. The molecular sieves were removed by filtration and the solvent by distillation. Water was then added to the residue and the product precipitated. It was filtered off and washed with water. Yield 14.1 g (64%) of 2,2-dimethyl-5-isopropylidene-4,6-dioxo-1,3-dioxane[7] (**2**, $R_1 = R_2 = CH_3$). Mp. 75.5—76.5° C.

Reaction of diazomethane with **2** ($R_1 = R_2 = CH_3$)

At — 15° C an ethereal solution of 3 eq. of CH_2N_2[8] was added to a solution of 1.5 g of 2,2-dimethyl-5-isopropylidene-4,6-dioxo-1,3-dioxane (**2**, $R_1 = R_2 = CH_3$) in 4 ml of ether. After evaporation of the ether, the residue was dissolved in 20 ml of CCl_4. A stream of ozone was then bubbled into this solution for about 8 hrs at 0° C. The solution was concentrated to about 3 ml and the mixture of ozonides was decomposed with water. The low boiling products were distilled off *in vacuo* and dried. Acetone, butanone, 2-pentanone and 3-pentanone were isolated by preparative gaschromatography and identified by comparison with authentic samples.

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[5] *M. Stiles* and *R. P. Mayer*, J. Amer. Chem. Soc. **81**, 1497 (1959).

[6] *A. N. Meldrum*, J. Chem. Soc. **93**, 598 (1908).

[7] *G. Swoboda-Adametz, J. Swoboda,* and *F. Wessely*, Mh. Chem. **95**, 1283 (1964).

[8] Organic Synthesis, John Wiley and Sons, Inc. (New York) **36**, 16 (1956), submitted by *Th. J. de Boer* and *H. J. Backer.*

Isopropylidenemalononitrile (**5**)

This compound was prepared according to *Prout*[9]. Yield 87%, B. P. 88—90° C/9 mm.

2-Pentylidenemalononitrile (**7**)

This product was obtained according to *Prout*[9]. Yield 91%.

3,3-Dicyano-4,4-dimethyl-1-pyrazoline (**8**) *from* **5** *by reaction with diazomethane at — 15° C*

An ethereal solution of CH_2N_2 (10 mmole) was added to 1.06 g (10 mmole) of isopropylidenemalononitrile (**5**) in 50 ml of ether at — 15° C. After 1½ hrs the ether was removed *in vacuo* at — 40° C. The colourless crystalline product was filtered off and washed with CCl_4 of — 20° C. 3,3-Dicyano-4,4-dimethyl-1-pyrazoline (**8**) was stable at this temperature. The NMR spectrum (in $CDCl_3$) at — 30° C showed a singlet at $\delta = 1.37$ ($—CH_3$) and a singlet at $\delta = 4.76$ ($—CH_2—$) with relative intensities of 3 : 1.

2,2-Dimethyl-1,1-cyclopropanedicarbonitrile (**9**) *by thermal decomposition of* **8**

At room temperature, the pyrazoline **8**, dissolved in ether, decomposed into N_2 and in a mixture of 2,2-dimethyl-1,1-cyclopropanedicarbonitrile (**9**) and of *sec.*-butylidenemalononitrile (**6**) in a ratio of 2 : 1 approximately (determined by gas chromatography). The reaction mixture was then cooled to — 35° C and 0.36 g of 2,2-dimethyl-1,1-cyclopropanedicarbonitrile (**9**) precipitated. **9** was recrystallized from a mixture of petroleum ether and CCl_4. M. P. 39—40° (lit. 39—40°)[10].

Reaction of isopropylidenemalononitrile (**5**) *with* CH_2N_2 *at room temperature*

At + 20° C an ethereal solution of CH_2N_2 was added to 1 g of isopropylidenemalononitrile (**5**), in 5 ml of ether. After about 4 hours the reaction was complete and the excess of CH_2N_2 and solvent were evaporated. The residual liquid was subjected to preparative gas chromatography using a 2 m 20% silicon oil column at 173° C. The products **9**—**13** were isolated. The molecular weights of the compounds were determined by mass spectrometry.

Infrared spectrum

The C≡N stretch vibration mode in compound **9** and **10** absorbs at 2260 cm^{-1} and in the products **11**, **12**, and **13** at 2290 cm^{-1}. The intensity of the absorption band of the CH_2-deformation mode in the region of 1450 cm^{-1} increases with increasing number of CH_2-groups. The C=C-stretch vibration band is absent. Weak bands above 3000 cm^{-1} indicate the presence of a cyclopropane ring[11].

NMR spectrum (CCl_4)

The chemical shift δ of the methyl and of the methylene protons in **9**—**13** are given in Table 1.

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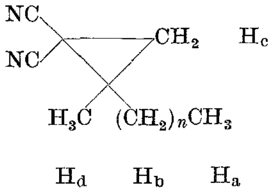
[9] *F. S. Prout*, J. Org. Chem. **18**, 928 (1953).

[10] *E. Ciganek*, J. Amer. Chem. Soc. **88**, 1979 (1966).

[11] *H. A. Szymanski*, Interpreted Infrared Spectra, Vol. 1, Plenum Press, New York, **1964**, p. 143.

Table 1



Compound	H_a	H_b	H_c	H_d
9	1.41	1.3—1.6	1.62	1.41
10	1.1		1.59	1.39
11	1.0		1.58	1.39
12	1.0		1.56	1.40
13	1.0		1.55	1.41

The methylene protons (H_b) display a multiplet, the cyclopropyl protons (H_c) and the α-methyl protons (H_d) a singlet, and the methyl protons (H_a) show a broad triplet.

The relative intensities of the protons H_a, H_b, H_c and H_d are in accordance with the assigned structure.

Reaction of 2-pentylidenemalononitrile (7) with diazomethane

This reaction was carried out in the same way as described above. After the work up, the products **11**—**13** were isolated.

Acknowledgement

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