acetylporphyrins 10 and 11: M^+ 1093 ± 1; λ_{max} 648, 595, 550 (sh), 519, 423 nm; ν_{max} (CH_2Cl_2) 3400, 1722, 1697 cm^{-1}; NMR ($CDCl_3$) δ 1.98 (s, 3 H), 3.8–4.7 (m, 16 H), 5.32, 5.45, 5.5, 5.55 (4s, 2 H), 7.3–8.0 (m, 16 H), 8.32–8.8 (m, 7 H). Similarly the isocyanates 12 and 13 could be prepared ($COCl_2$) and converted to stable ethylurethanes 14 and 15: M^+ 1123 ± 1; λ_{max} (CH_2Cl_2) 658, 595, 550, 518, 423 nm; ν_{max} 3300 cm^{-1}; NMR ($CDCl_3$) δ 5.35 (d, 2 H), 1.15 (t, 3 H, J = 7 Hz, ethyl group).

When the reduction of the zinc nitroporphyrin was carried out with $SnCl_2$–HCl in CH_2Cl_2 as cosolvent there was obtained after chromatography on silica gel (EtOAc–C_6H_6, 1:9 v/v) a 50% yield of the metal-free substance, tentatively suggested to be dione 16 [M^+ 1067 ± 1; ν_{max} 1720, 1601 cm^{-1}; λ_{max} (CH_2Cl_2) 655, 605, 578, 470 (sh), 412 nm; NMR ($CDCl_3$) δ −3.7 (1 H), 3.6–4.8 (m, 16 H), 5.26, 5.51, 5.55, 5.95 (4s, 2 H), 7.05–7.75 (m, 16 H), 8.34–8.72 (m, 6 H)], although the alternative isomeric possibilities are not excluded at this time.[9]
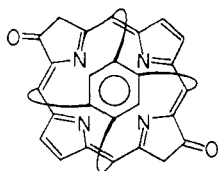
16

Presently we are attempting to elaborate these accessible functionalized capped porphyrins into species 5.

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(8) The presence and ratio of isomers is clearly defined by the NMR signals from the capping protons, which appear, with equal weight, as four singlets at δ 5.03, 5.78, 5.43, and 5.57, two for each isomer.
(9) Repetition of this reduction on a mononitrotetraphenylporphine, prepared essentially as above, cf. ref 6 above, gave a carbonyl frequency on the infrared, ν_{max} 1720 cm^{-1}, which is characteristic of an unsaturated five-ring ketone and is, in this case, not obscured by the ester functions implicit in 16.

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Prostanoid Endoperoxide Model Compounds: 2,3-Dioxabicyclo[2.2.1]heptane via Selective Diimide Reduction[1]

Summary: A convenient synthesis of 2,3-dioxabicyclo[2.2.1]-heptane (2) has been achieved in ∼30% yield by photosensitized singlet oxygenation of cyclopentadiene, followed by carefully controlled diimide reduction in nonpolar and nonprotic media at dry ice temperature.

Sir: The importance of prostaglandin endoperoxide (1) as precursor to the physiologically potent prostaglandins thromboxane and prostacyclin in the oxygenation of arachidonic acid has been well documented.[2] These pharmacologically significant substances originate from 1 by skeletal transformations of the 2,3-dioxabicyclo[2.2.1]heptane ring system (2); the prostaglandins PGE and PGF enzymatically

1   2
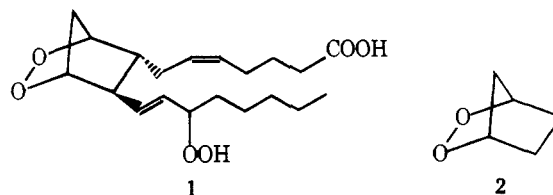
by base-catalyzed rearrangement and reduction,[3] the thromboxane A_2[4] and prostacyclin[5] presumably by enzymatic acid-catalyzed rearrangement. Thus, the synthesis of the parent endoperoxide skeleton 2 seemed timely and urgent in order to explore its chemistry in the interest of designing biologically active substitutes.

PGE   PGF

Thromboxane A_2 Prostacyclin
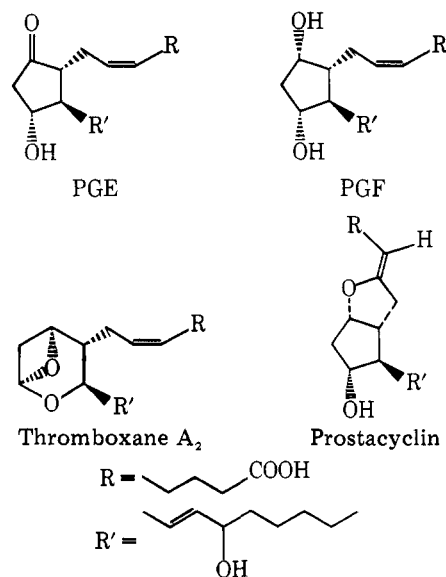
The endoperoxide 2 has been prepared by silver oxide reaction with 3-bromocyclopentyl hydroperoxide.[6,7] Simultaneously, an alternative synthetic method was reported which shows great promise for the preparation of the natural prostaglandin peroxide from PGF.[8] These successes urge us to communicate our results on the preparation of 2,3-dioxabicyclo[2.2.1]heptane (2) from cyclopentadiene (eq 1).

3   2

(1)
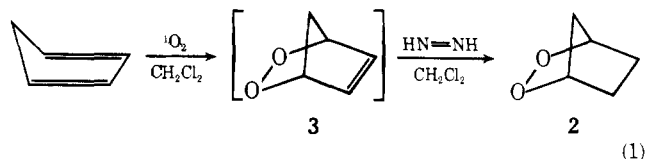
When cyclopentadiene is photooxygenated in methanol at −78 °C with rose bengal as sensitizer[9] and the resulting thermally labile cyclopentadiene endoperoxide (3) solution treated directly with tenfold excess of diimide, generated in situ from potassium azodicarboxylate and acetic acid[10] at dry ice temperature, only reduced decomposition and rearrangement products could be isolated. It was clear that the labile endoperoxide 2 had been formed, but it did not survive the polar and protic reduction conditions in methanol. Since these reduction conditions proved successful in the preparation of bridgehead-substituted derivatives of 2,[11] it was important to persist in this synthetic route for the parent endoperoxide.

As model substrate we chose ascaridole, which was reduced to dihydroascaridole[12] in ~40% by diimide, but employing methylene chloride instead of methanol as solvent and using 90% of the required stoichiometric amounts of acetic acid at dry ice temperature. Although these diimide reductions ran considerably slower, 2,3-dioxabicyclo[2.2.1]heptane (2) could be obtained in this manner in ~30% pure yield by silica gel column chromatography (at −20 °C and eluting with methylene chloride) of the photooxygenated cyclopentadiene reaction mixture after diimide reduction (eq 1). The endoperoxide 2, mp 41–43 °C (lit.[6] mp 42–43.5 °C), exhibited the reported[6] IR and NMR spectral data.[13] Catalytic hydrogenation over Pd/C afforded quantitatively *cis*-1,3-dihydroxycyclopentane, confirmed by IR and NMR comparison with an authentic sample prepared by diimide reduction of 1,4-dihydroxy-2-cyclopentene,[14] while treatment with KOH in methanol at 0 °C for 15 min gave the expected 3-hydroxycyclopentanone,[15] levulinaldehyde,[8] and traces of 2-cyclopentenone.

This convenient synthesis of 2 from the readily available cyclopentadiene should greatly facilitate the exploration of the chemistry of this novel bicyclic peroxide and make available prostanoid endoperoxide model compounds for pharmacological testing. The mild, peroxide bond-preserving diimide reduction method should prove useful in the synthesis of hitherto unknown, sensitive mono- and bicyclic peroxides.

Diimide Reduction (General Procedure). A 250-mL, two-neck, round-bottom flask equipped with magnetic spin bar, rubber septum, and pressure-equalizing dropping funnel was charged under a nitrogen atmosphere with 8.7 g (45 mmol) of dipotassium azodicarboxylate and 30 mL of CH_2Cl_2 (freshly distilled from CaH_2). While cooling with a dry ice–acetone bath and stirring magnetically are added dropwise within 20 min simultaneously a solution of 5.1 g (85 mmol) of acetic acid in 15 mL of CH_2Cl_2 from the dropping funnel and a solution of cyclopentadiene endoperoxide (prepared by photooxygenation of 0.560 g (8.5 mmol) of cyclopentadiene and 2 mg of tetraphenylporphyrin (as sensitizer) in 20 mL of CH_2Cl_2 at −78 °C for 5 h with a 150-W General Electric sodium lamp) by means of a steel capillary (15G) siphon from a dry ice cooled flask by applying a slight nitrogen pressure. After stirring at −78 °C for an additional 30 min, the reaction mixture was allowed to warm up slowly (~30 min) to 0 °C and stirred at this temperature another 120 min. The solids were removed by filtration, the solvent was rotoevaporated [0 °C (10 mm)], and the product bulb-to-bulb distilled [30 °C (0.1 mm)], affording a pale yellow semisolid which was purified by chromatography on silica gel at −20 °C, eluting with CH_2Cl_2.

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