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THE EXTRAORDINARY SELECTIVITY OF METHOXYPHENYLCARBENE; THE CASE OF THE CURIOUS "OLEFIN"

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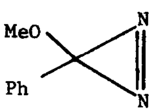
Summary. The reaction of MeOCPh with $Me_2C{=}CMe_2$ gives a low yield of the appropriate cyclopropane (3); however, aged olefin containing traces of the related hydroperoxide (8) or alcohol (9) impurities, selectively affords the formal O-H insertion products 7 or 4.

In our preliminary study of methoxyphenylcarbene (MeOCPh) as generated from 3-methoxy-3-phenyldiazirine, 1, we examined the carbene's additions to 4 alkenes: trans-2-butene, isobutene, trimethylethylene, and tetramethylethylene (TME).[2] Appropriate cyclopropanes were obtained in low yields from the first 3 substrates, but TME gave a product *tentatively* assigned as alkene 2. A detailed analysis of the reactivity of MeOCPh has now focused attention on the possible origins of 2.[3] Was it derived from the expected but undetected cyclopropane 3? Or was 2 the directly-formed primary product of a far more interesting "ene"-type reaction between MeOCPh and TME?

We have subjected the MeOCPh/TME reaction to very careful scrutiny, and now report that alkene 2 is *not* formed in this reaction. Rather, the compound originally assigned structure 2 is the closely related ene-acetal 4, probably formed by MeOCPh "insertion" into traces of 2,3-dimethyl-1-butene-3-ol that were present as an oxidative impurity in the TME substrate.

To assist in product analysis of the MeOCPh/TME reaction, we independently prepared cyclopropane 3 from its bromo analogue 5,[4] by exchange with t-BuLi (Et_2O/hexane, -60°C, 15 min), followed by reaction of the derived cyclopropyllithium with ethereal dimethyl peroxide[5] (30 min at -50°C, followed by warming to 25°C).[6] Cyclopropane 3 was obtained in 8% isolated yield[7] after aqueous/extractive workup,



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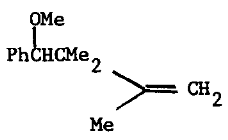

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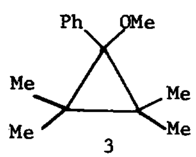

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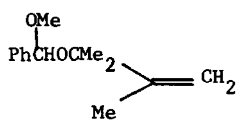

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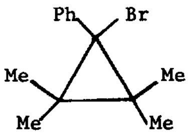

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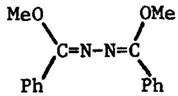

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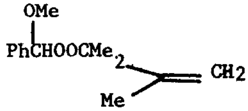

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silica gel chromatography (Et_2O/pentane), and kugelrohr distillation (40°C/0.5 mm-Hg). Its structure was established by high resolution mass spectroscopy, and proton nmr: δ($CDCl_3$) 0.94, 1.24 (2s, 4Me's), 3.04 (s, OMe), 7.30-7.33 (m, aryl).

Photolysis (25°C, 1 hr, Osram 200 W XE mercury lamp, Pyrex filter) or 25°C dark (1 hr) thermolysis of ~0.1 M diazirine 1 in 20 ml of TME (freshly distilled from $LiAlH_4$) gave 4-12% of adduct 3, high yields (40-70%) of azine 6,[8] and generally low yields (<5%) of benzaldehyde[2] and methyl benzoate.[2] These products are unexceptional for a carbene generated from a diazirine in an *unreactive* substrate. Importantly, a product with a gc retention time corresponding to 2 was absent (<1%).[9] However, when the TME substrate was <font=2> aged for several days to a week, 20-70% yields of peroxyacetal 7 were obtained. The latter was identified by gc and nmr comparisons with an authentic sample obtained in 75% yield from the thermolyis of diazirine 1 in 2,3-dimethyl-1-butene-3-hydroperoxide, 8.[10,11]

The origin of 7 in aged TME can be traced to the scavenging of MeOCPh by *traces* of 8, formed from TME by air oxidation (see below). Indeed when an insufficiency of diazirine 1 was thermally decomposed in 20 ml of TME, to which only 2 drops of hydroperoxide 8 had been added, peroxyacetal 7 was the sole product, isolated in at least 80% yield.[12] In a more quantitative, kinetic competition between 50 mmol of TME and 0.21 mmol of 8, only 7 and no 3 was detected in the product mixture by capillary gc; i.e., a 7/3 product ratio of >51 (electronic integration), from which we estimate that the relative reactivity of hydroperoxide 8 vs. TME exceeds (50/0.21) x 51 = 12,140.

Nevertheless, the product isolated in 1981 from our original[2] MeOCPh/TME experiment was not peroxyacetal 7, but the related acetal 4. We have now prepared 4 in 42% isolated yield by thermolysis of 1 in 2,3-dimethyl-1-butene-3-ol, 9. The acetal was purified by distillation (75°C/0.5 mm-Hg) and characterized by nmr and elemental analysis, wherein it is readily differentiated from 7.[13] The nmr spectrum of 4 matches that of the compound we originally isolated from the MeOCPh/TME reaction, and to which we assigned structure 2.[2]

The origin of 4 in the original study is problematical. It was observed in the *crude* reaction product,[2] so that it was not a gc-induced pyrolysis artifact. Moreover, cyclopropane 3 is stable under reaction/isolation conditions, and is not converted to 4 in the presence of hydroperoxide 8. In 20 reactions between MeOCPh and variously ill-treated TME, the major additive product was 7, not 4.[14] The formation of 7 is not surprising, because we consistently find hydroperoxide 8 in

$CH_2{=}CMeCMe_2OOH$ **8**

$CH_2{=}CMeCMe_2OH$ **9**

aged TME, and we now know that MeOCPh is highly selective toward **8** (see above). If the related alcohol **9**, were present in the TME,[15] acetal **4** might be expected to form. For example, competition experiments with MeOCPh give k_8/k_9 ~10, so that alcohol **9** should be at least 1000 times more reactive than TME toward the carbene. We have also found **4** as a product in control experiments where the TME substrate contained both **8** and 2,3-dimethyl-1-butene (another common TME impurity). Alcohol **9** may be formed from a free radical reaction of these two impurities.

In summary, then, the reaction of MeOCPh from diazirine **1** with highly purified TME gives low yields of addition product **3**.[16] Alkene **2** is not formed in this reaction, but if the TME has aged under air for several days, peroxyacetal **7** is formed. Under certain, ill-defined circumstances, acetal **4** can be produced, and it is most likely this compound that was originally taken for alkene **2**.[2]

In retrospect, it is the extraordinary nucleophilic selectivity of MeOCPh,[3] the consequent unreactivity of TME,[17] and the high reactivity of the carbene toward O-H groups,[12] that together result in the highly discriminating and deceptive O-H "insertions" of MeOCPh with traces of hydroperoxide or alcohol impurities present in great excesses of TME. In light of the present work, the reaction of nucleophilic MeOCOPh[18] with TME is unlikely to give an alkene analogous to **2**; the observed product[19] is probably comparable to **7** or **4**.

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References and Notes

(1) Visiting Scientist on leave from the Department of Food Technology, The Agricultural University, Warsaw, Poland.

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(6) For an analogous procedure, see R.A. Moss and D.P. Cox, Tetrahedron Lett., **26**, 1931 (1985).

(7) The major product was 1-phenyl-2,2,3,3-tetramethylcyclopropane.

(8) Azine **6**, mp 70-73°C, was purified by chromatography on silica gel (pentane), and characterized by nmr, mass spectroscopy, and elemental analysis.