

BENZYLIDENEMALONALDEHYDES: A REDOX REACTION DURING THE ATTEMPTED CYCLOADDITION ON NITROSOBENZENE

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Reaction of *p*-chlorobenzylidenemalonaldehyde with nitrosobenzene represents a reduction-oxidation process leading to 2-formyl-3-anilino-3-(4-chlorophenyl)acrylic acid (*III*). The structure of the product, including two intramolecular hydrogen bonds, has been proved by analysis of the ^1H and ^{13}C NMR spectra of the acid *III*, its deuterated form and the methyl ester obtained by reaction with diazomethane.

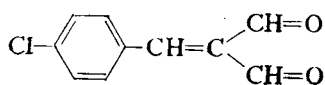
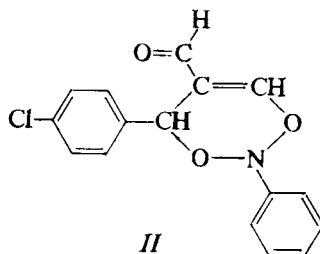
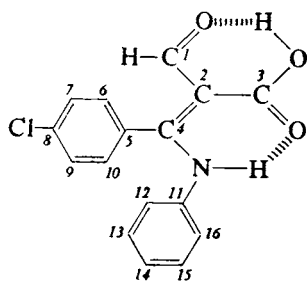
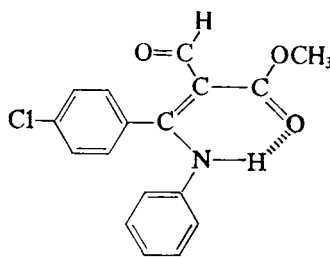
Benzylidenemalonaldehydes and some other methylenemalonaldehyde derivatives whose synthesis has recently been developed in our Laboratory¹⁻³ exhibit remarkable reactivity in cycloaddition reactions⁴, acting mainly as 4π -heterocomponents in the Diels-Alder reaction. In this communication we describe reaction of *p*-chlorobenzylidenemalonaldehyde with nitrosobenzene. Nitrosobenzene was included in our studies as a 2π component whose reaction with dienes was described for the first time by Wichterle^{5,6} and Arbuzov⁷.

p-Cl-Benzylidenemalonaldehyde reacts with nitrosobenzene in benzene to give a product of composition corresponding to a 1 : 1 adduct of both components. Like other cycloadditions of benzylidenemalonaldehydes⁴, also this reaction was catalyzed by traces of Lewis acids, such as boron trifluoride etherate. Formally, the studied addition could lead to a primary adduct with the hitherto undescribed structure *II*. However, the structure *II* was excluded already by the first physico-chemical data obtained. A detailed study of ^1H , ^2H and ^{13}C NMR spectra revealed that the addition product has the structure *III*, with two exchangeable protons.

In addition to the above-mentioned two exchangeable protons, the ^1H NMR spectrum exhibited a singlet due to the formyl proton at δ 8.89 and a complex multiplet of nine aromatic protons in the region δ 6.80–7.41 as required by the presence of a mono- and disubstituted phenyl group. Thus, the spectrum excluded the structure *II* without giving any data on structural details of the product.

Its proton-decoupled ^{13}C NMR spectrum exhibits 11 signals in the region δ 100 to 200, of which two correspond to two and one to four carbon atoms, as expected for a C_{16} molecule. The symmetrical equivalence of chemical shifts of the *ortho*-

and *meta*-carbon atoms in both the aromatic rings is obvious so that occurrence of four signals corresponding each to two carbon atoms may be expected. In our case, moreover, the chemical shifts of two two-carbon signals coincide. The ^{13}C NMR spectrum with off-resonance decoupling of protons proves that the mentioned signals have character of doublets and correspond to carbon atoms of the CH type. Of the remaining four signals of aromatic carbon atoms, three appears as singlets, corresponding to substituted atoms, and the fourth, a doublet at δ 127.2, can be unequivocally ascribed to the carbon atom in *para*-position of the monosubstituted phenyl. The four-carbon fragment originating from malonaldehyde afforded a doublet at δ 191.3 and singlets at δ 171.6, 170.8, and 101.9. The doublet at the lowest field can be ascribed to the formyl carbon atom (compare with the ^{13}C NMR data of *p*-chlorobenzylidenemalonaldehyde (*I*) in Table I). Also the singlets (according to their chemical shifts) must correspond to sp^2 -carbon atoms of which the first two apparently bear hetero atoms. On the basis of the ^1H and ^{13}C NMR data we suggested the structure *III*, containing exchangeable OH and NH protons – both bonded

*I**II**III**IV*

by intramolecular hydrogen bonds to the carbonyl oxygens which formally fits the NMR spectra. For a further confirmation of the suggested structure we made use of nondecoupled ^{13}C NMR spectrum, selective ^1H decouplings in the ^{13}C NMR spectra and ^{13}C NMR spectrum of the product after exchange with deuterium, studying particularly the atoms $\text{C}_{(1)}$ to $\text{C}_{(4)}$. The nondecoupled ^{13}C NMR spectrum,

together with selective decouplings of both the exchangeable protons and formyl hydrogen atom, enabled us to determine the coupling constants $J_{C,H}$ in the fragment $C_{(1)}$ to $C_{(4)}$ (Fig. 1) whose values agree with the suggested structure. The formyl carbon atom gives rise to a sharp doublet at δ 191.3 with $^1J_{C,H} = 179.1$ Hz which collapses on irradiation of the proton at δ 8.89 and shows no other $J_{C,H}$ interactions since in the given structure there are no hydrogens separated by two or three bonds from this carbon atom. The carbon at δ 171.6 interacts with the formyl hydrogen atom, one of the exchangeable protons (at δ 13.16) and with further two, presumably aromatic, hydrogen atoms ($J_{C,H} = 3$ Hz). Therefore, it must be bonded to the *para*-chlorophenyl substituent. The marked downfield shift is obviously caused by the directly bonded nitrogen atom and the signal at δ 13.16 can be ascribed to the NH-proton. The carbon signal, appearing at δ 170.8 as a doublet of doublets, interacts with the formyl hydrogen atom and the OH proton (at δ 14.46) and therefore it must correspond to the carboxyl carbon.

Finally, the atom, corresponding to the signal at δ 101.9, is involved in three $J_{C,H}$ interactions with all irradiated protons and, in accord with the proposed structure, this signal belongs to the sp^2 -carbon atom, bonded to the three above-discussed carbon atoms. The high value of its geminal coupling with the formyl hydrogen atom ($^2J_{C,H} = 18.8$ Hz) is typical for this grouping.

Further confirmation of the structure *III* was obtained from the NMR spectrum of the deuterated product. According to the spectrum, about 80% of the exchangeable protons were replaced by deuterium. The decoupled ^{13}C NMR spectrum exhibited isotopic shifts (-0.15 to -0.20 ppm) only for three atoms: $C_{(1)}$, $C_{(4)}$, and $C_{(11)}$ (double signals with intensities 80% and 20%) which, in accord with the structure *III*, are closest to the site of isotopic substitution (across two bonds). The nondecoupled ^{13}C NMR spectrum exhibited simpler multiplets of the atoms $C_{(1)}$, $C_{(2)}$ and $C_{(4)}$ for which the isotopic exchange eliminated the corresponding interactions $J_{C,H}$.

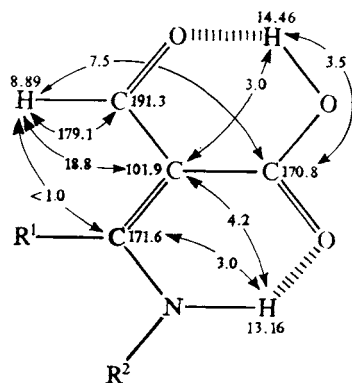


FIG. 1
 1H and ^{13}C NMR parameters of derivative *III*

To confirm the structure *III*, we prepared the methyl ester *IV* by treatment of *III* with diazomethane. The ^1H NMR spectrum of *IV* displayed a methyl ester singlet at δ 3.50, whereas the signal of one of the exchangeable hydrogen atoms disappeared. The formyl proton signal was markedly shifted downfield. This large shift (1.08 ppm) can be caused by the replacement of the hydroxyl proton by a methyl group which necessarily not only removes one of the hydrogen bonds but evidently also changes the conformation about the $\text{C}_{(2)}\text{—C}_{(3)}$ bond as a result of repulsive interactions of the two oxygen atoms (see formula *IV*). The formyl hydrogen atom is thus situated close to the methoxyl oxygen whose van der Waals effect may be responsible for the observed downfield shift. Also the ^{13}C NMR spectrum (Table I) is in accord with the ester structure *IV*. Compared with the spectrum of *III*, a new signal of the OCH_3 carbon atom appears at δ 51.1 and the signals of atoms $\text{C}_{(1)}$, $\text{C}_{(2)}$, $\text{C}_{(4)}$, and $\text{C}_{(5)}$ are shifted as a result of the esterified carboxyl. The other signals are affected only little (< 1 ppm).

Reduction–oxydation processes in the nitrosobenzene chemistry are not rare. As a process analogous to that found by us we may mention *e.g.* the reaction of nitrosobenzene with diethyl methylenemalonate⁸ in boiling chloroform which affords a product whose structure corresponds to a condensation product of phenylhydroxylamine with diethyl hydroxymethylenemalonate.

EXPERIMENTAL

Melting points were determined on a Kofler block, IR spectra were taken on a Zeiss UR 20 spectrometer, UV spectra on a Unicam 8000 instrument, and mass spectrum on an MS 902 spectrometer. Measurements of ^1H and ^{13}C NMR spectra were performed in the FT mode on Varian XL-200 (200 MHz for ^1H and 50.31 MHz for ^{13}C) and on Tesla BS-497 (100 MHz for ^1H ; 25.17 MHz for ^{13}C) instruments. The compounds were dissolved in deuteriochloroform and measured at room temperature (about 22°C) with tetramethylsilane as internal standard.

2-Formyl-3-anilino-3-(4-chlorophenyl)acrylic Acid (*III*)

A drop of boron trifluoride etherate was added to a stirred solution of 4-chlorobenzylidenemalon-aldehyde (0.78 g; 4 mmol) and nitrosobenzene (0.6 g; 5.6 mmol) in benzene (4 ml). After stirring for 2 h and standing overnight at room temperature, the mixture was diluted with benzene and filtered through silica gel. Evaporation of the solvent and crystallization from benzene–light petroleum afforded 0.78 g (81%) of the product, m.p. 171–174°C. For $\text{C}_{16}\text{H}_{12}\text{ClNO}_3$ (301.5) calculated: 63.68% C, 3.98% H, 11.77% Cl, 4.64% N; found: 63.59% C, 3.87% H, 11.87% Cl, 4.36% N. Mass spectrum (m/e): 301 (M^+), 227, 254, 193. IR spectrum (CHCl_3), cm^{-1} : 2 750 vw, 1 680 s, 1 599 s, 1 497 m, sh, 1 574 s, 1 560 s. UV spectrum (ethanol), nm ($\epsilon \cdot 10^{-3}$): λ_{max} 306 (18.8).

Deuteration. The acid *III* (0.2 g; 0.663 mmol) in acetonitrile (1 ml) was mixed with $^2\text{H}_2\text{O}$ (0.1 ml) and the solution was taken down *in vacuo*. This procedure was repeated five times. The thus-obtained product contained about 80% of the exchangeable protons replaced by deuterium.

Methyl 2-Formyl-3-anilino-3-(4-chlorophenyl)acrylate (IV)

Diazomethane in ether had been slowly added to a solution of the acid III (0.45 g; 1.49 mmol) in chloroform (4 ml) until the evolution of nitrogen ceased. The solvent was evaporated *in vacuo* and the residue crystallized from cyclohexane, affording 0.34 g (72%) of the product, m.p. 121 to 123°C. For $C_{17}H_{14}ClNO_3$ (315.5) calculated: 64.66% C, 4.44% H, 11.15% Cl, 4.44% N; found: 64.42% C, 4.48% H, 11.05% Cl, 4.54% N.

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