2,6,9-Trioxabicyclo[3.3.1]nona-3,7-diene-4,8-dicarbaldehyde, a Dissymmetric Propeller-like Molecule. The Structure and Chirality Proof

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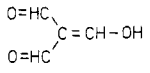
We report spectroscopic proof that the compound formed from two molecules of triformylmethane (1) by extrusion of one molecule water, and described earlier[1] as 2,6-diformyl-4-oxa-2,5-heptadienedial (2), possesses a bicyclic propeller-like structure 3 and exhibits axial chirality.

The simplest trialdehyde, triformylmethane (1), obtained in our laboratory as early as in 1960,[1,2] proved to be a strong acid (pK_a = 2.0).[3] When treated with carbonyl chloride it was converted to a stable derivative melting at 175–6 °C with elemental analysis corresponding to $C_8H_6O_5$ and regenerating the starting trialdehyde on heating in water. On the basis of this behavior resembling that of acid anhydrides, we proposed[1] for this compound the structure 2. In view of the more recent investigations[4,5] revealing that compounds with a methylenemalonaldehyde moiety exhibit a very high reactivity, some of them being extremely unstable, it became evident that the structure 2 required reinvestigation.



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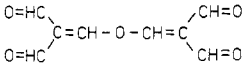

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Applying ^1H and ^{13}C NMR spectroscopy, we have now proven that the above-mentioned anhydro compound has the bicyclic structure 3. This is also in accord with MS, IR, and UV spectra. The proton NMR spectrum (200 MHz, $CDCl_3$) exhibits three singlets at δ 9.34, 7.61, and 6.32 with an intensity ratio of 1:1:1, which indicates the high symmetry of the molecule. Proton-decoupled ^{13}C NMR spectrum (50.3 MHz, DMSO-d_6) exhibited four signals at δ 187.6, 162.7, 117.0, and 86.5, again in general agreement with formula 3. However, the most important information on the topology of the molecule 3 was obtained from $J(^{13}C,^1H)$ values (Figure 1) in the proton-coupled ^{13}C NMR spectrum. All couplings were assigned by a selective $^{13}C\{^1H\}$ decoupling experiments, proving thus unambiguously the structure 3.

Possessing a 2-fold rotational axis as the only element of symmetry, the structure 3 should be chiral in accord with the observed chirality of 1,3,5,7-tetramethyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene, described earlier.[6–9] Indeed, when the chiral shift reagent (tris[3-[(trifluoromethyl)hydroxymethylene]-(+)-camphorato]europium-(III))[10] was employed, a nice splitting of all the three sin-

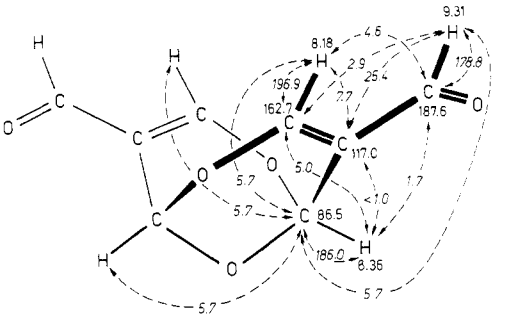
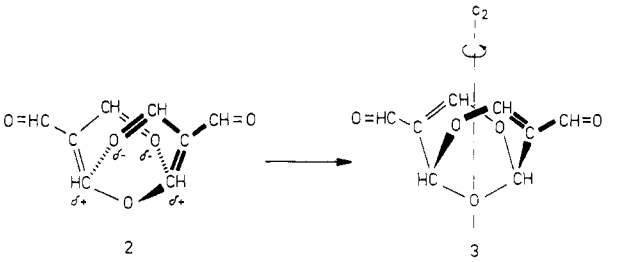


Figure 1. Proton and carbon-13 NMR parameters of compound 3 in DMSO-d_6. Chemical shift values (in ppm) are given at individual protons and carbon atoms and coupling constants J(C,H) are indicated by dotted lines with corresponding values (in hertz).

Scheme I



2 3

glets in ^1H NMR spectrum was observed (see the Experimental Section). The more pronounced induced shifts, observed for protons CH=O and OCHO (in comparison with CH=C), are in agreement with the expected more effective complexation of metal ion to aldehyde carbonyls. This also indicates the preferred s-trans orientation of the CH=CCH=O fragment (in accordance with the ^3J(C,H) values of formyl protons: 2.9 and 5.7 Hz for cis- and trans-oriented carbon atoms).

The heterocyclic system identified in the present study is rather rare. The only other reported compound of this type, 1,3,5,7-tetramethyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene, was formed from a platinum(II) organometallic intermediate of acetylacetone.[6–8] Somewhat later, its separation into enantiomers has been achieved via rhodium complexes.[9] In contrast to the above-mentioned 1,3,5,7-tetramethyl derivative, the formation of our bicyclic dialdehyde 3 proceeds with remarkable ease. In this work we confirm the propensity of the methylenemalonaldehyde moiety, both in triformylmethane and its anhydro form 2, to undergo cycloadditions.[4,5,11] In Scheme I the conversion of the anhydro form 2 into bicyclic compound 3 is visualized, the formation of the two new bonds being marked by dotted lines.

It can be concluded that the 2,6,9-trioxabicyclo[3.3.1]-nona-3,7-diene system, identified so far only in the two cases discussed above, may be expected to be a stable byproduct of the chemistry of other 1,3-dicarbonyl compounds, in particular, the triacylmethane family.

Experimental Section

Melting points were determined on a Kofler block and are uncorrected. Solvents and common reagents were obtained

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commercially. Triformylmethane was prepared by a described method[1,2] with use of the modified procedure given below. ^1H and ^{13}C NMR spectra were measured on a Varian XL-200 FT-NMR spectrometer.

Triformylmethane. To a solution of bromoacetic acid (34.74 g, 0.25 mol) in 100 mL of dimethylformamide was added $POCl_3$ (82 mL, 0.875 mol) at 15–18 °C during 2 h. After standing for 1 h the reaction mixture was heated at 75 °C for 2 h and then at 90 °C for 10 h. The reaction mixture was cooled and worked up at −25 °C by adding ethanol (100 mL) followed by water (200 mL) and 70% $HClO_4$ (50 mL). After the mixture was stirred for 2 h at −20 °C, the precipitate formed was separated by succion, washed with ethanol, followed by ethanol saturated with SO_2, and dried in vacuo. The crude diperchlorate[2] $C_{10}H_{21}Cl_2N_3O_8$ (382.2), obtained in about 55–65% yield, could be crystallized from acetonitrile (mp 224 °C), but for further procedure this purification was not necessary. The diperchlorate (3.82 g, 0.01 mol) was treated in 2 mL of CH_3OH with 4 N $NaOH/CH_3OH$ in two successive portions; the first one (5 mL) dissolved the diperchlorate, and the second one (3 mL) precipitated the sodium salt of triformylmethane. This was separated by succion and washed with a small portion of CH_3OH. The sodium salt was stirred for 1 h with a mixture of dichloromethane (15 mL), water (1 mL), and concentrated HCl (1 mL). The organic layer was separated, the aqueous layer was extracted twice with dichloromethane (8 mL), and the combined extracts were dried over anhydrous $MgSO_4$ and filtered. The solvent was removed with use of a small distillation column, and the residue was sublimed in vacuo. Yield 0.8 g (80%), mp 101–103 °C (ref 1).

2,6,9-Trioxabicyclo[3.3.1]nona-3,7-diene-4,8-dicarbaldehyde. A mixture of triformylmethane (0.5 g, 0.005 mol), dry ether (20 mL), and thionyl chloride (3.65 mL, 0.05 mol) was stirred overnight, the ether and the excess thionyl chloride were removed in vacuo, and the residue was purified by sublimation (130 °C, 26 Pa) and crystallization from 1,2-dichloroethane: yield 0.27 g (60%); mp 180 °C; MS, e/z (percent) 182 (M^+, 17.5), 154 (31), 72 (29), 71 (28), 55 (82), 53 (44), 29 (100), 27 (40); UV (CH_3CN) λ_{max} 230 nm, ϵ 3.9×10^4; IR (KBr disk, selected bands): 3067 (m), 3050 (w), 3019 (m) (ν_{C-H} of CH=C), 2853 (m), 2754 (vw), 2740 (vw) (ν_{C-H} of CH=O), 1661 (s), 1681 (s) ($\nu_{C=O}$), 1631 (vs) ($\nu_{C=C}$), 1245 (vs) (ν_{ring}), 987 (s), 930 (s), 895 (s), 860 (s); ^1H NMR (a) in $CDCl_3$ δ 6.32 (s, OCHO), 7.61 (s, CH=), 9.34 (s, CH=O); (b) +Eu[tfc]$_3$ (L/S $\approx$ 0.5) δ 6.95 and 6.96 (s, OCHO), 7.92 and 7.96 (s, NCH=), 9.98 and 10.02 (s, CH=O).

Registry No. 1, 18655-47-5; 1·Na^+, 79341-66-5; 2, 116149-13-4; 3, 116149-12-3; $(Me_2N^+{=}CH)_2C{=}CHNMe_2{\cdot}2ClO_4^-$, 2009-81-6; bromoacetic acid, 79-08-3.

Conversion of Isocyanates to Nitro Compounds with Dimethyldioxirane in Wet Acetone

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The standard reaction sequence for transformation of a carboxylic acid into a nitro group is lengthy: acid–acylazide→isocyanate→carbamate→amine→nitro. It occurred to us that this "classical" route would be much simplified if a reagent could be found for direct oxidation of the intermediate isocyanate to the desired nitro compound. This would also obviate the necessity of working with the free amine, an important advantage as this electron-rich group is often a point of weakness in strained molecules, triggering the breakdown of the skeleton. Conveniently, the advent of azidotrimethylsilane has made isocyanates exceptionally easy to prepare *and* isolate.[1]

Table I. Oxidation of Isocyanates with Dimethyldioxirane[a]

	no water added		15% H_2O added		15% H_2O with $PhCH_2NMe_3OH$	
isocyanate	time	yield, %	time	yield[c], %	time	yield,[c] %
phenyl	no reaction		30 min	95 (65)[b]		
cubane-1,4-di	no reaction		1 h	85[b]		
n-butyl			24 h	34	1 h	89
cyclohexyl			24 h	16	3 h	94
tert-butyl			24 h	<5	8 h	83

[a] Reaction conditions: 0.08 M dimethyldioxirane in acetone solution; room temperature; dark. [b] Isolated yield. [c] By calibrated GLC analysis.

Unfortunately, little has been reported about the oxidation of isocyanates.[2]

We undertook a brief survey of the reactions of cyclohexyl isocyanate with common oxidizing agents. Ozone did not react with the isocyanate under a variety of conditions. Oxidation with potassium permanganate or with *m*-chloroperbenzoic acid gave complex mixtures of products, but these contained little or no nitrocyclohexane. Oxidation of cyclohexyl isocyanate with ruthenium tetroxide in carbon tetrachloride did give a 1:1 mixture of nitrocyclohexane and cyclohexanone. In all probability this oxidation proceeds via cyclohexanone oxime and requires the presence of hydrogen α to the isocyanate. Although certainly this reagent qualifies for further consideration, in the case of real interest to us, the oxidation of 1,4-diisocyanatocubane, the reaction with ruthenium dioxide took an obscure course and destroyed the ring system entirely.[3] After this failure, we turned to dimethyldioxirane, an oxidizing agent of extraordinary properties.[4]

Dimethyldioxirane was prepared by reaction of OXONE (DuPont trademark), $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$, with buffered aqueous acetone, fairly much following the procedure described by Murray and Jeyaraman.[5a] The dimethyldioxirane was entrained along with other volatiles in a room temperature nitrogen stream; subsequent condensation gave a wet acetone solution about 0.1 M in oxidant.

Our results for the oxidation of some representative isocyanates with dimethyldioxirane in acetone are summarized in Table I. Primary, secondary, and tertiary aliphatic isocyanates, as well as phenyl isocyanate, are all cleanly converted to the corresponding nitro compounds in good yield. Water is an essential ingredient; oxidation does not occur (the isocyanate can be recovered unchanged) if the dimethyldioxirane/acetone solution is dried before use over 4A molecular sieves. On the other hand, if water is purposely added, the conversions occur quickly at rates roughly dependent on the obvious steric factors. Thus, it is clear that the electron-poor isocyanate itself is not directly oxidized, but rather is hydrolyzed first to the carbamic acid. This appears to be the rate-limiting step, for the overall rate of oxidation is increased dramatically, as shown in the table, if a catalytic amount of benzyltrimethylammonium hydroxide is added to the reaction so-

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