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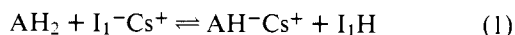
Carbon Acidity. 59. First and Second Ion-Pair Acidity Constants for 9,10-Dihydroanthracene with Cesium Cyclohexylamide¹

Sir:

Although dimetalated and even more highly metalated hydrocarbons are not uncommon,² no equilibrium constants for such higher metalations have previously been measured. We report here both the first and second acidity constants for 9,10-dihydroanthracene (DHA) expressed as pK_{CsCHA} values in the cesium cyclohexylamide (CsCHA)-cyclohexylamine (CHA) system.³

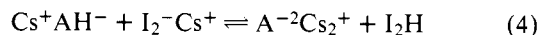
The procedure for measuring the spectra of the cesium salts was essentially that used previously,⁴ and the relevant data are summarized in Table I. Commercially obtained DHA was purified by recrystallization from ethanol followed by vacuum sublimation. UV analysis showed the presence of <0.01% anthracene. The absorptions of 9,10-dihydroanthracyl 9 anion⁵ (DHA⁻) and 9,10-dihydroanthracene 9,10 dianion⁶ (anthracene dianion, A⁻²) lie well separated in the visible region with extinction coefficients of comparable magnitude and permit the determination of the pK leading to the dianion. Formation of the dianion with CsCHA is rapid and quantitative; successive additions of base yielded a constant final absorption value with an isosbestic point between the monoanion and dianion peaks. No absorptions due to anthracene radical anion were observed.⁷ The λ_{max} values of the tight ion-paired and solvent-separated lithium salts of DHA⁻ occur at 400 nm and 450 nm, respectively;⁸ we find that the cesium salt absorbs at 444 nm. Extrapolating from the ion-pair studies of Hogen-Esch and Smid,⁹ this value is about what one would expect for a contact ion pair with a cation of large radius.

The pK measurement technique is based on competitive equilibria with cesium cyclohexylamide (CsCHA) in cyclohexylamine (CHA):^{4,10}



$$K_1 = [I_1H][AH^-Cs^+]/[AH_2][I_1^-Cs^+] \quad (2)$$

$$\log K_1 = pK_{CsCHA}(I_1H) - pK_{CsCHA}(AH_2) \quad (3)$$



$$K_2 = [I_2H][A^{-2}Cs_2^+]/[AH^-Cs^+][I_2^-Cs^+] \quad (5)$$

$$\log K_2 = pK_{CsCHA}(I_2H) - pK_{CsCHA}(AH^-Cs^+) \quad (6)$$

Determination of the second pK_{CsCHA} value involved a more indirect technique than usual because the indicators used and DHA⁻ absorb at the same wavelength. Therefore, the 444-nm peak had to be factored into the two components by calculating the concentration of A⁻² from the 633-nm peak and deriving the DHA⁻ concentration from mass balance with the initial quantity of anthracene (eq 7-9) where ϵ_1 , ϵ_2 , and ϵ_3 refer to the independently determined extinction coefficients of 9,10-dihydroanthracylcesium (AH⁻Cs⁺), indicator (I⁻Cs⁺), and

Table I. Absorbance and pK_{CsCHA} Values of Indicators and DHA

hydrocarbon, ^a RH	λ_{max} (R ⁻ Cs ⁺), nm	$10^{-3}\epsilon$	pK_{CsCHA} (per H) ^b
BDPM	573	44.3	30.2
DXM	448	37.7 ^c	36.3
DpTM	446	44.0	35.1
DmTM	447	47.9	34.8
DHA	444	24.2	30.3
DHA ⁻ Cs ⁺	633	18.3	34.1

^a Abbreviations follow: BDPM, *p*-biphenyldiphenylmethane; DXM, bis(2,4-dimethylphenyl)methane (or dixilylmethane); DpTM, di-*p*-tolylmethane; DmTM, di-*m*-tolylmethane; DHA, 9,10-dihydroanthracene; DHA⁻, 9,10-dihydroanthracyl anion. ^b Error limits are within ± 0.2 . ^c This value was redetermined and is a correction to the previously published number.¹⁰

9,10-dihydroanthracene dicesium (A⁻²Cs₂⁺) in that order. Several runs were made with each of three indicators, DpTM, DXM, and DmTM, and consistent results were obtained.

$$[AH^-Cs^+] = [AH_2]_0 - [A^{-2}Cs_2^+] \quad (7)$$

$$[I_2^-Cs^+] = (Abs_{444} - \epsilon_1[AH^-])/ \epsilon_2 \quad (8)$$

$$[A^{-2}Cs_2^+] = Abs_{633}/ \epsilon_3 \quad (9)$$

The first pK_{CsCHA} of DHA, 30.3, is not significantly different from that previously measured for 9,9-dimethyl-9,10-dihydroanthracene (30.25).¹⁰ This result provides a check on the present experimental technique and shows that the effects of a dimethylmethylene bridge are similar to a simple methylene bridge in this system, but the truly novel result of the present work is the discovery of such a small difference of only 4 pK units between the first and second dissociations; with a pK_{CsCHA} of 34.1, DHA⁻Cs⁺ is almost as acidic as diphenylmethane itself ($pK_{CsCHA} = 33.4$).¹⁰

One factor contributing to this relatively high acidity is the high delocalization of the dianion. Anthracene dianion is a 16-electron system with a considerable paratropic ring current;¹¹ however, this anti-aromatic character clearly does not seriously offset the net stabilization provided by the delocalized π system and illustrates the point made by Haddon, Kaplan, and Marshall¹² that classification of aromatic character by any one criterion does not necessarily reflect on the other properties. Ring current effects in particular are so sensitive to small perturbations that they have little correlation with thermodynamics.¹³

The other important factor in this system is that the dianion is undoubtedly a contact ion triplet in which the cesium cations are located on opposite sides of the anthracene dianion.¹⁴ The electrostatic stabilization in such a system is clearly of dominating importance. The quantitative resultant of these effects as given in the present experiments also helps to rationalize the polymetalation observed in many organolithium compounds.²

References and Notes

- This research was supported in part by U.S. Public Health Service, National Institutes of Health, Grant No. GM-12855.
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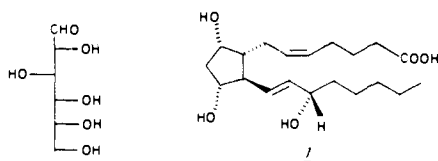
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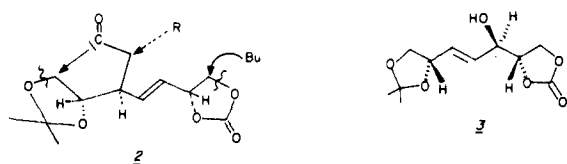
Total Synthesis of Prostaglandin F_{2α} by Chirality Transfer from D-Glucose^{1,2}

Sir:

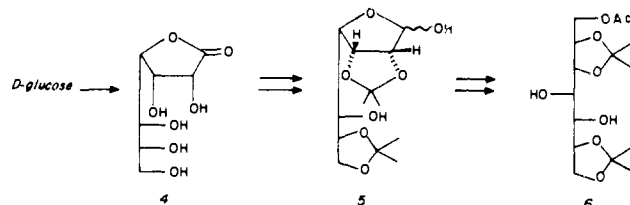
We describe herein the successful construction of prostaglandin PGF_{2α} (**1**) from D-glucose.



The synthetic plan involves the assumption that the transformations shown by arrows on **2** could be effected. A molecule of type **2** should in turn result from C–O → C–C chirality transfer from **3**. It is this molecule which thus became our initial synthetic target.

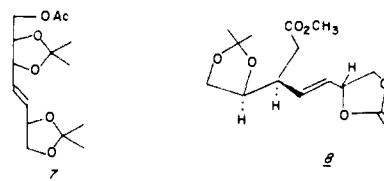


The product of the addition of HCN to D-glucose, the commercially available³ D-glycero-D-guloheptono-1,4-lactone (**4**), was reduced with aqueous sodium borohydride (pH kept at 3–3.5 by simultaneous addition of 10% H₂SO₄) to give (~90% yield) D-glycero-D-guloheptose⁴ from which the required 2,3,6,7-diisopropylidene-D-glycero-D-guloheptose (**5**)

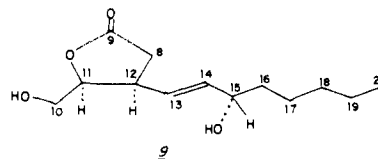


was formed⁵ in 75% yield together with 15% isomeric 3,5,6,7-diisopropylidene derivative.⁶ Reduction to the corresponding diisopropylideneheptitol⁷ (sodium borohydride in

methanol, 10~15 °C, 1.5 h, then acetic acid to pH 7) was followed by acetylation of the primary alcohol to give **6**⁸ (1.2 equiv each of acetic anhydride and pyridine, chloroform, –7 °C, 18 h) and elimination of the adjacent hydroxyl groups by thermolysis of the dimethylformamide cyclic acetal⁹ derived from **6** in the presence of acetic anhydride to produce in ~40% overall yield from **4** the acetoxy trans olefin **7** (purified either



by vacuum distillation or silica gel chromatography); NMR (220 MHz) δ 5.07 (dd, *J* = 6, 16 Hz, 1 H) 5.15 (dd, *J* = 6, 15.5 Hz, 1 H). Freeing of the secondary allylic alcohol required for chirality transfer from C–O to C–C was done by following lines previously laid down in our synthesis of PGA₂ from L-erythrose.^{2a} Removal of the acetate with base was followed by formation of the mixed carbonate (1.5 equiv of methyl chloroformate, pyridine, 0 °C, 2.5 h) which finally led after hydrolysis of the isopropylidene groups (cupric sulfate, aqueous methanol, 24-h reflux) to the necessary terminal five-membered carbonate (addition and removal of benzene-methanol). Transformation of the remaining vicinal glycol to its acetone (acetone, sulfuric acid catalysis, 2 h at room temperature), and then neutralization with ammonia gas and silica gel chromatography (40% ethyl acetate-hexane) now led, in ~54% yield from **7**, to the key intermediate **3**; mp 69–70 °C; [α]_D²⁵ +15.3° (*c* 1.88, CH₃OH); *R*_f 0.46 in ether; NMR δ 1.44 (3 H, s), 1.47 (3 H, s), 3.5 (1 H, br, OH), 3.63 (1 H, dd, *J* = 7, 7 Hz), 6.0 (1 H, ddd, *J* = 1.5, 6.15 Hz). Establishment of the proper chirality at the eventual C₁₂ center was effected by the ortho ester Claisen method¹⁰ to give **8** (80% from silica gel with



CH₂Cl₂), on which the construction of the allylic alcohol side chain was completed essentially by the sequence used in a related case:^{2a} basic hydrolysis of the cyclic carbonate, formation of the primary monotosylate,¹¹ protection of the secondary alcohol with ethyl vinyl ether, and coupling with lithium dibutylcuprate (10 equiv, ether, –40 °C, 2 h). The crude cuprate coupling product was then simultaneously deprotected and lactonized to **9** (aqueous sulfuric acid, THF, 15 h, room temperature) obtained from silica gel with 97:3 CH₂Cl₂-CH₃OH in ~35% overall yield from **8**. The sirupy **9** had [α]_D²⁵ +42.6° (*c* 1.55, MeOH) and was a single substance by ¹³C NMR: δ 14.7, 14.47, 31.78, 25.13, 37.09, 71.87, 126.21, 137.44, 40.73, 83.47, 61.39, 177.87, and 35.24 for carbons¹² 20 through 8, respectively. The trans 13,14 double bond in the ¹H NMR showed *J* = 15 Hz.

Alkylation of the bis(ethoxyethyl) ether of **9** with the diphenyl *tert*-butylsilyl ether¹³ of 7-bromo-*cis*-5-hepten-1-ol¹⁴ (1.1 equiv of lithium hexamethyldisilazane, THF, –78 °C, and then 3 equiv of bromide in THF-HMPA (final THF-HMPA, ~92:8) at –40 to –20 °C, 2 h) gave 71% of the monoalkylated product **10** (NMR *J*_{8,12} = 16 Hz, (*J*_{11,12} = 7 Hz), together with 13% of the more rapidly eluted (silica gel, 10:5:1-2) cyclohexane-pentane-ethyl acetate dialkylated material.

The construction of the cyclopentanone ring from the lactone was carried out by the protected cyanohydrin method.^{2b,15} Reduction of the lactone of **10** to the hemiacetal (diisobutylaluminum hydride), cyanohydrin formation (HCN, eth-