The Chemistry of 2-Oxopropanedinitrile (Carbonyl Cyanide); XIX[1]. The Ene Synthesis Using 2-Oxopropanedinitrile and 1,3-Dicarbonyl Compounds

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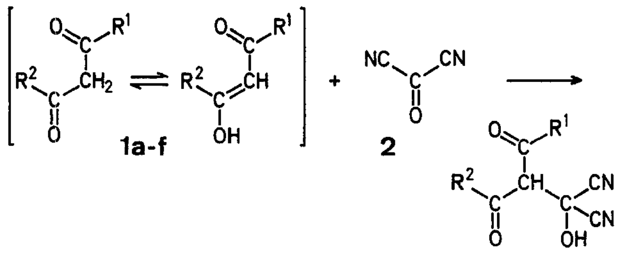
In the ene synthesis a variety of carbonyl compounds has been employed as enophiles[2]. On the other hand, only few examples are reported in which a carbonyl compound reacts as the ene component. Thus, the formation of adducts in the reaction of β-oxo-*s*-triazines with dimethyl acetylenedicarboxylate, ethyl azodicarboxylate, and acrylonitrile was explained by an ene synthesis mechanism involving hydrogen transfer from the enol of β-oxo-*s*-triazine to a carbon atom of the enophile[3]. The same enol hydrogen transfer was also found in the thermal cyclization of unsaturated ketones[4].

Previously[5] we described a further example of the ene synthesis in which a monoketone was shown to combine, as ene component, with 2-oxopropanedinitrile (also known as mesoxalodinitrile or carbonyl cyanide), a highly reactive enophile[2]. Our present study has revealed that the reaction is capable of considerable generalization since 2-oxopropanedinitrile (**2**) has been found to react under mild conditions with 1,3-dicarbonyl compounds such as 1,3-diphenyl-1,3-propanedione (**1a**), 1,3-bis[2,4,6-trichlorophenyl]-1,3-propanedione (**1b**), 1-phenyl-1,3-butanedione (**1c**), 4,4,4-trifluoro-1-phenyl-1,3-butanedione (**1d**), 2,4-pentanedione (**1e**), and diethyl malonate (**1f**). Combination of **1a–e** and carbonyl cyanide (**2**) in diethyl ether solution at 0° resulted in the rapid disappearance of **2**, and formation of a product analysis of which indicated that the reaction of the 1,3-diketones **1a–e** involved one mol of 2-oxopropanedinitrile (**2**) and one mol of diethyl ether bound in the form of the etherate.

For all compounds, structures of the ene adduct type **3** were advanced (Scheme A), based on spectral evidence (see Table) and chemical degradation.



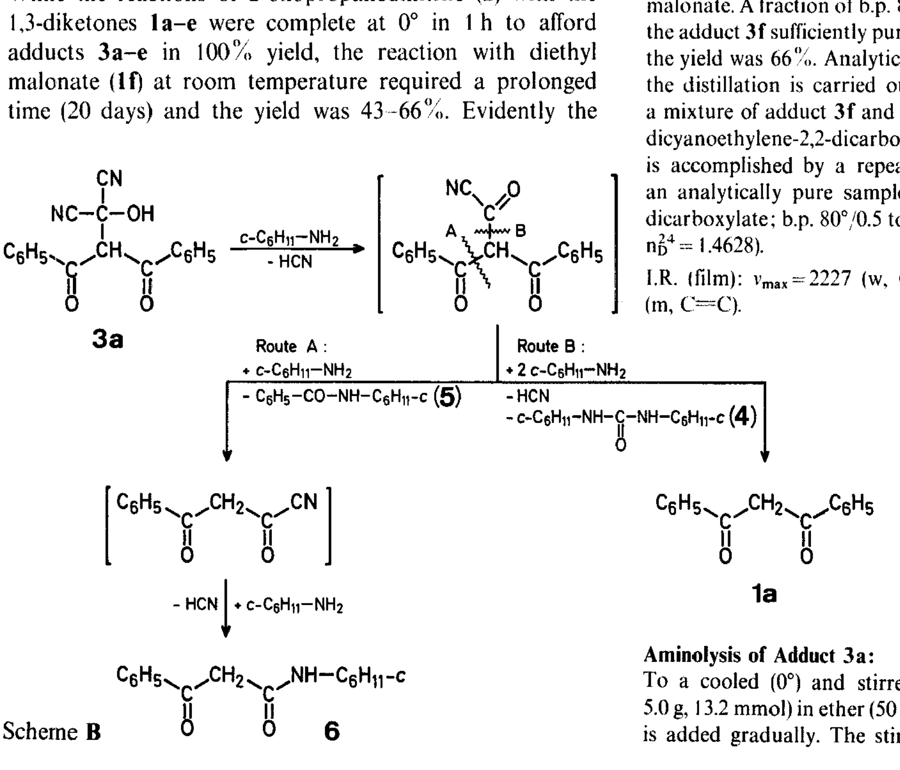
Scheme A

1, 3	R^1	R^2
a	C_6H_5	C_6H_5
b	2,4,6-tri-Cl—C_6H_2	2,4,6-tri-Cl—C_6H_2
c	CH_3	C_6H_5
d	CF_3	C_6H_5
e	CH_3	CH_3
f	OC_2H_5	OC_2H_5

It should be pointed out that the crude adducts **3** were not contaminated with *O*-substituted derivatives of enols. This result has special significance in light of its mechanistic consequence, because a lack of *O*-substituted products is in favour of the assumed ene synthesis mechanism involving a concerted pericyclic reaction, which is thermally allowed by orbital symmetry rules.

The ene adducts derived from 1,3-diketones were rather unstable, and we encountered difficulties in their isolation; however, in the cases of the reactions carried out in ether we succeeded in obtaining analytically pure etherates of **3a–d**. When ether was replaced by chloroform, the reaction yielded the free products **3a–d**, however, these were too unstable to survive a purification procedure.

While the reactions of 2-oxopropanedinitrile (**2**) with the 1,3-diketones **1a–e** were complete at 0° in 1 h to afford adducts **3a–e** in 100% yield, the reaction with diethyl malonate (**1f**) at room temperature required a prolonged time (20 days) and the yield was 43–66%. Evidently the high proportion of the enol form in **1a–e** facilitated the ene synthesis. All adducts **3** are new compounds; their reactivity is exemplified by the degradation of adduct **3a** by means of cyclohexylamine, resulting in splitting of all HC—CO bonds and formation of *N*,*N*-dicyclohexylurea (**4**), 1,3-diphenyl-1,3-propanedione (**1a**), *N*-cyclohexylbenzamide (**5**) and *N*-cyclohexylbenzoylacetamide (**6**), Scheme **B**.



Scheme **B**

A specific feature of the adduct **3f** obtained from 2-oxopropanedinitrile and diethyl malonate is its dehydration to diethyl 1,1-dicyanoethylene-2,2-dicarboxylate which is accomplished by heating of **3f**. Reaction of **3f** with aniline causes elimination of hydrogen cyanide followed by splitting of the C—CN bond and formation of diethyl phenylaminocarbonylmalonate and second molecule of hydrogen cyanide.

Reaction of 2-Oxopropanedinitrile (2) with 1,3-Diketones 1a–e; General Procedure:

Throughout the reaction, atmospheric moisture is excluded by use of drying tubes containing phosphorus pentoxide. The 1,3-diketone (30 mmol) is placed in a three-necked flask equipped with a thermometer, a magnetic stirring bar, and a dropping funnel. Dried ether (10–15 ml) is added to dissolve the 1,3-diketone and the solution is cooled to 0°. 2-Oxopropanedinitrile (30 mmol) is added dropwise. Reactions with all 1,3-diketones are exothermic and the reaction vessel is cooled to prevent the temperature from exceeding 0°. Stirring is continued for 1 h. Adducts **3a, b** crystallize from the reaction mixture; careful evaporation (0°) of the ether at reduced pressure yields a second crop of crystalline **3a, b**. Adducts **3c, d** are soluble in ether; they are isolated by evaporation of the ether under reduced pressure (oil pump) at 0°. The above isolation procedures gives the etherate of **3a–d** in sufficient purity for analysis. Adduct **3e** is soluble in ether; after evaporation of ether, the oily product decomposes even below 0°. Yields and physical properties are given in the Table.

Reaction of 2-Oxopropanedinitrile (2) with Diethyl Malonate (1f):

A flask containing diethyl malonate (**1f**; 3.65 g, 23 mmol) and 2-oxopropanedinitrile (**2**; 2.2 g, 27 mmol) is set aside at room temperature for 20 days; the mixture acquires a dark-brown coloration. Distillation at reduced pressure affords a fraction of b.p. 40–50°/0.1 torr (0.4 g) containing mainly unreacted diethyl malonate. A fraction of b.p. 80–90°/0.1 torr (2.35 g, 43%) contains the adduct **3f** sufficiently pure for analysis. In another experiment, the yield was 66%. Analytical data are given in the Table. When the distillation is carried out at the pressure of 1 torr, it gives a mixture of adduct **3f** and its dehydration product, diethyl 1,1-dicyanoethylene-2,2-dicarboxylate. Complete dehydration of **3f** is accomplished by a repeated distillation (yield 82%) to give an analytically pure sample of diethyl 1,1-dicyanoethylene-2,2-dicarboxylate; b.p. 80°/0.5 torr; $n_D^{20} = 1.4638$ (Lit.[6] b.p. 86°/1 torr; $n_D^{24} = 1.4628$).

I.R. (film): $\nu_{max} = 2227$ (w, C≡N); 1740 (s, C=O); 1600 cm^{-1} (m, C=C).

Aminolysis of Adduct 3a:

To a cooled (0°) and stirred solution of adduct **3a** (etherate, 5.0 g, 13.2 mmol) in ether (50 ml), cyclohexylamine (7.9 g, 80 mmol) is added gradually. The stirring is continued for 1 h at 0° and

Table. Adducts **3** obtained from 1,3-Dicarbonyl Compounds (**1**) and 2-Oxopropanedinitrile (**2**)

Product	Yield [%]	m.p.	Molecular formula[a]	I.R.[b] ν_{max} [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$)[c] δ [ppm]
3a$\cdot$O(C$_2$H$_5$)$_2$	100	>70° (dec.)	$C_{22}H_{22}N_2O_4$ (378.4)	2950 (vs, br, OH); 2240 (vw, C≡N); 1680 (vs, C=O); 1600, 1584 (s, C=C arom); 1085 (s, C—OH) 688 (s, def. arom)	1.25 (t, 6H, OCH$_2$C$\underline{H}_3$); 3.55 (q, 4H, OC$\underline{H}_2$CH$_3$); 6.08 (s, 1H, >CH—); 7.70 (m, 10H$_{arom}$)
3b$\cdot$O(C$_2$H$_5$)$_2$	100	>78° (dec.)	$C_{22}H_{16}Cl_6N_2O_4$ (585.1)	2980 (vs, br, OH); 2244 (vw, C≡H); 1678 (vs, C=O)	1.26 (t, 6H, OCH$_2$C$\underline{H}_3$); 3.55 (q, 4H, OC$\underline{H}_2$CH$_3$); 6.01 (s, 1H, >CH—)
3c$\cdot$O(C$_2$H$_5$)$_2$	100	>30° (dec.)	$C_{17}H_{20}N_2O_4$[d] (316.4)	3000 (vs, br, OH); 2235 (vw, C≡N); 1725 (vs, C=O); 1676 (vs, C=O)[d]	1.25 (t, 6H, OCH$_2$C$\underline{H}_3$) 2.32 (s, 3H, C$\underline{H}_3$—C); 3.35 (q, 4H, OC$\underline{H}_2$CH$_3$); 5.35 (s, 1H, >CH—); 7.80 (m, 5H$_{arom}$)[d]
3d$\cdot$O(C$_2$H$_5$)$_2$	100	>28° (dec.)	$C_{17}H_{17}F_3N_2O_4$[d] (351.3)	2990 (vs, br, OH); 2238 (vw, C≡N); 1745 (vs, C=O); 1680 (vs, C=O)[d]	1.25 (t, 6H, OCH$_2$C$\underline{H}_3$); 3.55 (q, 4H, OC$\underline{H}_2$CH$_3$); 5.80 (s, 1H, >CH—); 7.75 (m, 5H$_{arom}$)[d]
3e	100	oil	—[e]	—	—
3f	43–66	—[f]	$C_{10}H_{12}N_2O_5$ (240.2)	3333 (m, br, OH); 2985 (m, CH); 2257 (w, C≡N); 1745 (s, br, C=O); 1372 (m, CH); 1302, 1250 (s, —CO—O—C); 1095 (m, —CO—O—C); 1020 (s, —C—OH)[g]	1.41 (t, 6H, OCH$_2$C$\underline{H}_3$); 3.31 (s, 1H, >CH—); 4.50 (q, 4H, OC$\underline{H}_2$CH$_3$); 12.60 (br.s, 1H, OH)

[a] Unless otherwise stated, products gave satisfactory microanalyses (C ±0.5%, H ±0.5%, and/or N ±0.6%).

[b] The I.R. spectra were recorded on a Spectromom 2000 (MOM Budapest) spectrophotometer in Nujol unless otherwise stated.

[c] The ^{1}H-N.M.R. spectra were measured at 60 MHz with a Jeol JNM C60 HL spectrometer using TMS as internal standard. Abbreviations used: s, singlet; br.s, broad singlet; t, triplet; q, quartet; m, multiplet.

[d] Analysis or spectrum performed immediately after the reaction. The sample was stored below 0°.

[e] Product is too unstable at 0° to be analysed.

[f] b.p. 80–90°/0.1 torr; $n_D^{20} = 1.4490$.

[g] Measured as film.

for 1 h at room temperature. *N,N'*-Dicyclohexylurea (**4**) which precipitates during the reaction is filtered off. Partial evaporation of the filtrate yields a second crop of *N,N'*-dicyclohexylurea (**4**) identified by comparison (I.R.) with an authentic sample; yield of **4**: 2.16 g (73%); m.p. 220–225°.

The ether filtrate is washed with dilute hydrochloric acid, water, and dried before being evaporated. The residue is separated by column chromatography (Silica Gel G, benzene/methanol 9:1) to give the starting 1,3-diphenyl-1,3-propanedione **1a** (1.96 g, 66%), *N*-cyclohexylbenzamide **5** (0.4 g; m.p. 145–147°), and a fraction (0.35 g) containing *N*-cyclohexylbenzoylacetamide (**6**) contaminated with **5**. *N*-Cyclohexylbenzoylacetamide is identified by means of T.L.C. (light petroleum/chloroform, iodine).

Aminolysis of Adduct 3f:

To a solution of the crude adduct **3f** (4 g) in benzene (50 ml), aniline (4 g) is added. After 2 h, the mixture is filtered, washed twice with dilute hydrochloric acid, water, and then dried with magnesium sulphate. Evaporation yields a dark oily residue which is crystallized from light petroleum/benzene (4:1); recrystallization gives diethyl phenylaminocarbonylmalonate; yield: 1.35 g (30%); m.p. 122–124° (Lit.[7] 123–124°).

^{1}H-N.M.R. (CDCl$_3$): δ = 1.34 (t, 6H, CH$_2$—C$\underline{H}_3$); 4.28 (q, 4H, C$\underline{H}_2$—CH$_3$); 4.43 (s, 1H, >CH—); 7.34 (m, 5H$_{arom}$); 9.23 ppm (br.s, 1H, NH).

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