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TRAPPING OF UNSATURATED FULVENE ENDOPEROXIDES WITH DIMETHYL 1,2,4,5-TETRAZINE-3,6-DICARBOXYLATE: A NEW SYNTHESIS OF ALKYLIDENE- AND ARYLIDENEMALONALDEHYDES

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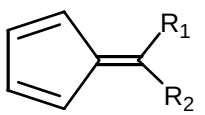
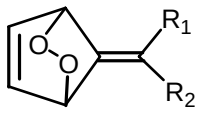
Abstract - Unsaturated fulvene endoperoxides (**2a-e**) were trapped with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (**4**). The formed saturated fulvene endoperoxides containig 1,2-dihydropyridazine ring (**6a-e**) were characterised by spectroscopic methods. Treatment of (**6a-e**) with cobalt(II) tetraphenylporphyrin (CoTPP) provided alkylidene- and arylidenemalonaldehydes (**9a-e**).

Unsaturated bicyclic endoperoxides are readily available by cycloaddition of singlet oxygen with cyclic 1,3-dienes.[1] The photooxygenation of fulvenes has been one of the most intriguing reactions in singlet oxygen chemistry.[2] Thus, the reaction of singlet oxygen with the 6,6-disubstituted fulvenes (**1**) provides a useful method for the preparation of substituted oxepinones.[3] Unstable fulvene endoperoxides (**2**) can be conveniently and selectively reduced to their respective stable dihydrofulvene endoperoxides (**3**).[4] Erden *et al.*[5] have shown that the thermolysis of the saturated fulvene endoperoxides derived from 6-vinylfulvenes proved to be excellent precursors of substituted cyclopentenones. Allene oxides and/or cyclopropanones are postulated as intermediates in this reactions.[5]



1



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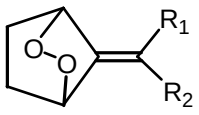
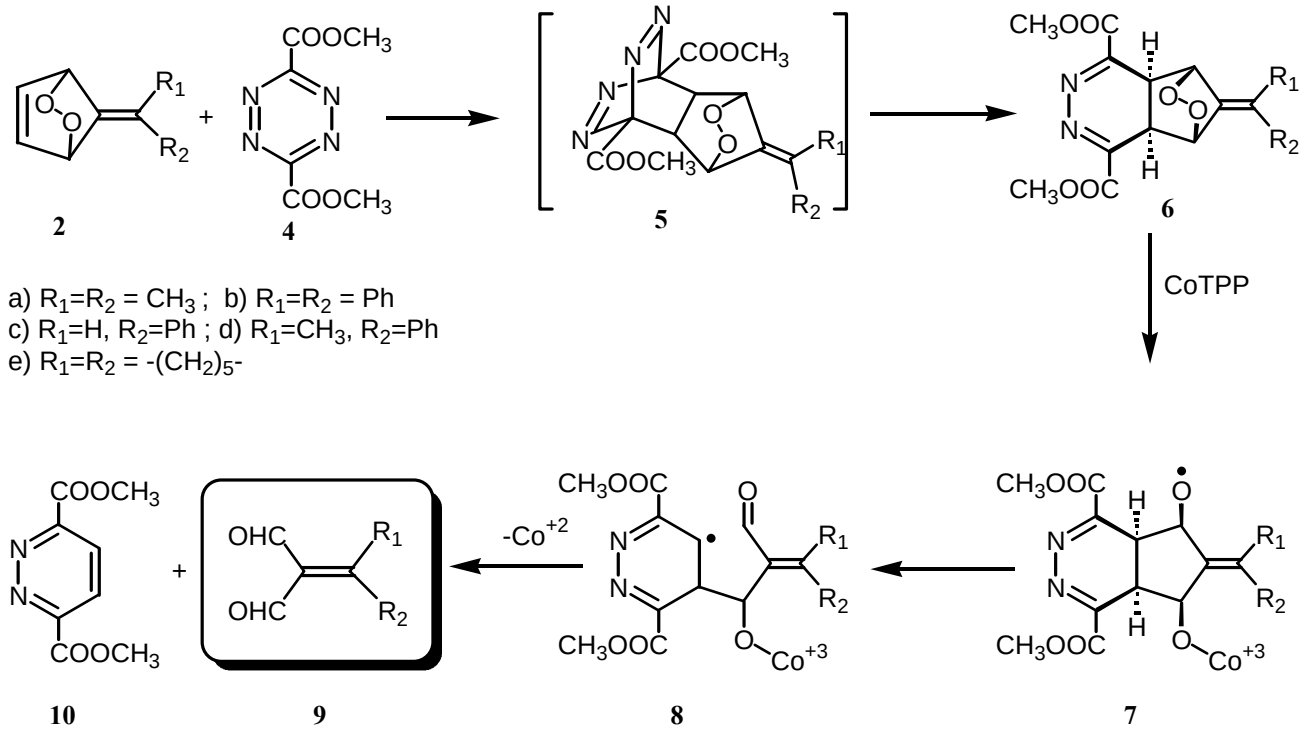


3

a) $R_1=R_2 = CH_3$; b) $R_1=R_2 = Ph$
c) $R_1=H$, $R_2=Ph$; d) $R_1=CH_3$, $R_2=Ph$
e) $R_1=R_2 = -(CH_2)_5-$

In this communication we describe an applicability of the dihydrofulvene endoperoxides to the synthesis of alkylidene- and arylidenemalonaldehydes. The methodology is based on trapping of highly reactive fulvene endoperoxides (**2**) with tetrazine (**4**) and the CoTPP-catalysed decomposition of the formed compounds.

More recently, we succeeded in the synthesis of some interesting bicyclic endoperoxides, which contain heteroaromatic ring[6] by reacting of suitable unsaturated bicyclic endoperoxides with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (**4**). The 'inverse electron-demand' Diels-Alder reaction of 1,2,4,5-tetrazines with alkenes provides a useful synthetic route to substituted dihydropyridazines.[7] We first reacted the disubstituted fulvene endoperoxide (**2**), obtained by photooxygenation of the appropriate fulvenes (**1**) in dry $CHCl_3$ at -50 ^oC in the presence of tetraphenylporphyrine, with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate. The isolated products were formed upon nitrogen extrusion from the initial formed tricyclic adducts (**5**) in quantitative yields (Scheme 1). The spectral data supported the proposed structures and preservation of peroxide linkage.



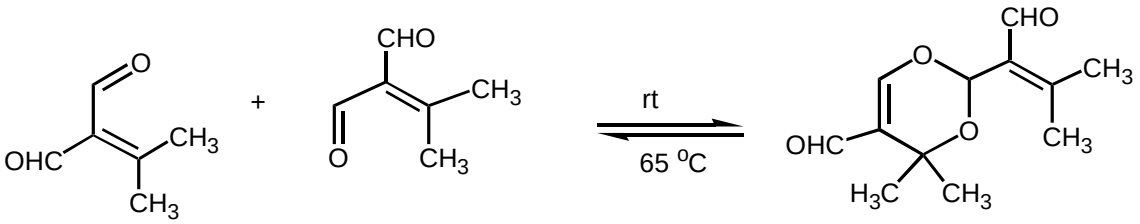
2 **4** **5** **6** **7** **8** **9** **10**

Scheme 1

^{13}C NMR data of **6a** were consistent with the proposed structure showing 4 aliphatic and 3 olefinic and 1 carbonyl carbons. ^1H NMR spectrum consists of four group signals. The peroxide-bridgehead protons and the dihydropyridazine ring protons appear as broad singlets at 5.28 and 3.63 ppm, respectively. The methoxyl and methyl protons were displayed as singlets. The structure of the dihydroprydazine-fulvene endoperoxides (**6b-e**) were also determined by ^1H and ^{13}C NMR spectral data. The stereochemistry of **6** was not determined. Sasaki *et al.*[8] have shown that disubstituted fulvene derivatives having structure like **2** undergo cycloaddition reaction with dienes to give exclusively exo-products. On the basis of these results we assume that **6** has also exo-configuration.

Next, we turned our attention to the CoTPP-catalysed rearrangement[9] of these endoperoxides. The 1,2-dihydroprydazine-fulvene endoperoxides (**6a-e**) were exposed to CoTPP in $CHCl_3$ for 1 h at –50 °C. In all cases, dihydrofulvene endoperoxides (**6a-e**) underwent a fragmentation to form alkylidene- or arylidenemalonaldehydes[10] (**9a-e**) and pyridazine (**10**) where cleavage of C-C bonds are involved (Scheme 1). At this stage, we postulate a radical mechanism for the formation of these products. We assume that the radical (**7**) resulting from electron-transfer reaction between Co^{2+} species and endoperoxides (**6**) serves as a key intermediate. Cleavage of the C-C bond can generate allyl radical and first formyl group. Consequently, this intermediate (**8**) can undergo a second C-C cleavage followed by or following elimination of Co^{2+} species to provide dialdehydes (**9a-e**).

The arylidenemalonaldehydes represent an important class of compounds, which are of considerable preparative and theoretical interest.[11] The first general synthesis of substituted methylidenemalonaldehydes has been developed by Arnold *et al*.[12] However, This synthesis is limited to the preparation of at the benzene ring substituted arylmethylenemalonaldehydes and their heterocyclic analogues. However, our synthesis can be applied to the generation of a variety of alkylidene- or arylidenemalonaldehydes.



9a **11**

Scheme 2

The structural and dynamical properties of alkylidene- and arylidenemalonaldehydes are also of considerable experimental and theoretical interest.[11] We observed that dimethylidenemalonaldehyde (**9a**) dimerizes smoothly at room temperature involving a [2+4] cycloaddition reaction to give **11** which can undergo a cycloreversion reaction at 65 °C to form the starting material. However, the dialdehydes (**9b-e**) are stable at room temperature.

In summary, we have developed an efficient strategy to access a series of alkylidene- and arylidenemalonaldehydes from readily available starting materials. Further development of this chemistry is on going.

ACKNOWLEDGMENT

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10. Selected spectroscopic data for aldehydes (**9a-e**): **9a** (66%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.20 (s, 2 H), 2.40 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 193.12, 174.18, 134.92, 25.39. **9b** (70%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.56 (s, 2H), 7.61-7.22 (m, 10 H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.37, 171.56, 138.57, 136.08, 133.13, 132.95, 129.83. **9c** (54%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.19 (s, 1H), 10.06 (s, 1H), 8.19 (s, 1H), 7.63-7.50 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 192.57, 191.90, 156.49, 136.07, 134.45, 134.02, 133.58, 131.08. **9d/d'**(enol form) (57%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.24 (s, 1H), 9.56 (s, 1H), 8.43, (s, 2H), 7.51-7.29 (m, 10H), 5.30 (bs, 1H), 5.23 (bs, 1H), 2.73 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.03, 193.88, 183.47, 172.63, 140.87, 135.30, 132.33 (2C), 130.69 (2C), 130.59 (2C), 130.49, 130.37, 129.55, 114.51, 25.80. **9e** (47%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.39 (bs, 2H), 5.65 (m, 1H), 2.06-1.44 (m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 181.77, 154.61, 131.95, 125.39, 121.07, 29.77, 27.47, 24.70, 23.73. Spectroscopic data for dimer **11:** ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.04 (s,1H), 9.13 (s, 1H), 7.35 (s, 1H), 6.14 (s, 1H), 2.30 (s, 3H), 2.19 (s, 3H), 1.54 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.78, 190.15, 166.72, 165.36, 133.06, 129.19, 93.22, 77.86, 28.63, 27.22, 25.83, 22.84.
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