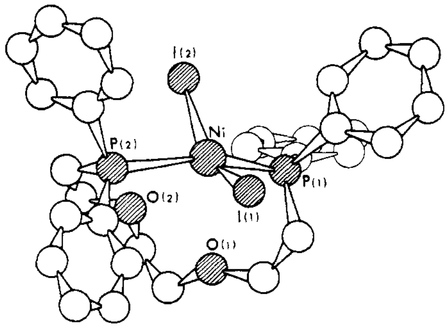

Figure 2. A perspective view of the $\mathrm{Ni(POOP)I_2}$ molecule.

The structure consists of discrete molecules of $\mathrm{Ni(POOP)I_2}$ (Figure 2). The nickel atom is tetracoordinated and linked to the two phosphorus atoms and the two iodine atoms. Each oxygen atom occupies statistically two positions differing for orientation about the C···C axis in the C–O–C moiety. Occupancy factors are close to 50% for the two positions as evidenced by a ΔF Fourier synthesis and by the subsequent refinement. Temperature factors for O(1) and O(2) dropped from 9.60 and 10.70 Å^2, respectively, to 4.75 and 5.17 Å^2 [O(1) and O(1)′] and to 3.83 and 5.11 Å^2 [O(2) and O(2)′] after disordering was considered.

The shortest distance of each oxygen atom from the metal atom is equal to 3.2 Å. The coordination geometry about the nickel atom can be described as intermediate between square planar and tetrahedral. In fact, the angles about the nickel are: I(1)–Ni–I(2), 143.5; I(1)–Ni–P(1), 89.2; I(1)–Ni–P(2), 94.3; I(2)–Ni–P(1), 97.6; I(2)–Ni–P(2), 90.0; and P(1)–Ni–P(2), 162.1° (average σ 0.2°). The distances of the ligand atoms from the metal atom are the following: Ni–I(1), 2.51; Ni–I(2), 2.49; Ni–P(1), 2.24; and Ni–P(2), 2.24 Å (average σ 0.007 Å). Considering the least-squares plane calculated by the positions of the nickel, the two iodine, and the two phosphorus atoms, the following displacements from this plane were found: Ni, −0.17; I(1), +0.61; I(2), +0.60; P(1), −0.52; and P(2) −0.52 Å. The angle between the plane containing Ni, I(1), and I(2), and the plane containing Ni, P(1), and P(2) is 86°.

Until now, X-ray structural determinations have shown all low-spin tetracoordinate nickel(II) complexes to be either perfectly planar or only very slightly distorted, with the greatest tetrahedral distorsion being 173°, as found in the biacetylbis(mercaptoethylimine)-nickel(II) complex.[12] The complex $\mathrm{Ni(POOP)I_2}$, therefore, shows the largest distorsion toward a tetrahedron of all the low-spin tetracoordinated nickel(II) complexes analyzed by X-rays so far. The closeness of this geometry to the tetrahedral one is again more evident if the I–Ni–I angle (143.5°) is compared not with the theoretical value of 109° 28′, but with those found in the distorted tetrahedral $\mathrm{(Ph_3P)_2NiX_2}$ complexes, *e.g.*, Br–Ni–Br (126°) and Cl–Ni–Cl (123°) taking into account, furthermore, that a greater value for I–Ni–I angle would be expected.

Since the chain between the two phosphorus atoms in the POOP ligand has nearly the same length as the $\mathrm{-(CH_2)_8-}$ chain in $\mathrm{Ph_2P(CH_2)_8PPh_2}$ (C–C = 1.54, C–O = 1.43 Å), which forms high-spin tetrahedral complexes, the distorsion in the $\mathrm{Ni(POOP)I_2}$ complex may be attributed to a different disposition of the chain. This different disposition is probably due to an electrostatic interaction of the oxygen atoms with the metal atom. In fact, of all the atoms in the chain, the oxygen atoms are the nearest to the metal (3.2 Å).

This distortion from planarity can account for the low-energy shift observed in the crystal-field band in the $\mathrm{Ni(POOP)I_2}$. In effect the distortion of the coordination polyhedron toward a tetrahedral geometry causes less destabilization of the $d_{x^2-y^2}$ orbital (with respect to planar complexes), with consequent reduction in frequency of the $d_{xy} \rightarrow d_{x^2-y^2}$ transition, to which the observed band is assigned.[13]

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A New Route to Tropones Based on the 1,3-Dipolar Reactivity of Heteroaromatic Betaines

Sir:

We wish to report (a) that anhydro-3-hydroxy-1-methylpyridinium hydroxide (**1**) reacts with N-phenylmaleimide, acrylonitrile, and methyl acrylate to yield the adducts **2**, **3a**, and **3b**, respectively, and (b) a new synthesis of tropones and tropolones from the methiodides of these adducts.

The reactions of type a are the first examples of the C(6)–N–C(2) unit of a simple pyridine ring acting as the 1,3-dipole in a dipolar addition. Indeed electrocyclic reactions in pyridine chemistry are rare; thus pyridine adds 2 mol of dimethyl acetylenedicarboxylate across the –C=N– bond *via* a two-step addition–cyclization mechanism.[1] However, the conversions **1** → **2**, **3** were sought as mesoionic compounds such as sydnone have long been known to behave as 1,3 dipoles,[2] and it has recently been shown[3,4] that corresponding derivatives with six-membered rings react analogously (certain pyrimidinium betaines dimerize by an alternative path[5]). One of us pointed out many years ago[6] that "mesoionic" structures were mesomeric betaines with aromatic character. Hence mesomeric betaines of type **1** should also show 1,3-dipolar character. Ullman[7] has found such reactivity for benzpyrylium oxides and aziridines can ring-open to dipolar azomethine ylides.[8]

The adducts (**2**, **3**) bear an obvious resemblance to tropane alkaloids, which have been converted by successive Hofmann eliminations into cycloheptane derivatives.[9] In the present case Hofmann elimination

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(1) R. M. Acheson, *Advan. Heterocycl. Chem.*, **1**, 125 (1963).

(2) R. Huisgen and H. Gotthardt, *Chem. Ber.*, **101**, 1059 (1968), and references therein.

(3) J. Honzl and M. Šorm, *Tetrahedron Lett.*, 3339 (1969).

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(6) A. R. Katritzky, *Chem. Ind.* (London), 521 (1955).

(7) E. F. Ullman and J. E. Milks, *J. Amer. Chem. Soc.*, **84**, 1313 (1962).

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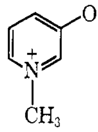
should be particularly easy as one of the relevant protons is activated by an electron-withdrawing group. Indeed, adducts **3a** and **3b** form quaternary methiodides **4a** and **4b** which undergo elimination with silver oxide or sodium bicarbonate. However, in place of the simple tropones (**5a,b**) expected, the products are easily



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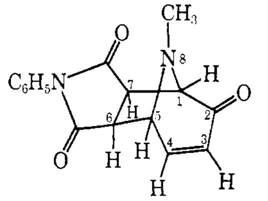

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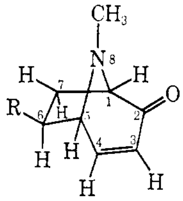

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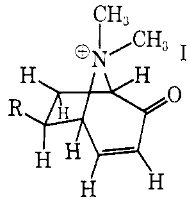

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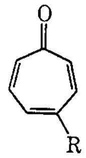
a, $R = CN$; **b**, $R = CO_2CH_3$



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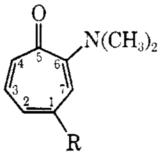

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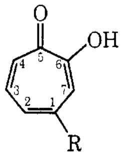

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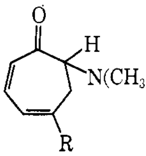

8

separated mixtures of the dimethylaminotropones (**6a,b**) and the corresponding tropolones (**7a,b**). Evidently, the intermediate dihydrotropones **8a,b** are rapidly oxidized to the dimethylaminotropones (**6a,b**) and these, as was shown in a separate experiment, are partially hydrolyzed under the reaction conditions to **7a,b**.

The adduct **2**, which was prepared (60%) by heating **1**[10] and N-phenylmaleimide under reflux in THF until most of **1** disappeared, followed by routine work-up and recrystallization from EtOH, forms pale yellow needles, mp 164–165° dec; *m/e* 282. *Anal.* Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.93. Found: C, 68.13; H, 4.70; N, 9.70. The structure was confirmed by the nmr spectrum: $\delta_{TMS}^{CDCl_3}$ 2.47 (s, 3 H, -NCH_3), 3.21 (d, 1 H, H_7, $J_{6,7}$ = 7.6 Hz), 3.41 (d, 1 H, H_6), 3.88 (s, 1 H, H_1), 4.13 (d, 1 H, H_5, $J_{4,5}$ = 4.8 Hz), 6.13 (dd, 1 H, H_3, $J_{3,4}$ = 10.0 Hz; $J_{1,3}$ = 1.6 Hz), 7.03 (dd, 1 H, H_4). The detailed assignment was confirmed by double resonance.[11] The absence of appreciable coupling between $H_{1,7}$ and $H_{5,6}$ indicates the *exo* configuration shown in **2**.

In a similar manner, adduct **3a** was obtained (75%) by heating **1** and acrylonitrile in THF in the presence of hydroquinone: **3a** formed yellow needles: mp 95–97°; ν_{max}^{Nujol} 1605, 1690, and 2225 cm^{-1}; *m/e* 162. *Anal.* Calcd for $C_9H_{10}N_2O$: C, 66.65; H, 6.22; N, 17.27. Found: C, 67.08; H, 5.95; N, 17.47. The *exo* configuration **3a** and stereochemical purity was again confirmed by the nmr (and nmdr) spectrum: $\delta_{TMS}^{CDCl_3}$ 2.10 (octet, H_{7endo}, $J_{7endo,7exo}$ = 13.8 Hz, $J_{6,7endo}$ = 9.3 Hz, $J_{1,7endo}$ = 1.0 Hz), 2.50 (s, 3 H, -NCH_3), 2.72 (octet, H_{7exo}, J_{17exo} = 7.9 Hz, $J_{6,7exo}$ = 3.5 Hz), 2.94 (q, H_6), 3.66 (q with structure, H_1), 4.01 (d, H_5, $J_{4,5}$ = 5.0 Hz), 6.06 (q, H_3, $J_{1,3}$ = 1.5 Hz, $J_{3,4}$ = 9.9 Hz), 6.94 (q, H_4). By mixing **3a** with methyl iodide in ethyl acetate, methiodide **4a** was obtained in quantitative yield as faintly yellow crystals, mp 132–133° dec. *Anal.* Calcd for $C_{10}H_{13}N_2OI$: C, 39.49; H, 4.31; N, 9.21; I, 41.73. Found: C, 39.29; H 4.21; N, 9.38; I, 42.00. Treatment of aqueous **4a** with silver oxide followed by ether extraction afforded 6-dimethylamino-5-oxo-1,3,6-cycloheptatriene-1-carbonitrile (**6a**; 21%), golden yellow needles, mp 72–73°; *m/e* 174; $\nu_{max}^{CCl_4}$ 1580, 1615, and 2220 cm^{-1}. *Anal.* Calcd for $C_{10}H_{10}N_2O$: C, 68.85; H, 5.79; N, 16.08. Found: C, 69.98; H, 5.99; N, 15.51. Repeated analyses gave inconsistent results probably because of deterioration of the sample on standing (dark color developed). The nmr spectrum is consistent with the proposed structure: $\delta_{TMS}^{CCl_4}$ 6.23 (H_7), 6.67 H_2, 6.73 (H_4), 6.91 (H_3); $J_{2,3}$ = 8.73 Hz, $J_{2,4}$ = 0.95 Hz, $J_{3,4}$ = 12.23 Hz (these *J* values were obtained by LAOCOON III analysis of the ABC spectrum obtained when H_7 was irradiated). In particular, the coupling constants agree well with those reported for tropones and tropolones.[12,13] Acidification of the mother liquor (after ether extraction) followed by routine work-up gave 6-hydroxy-5-oxo-1,3,6-cycloheptriene-1-carbonitrile (**7a**; 27%), yellow needles, mp 194–195° (lit.[14] mp 194–195°); ν_{max}^{Nujol} 1570, 1580, 1620, 2220, and 3230 cm^{-1}; *m/e* 147. *Anal.* Calcd for $C_8H_5NO_2$: C, 65.31; H, 3.43; N, 9.52. Found: C, 65.40; H, 3.17; N, 9.36.

1 was heated 40 hr with methyl acrylate and the glassy product converted to the methiodide **4b**, faintly yellow flakes, mp 151–153° dec. *Anal.* Calcd for $C_{11}H_{16}NO_3I$: C, 39.18; H, 4.78; N, 4.16; I, 37.64. Found: C, 39.19; H, 4.70; N, 4.03; I, 38.07. The nmr spectrum of **4b** (and that of the crude amine **3b**) indicates that the adduct is a *ca.* 1:1 mixture of *exo* and *endo* isomers contrasting with the stereochemically pure **3a**. Stirring **4b** in dilute $NaHCO_3$ for 3 hr at 20° gave methyl 6-dimethylamino-5-oxo-1,3,6-cycloheptatriene-1-carboxylate (**6b**; 33%; golden yellow needles; mp 66–67°; $\nu_{max}^{CCl_4}$ 1570, 1610, and 1720 cm^{-1}; *m/e* 207. *Anal.* Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32, N, 6.76. Found: C, 63.89; H, 6.15; N, 6.72) and methyl 6-hydroxy-5-oxo-1,3,6-cycloheptatriene-1-carboxylate (**7b**; 40%; yellow needles; mp 116–118° (lit.[15] mp 117–118°); $\nu_{max}^{CCl_4}$ 1560, 1620, 1735, and 3180 cm^{-1}; *m/e* 180. *Anal.* Calcd for $C_9H_8O_4$: C, 60.00; H, 4.48. Found: C, 59.89; H, 4.38).

The final sequence yields 73% of cycloheptatrienone derivatives. This synthetic route is thus of preparative significance in view of the tedious methods previously employed to prepare such compounds.[14–16]

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(9) J. Meinwald and O. L. Chapman, *J. Amer. Chem. Soc.*, **80**, 633 (1958), and references therein.

(10) Advantageously prepared by ion exchange from the quaternary iodide.

(11) Details will be given in the full communication.

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We believe that the present work also illuminates the structural characteristics required to endow 1,3-dipole reactivity and suggests interesting extensions. Further work is in progress.

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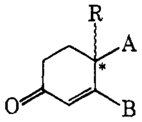
The Substrate Selectivity of the Steroid Dehydrogenase of *Arthrobacter simplex*. Its Use for the Resolution and Determination of Absolute and Relative Configuration in Total Synthesis

Sir:

The total synthesis of polycyclic hydroaromatic systems, including steroids and other terpenoids, involves the more or less stereoselective generation of new asymmetric centers whose stereochemistry relative to the remaining centers is often unknown. Available methodology for ascertaining the configuration of the new center is limited, X-ray crystallography often constituting the only reliable procedure.

We wish to report a novel and rapid procedure, which resolves racemic mixtures, indicating in the process the absolute configuration of the two enantiomers at the newly generated center, and by ORD or CD measurements provides the absolute configuration of the remaining centers, the net result being the complete stereochemical description of both enantiomers. The systems amenable to such treatment are α,β-unsaturated ketones of the general structure I where R may be H or CH_3 and A and B together represent the remaining elements of a polycyclic system totaling two, three, or four rings, the latter being either five or six membered. Such systems may be the result of a Birch reduction, of a Robinson or Stork annellation, etc.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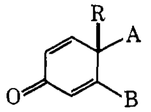
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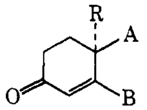
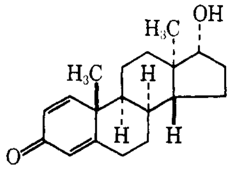

III

The critical reagent is the steroid dehydrogenase of *Arthrobacter simplex*, which in the form of an acetone-dried cell powder represents a stable material. We have found that in all cases examined the enzyme attacks preferentially that antipode of a racemate which possesses the center marked with an asterisk in the configuration corresponding to that of C-10 in "natural" steroids[1] to form II,[2] leaving unchanged III. The following is typical of this enzymatic resolution. To 30 ml of a suspension of *A. simplex* cells[3,4] (40 mg/ml) in 0.01 *M* pH 7.0 phosphate buffer prepared with the aid of a Waring blender was added with stirring a solution of 15 mg of *rac*-$9\beta,10\alpha$-testosterone and 2 mg of 2-methyl-1,4-naphthoquinone in 1.5 ml of ethanol. After stirring for 24 hr at 25° the mixture was extracted with ethyl acetate–acetone (1:1, 30 ml) and centrifuged, and the organic layer separated. After two more extractions with ethyl acetate the organic layers were washed with water, dried, and evaporated *in vacuo*. The residue (20.2 mg) after tlc on silica gel (ethyl acetate–chloroform 1:9, developed three times) yielded IV [(4.4 mg), mp 175–176°; $[\alpha]_D$ +16.5°;[5] M^+ 286] and "natural" *l*-$9\beta,10\alpha$-testosterone, mp 150–152°; $[\alpha]_D$ −138°; reported[6] mp 154–156°; $[\alpha]^{diox}_D$ −141°. From the above result and the fact that *l*-nortestosterone remains unchanged during incubation with a cell-free preparation of *A. simplex*,[7] while its "natural" enantiomer is converted to estradiol, it was conjectured that chirality at C-10 was decisive for recognition of the substrate by the enzyme. This was verified with all substrates examined and will be illustrated in connection with the total synthesis of the C-nor-D-homosteroids *rac*-V and *rac*-VI described recently.[8]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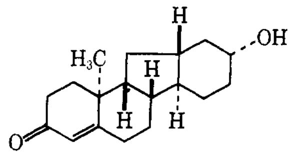
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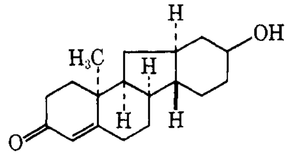
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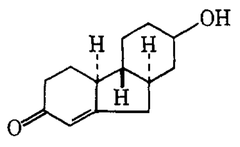
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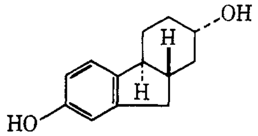
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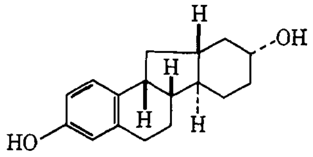
IXa

Starting material was the tricyclic ketone *rac*-VII whose configuration at C-10 was uncertain.[9] Enzymatic dehydrogenation of *rac*-VII for 5 days gave after tlc separation the phenol VIII and recovered VII. The phenolic methyl ether of VIII had CD, $[\theta]_{225}$ +7100, $[\theta]_{280}$ +960, B-norestradiol, $[\theta]_{227}$ +7100, $[\theta]_{284}$ +2000. Jones oxidation of the methyl ether afforded the ketone,[8] CD, $[\theta]_{220}$ +7800, $[\theta]_{288}$ +5800, the increase in θ_{288} indicating the strong positive Cotton effect due to the new keto group. The recovered VII had $[\theta]_{320}$ −180. "Natural" B-nor-Δ^4-cholestenone possesses a positive Cotton effect near 320 nm.[10] The above CD data establish the absolute configuration of VIII and of the corresponding chiral centers in VII.

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(1) In most cases this is the *R* configuration.

(2) All structural formulae designate the enantiomer whose absolute configuration is shown.

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