The lowest C–M transition temperature reported by Steinsträsser was 89° for *p*-*n*-butylphenyl *p*-*n*-butylbenzoyloxybenzoate. We have been able to obtain liquid crystals with C–M transition temperatures as low as 39° (compound **2**, Table I) as a result of a lateral chloro substituent. The nematic range (83°) for compound **2** is the largest range yet obtained for a single component with a C–M transition temperature below 40°. The most effective location for the lateral substituent in terms of lowering the C–M transition temperatures appears to be ortho to the carbonyl group of the ester linkage (compare compounds **2**, **3**, and **6**, **7** in Table I).

The preparation of additional liquid crystals in the phenyl *p*-benzoyloxybenzoate system is in progress and will be reported later.

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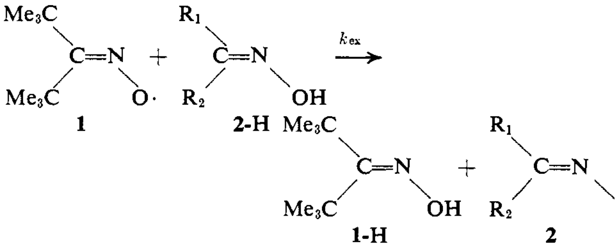
Received September 23, 1972

The Oxime–Iminoxy Radical Reaction[1]

Sir:

As part of our work on the free radical di-*tert*-butyliminoxy[2] (**1**), we have studied the exchange reaction between this radical and some oximes.



a, $R_1 = R_2 = Me$
b, $R_1 = Ph$; $R_2 = H$
c, $R_1 = Me_3C$; $R_2 = Me_2CH$

Benzene solutions of **1** (10^{-3} *M*) and **2a**-H or **2b**-H (0.1 *M*) displayed only a well-resolved epr spectrum of **1** that decayed with half-lives of 1 or 2 hr at room temperature. With **2a**-H the decomposition of **1** followed first-order kinetics over a tenfold concentration range. Between 25 and 51° the observed rate constant for decay could be represented by

$$k_{obsd} = 1.2 \times 10^9 \exp(-17{,}900\ (\text{cal mol}^{-1})/RT)\ \text{sec}^{-1}$$

Comparable results were obtained in 95% ethanol. With **2b**-H the radical decayed by half after 1.2 hr, but the rate accelerated with time. We had not anticipated such slow reactions. The iminoxy radical **2a** decays rapidly with first-order kinetics($k_{decay}^{25°} = 0.04$ sec⁻¹) when generated photochemically under similar conditions.[3] Radical **2b** decays rapidly but with second-order kinetics ($k_{decay}^{25°} = 9 \times 10^7\ M^{-1}\ \text{sec}^{-1}$).

With **2c**-H in benzene, *o*-dichlorobenzene, CCl_4, or 95% ethanol **1** decayed and radical **2c** appeared. An equilibrium was attained within a few *minutes* which favored **1** over **2c**. The equilibrium mixture is stable for hours. The spectra of **1** and **2c** overlap but differ sufficiently for the equilibrium constant to be estimated by double integration of the highest field components of the triplets. In benzene at 25° values of [**1**][**2c**-H]/[**1**-H][**2c**] = $K_{eq}^{25°}$ ranged from 130 to 900 depending on the exact procedure used to estimate the concentrations of **1** and **2c**. This equilibrium could be approached from the opposite direction by brief irradiation (λ >313 nm) of a degassed benzene solution of **2c**-H (0.1 *M*) and **1**-H (8×10^{-4} *M*) containing di-*tert*-butyl peroxide. The mixture of **1** and **2c** that resulted was initially rich in **2c**. Equilibration again occurred within a few minutes[4] and two determinations gave $K_{eq}^{25°} = 380$ and 500 in good agreement with the first method.[5] The free energy for the formation of **2c** from **2c**-H is therefore *ca.* 3 kcal/mol less favorable than that for the formation of **1** from **1**-H.[6]

To determine the exchange rate for the thermoneutral reaction, **1** was isotopically labeled with ^{17}O by photolysis of di-*tert*-butyl peroxide and di-*tert*-butylketimine in benzene in the presence of oxygen[7,8] enriched with ^{17}O. After addition of excess **1**-H to the ^{17}O-labeled **1** [$a(^{17}O) = 22.6$ G[10]], we observed a pseudo-first-order decay of the lowest field satellite of the **1**-^{17}O.

$$(Me_3C)_2C{=}NH \xrightarrow[^{34}O_2,\ h\nu]{Me_3COOCMe_3} (Me_3C)_2C{=}N{-}^{17}O\cdot$$

$$(Me_3C)_2C{=}N{-}^{17}O\cdot + (Me_3C)_2C{=}NOH \xrightarrow{k_{ex}} (Me_3C)_2C{=}N{-}^{17}OH + (Me_3C)_2C{=}NO\cdot$$

The average of five determinations gave $k_{ex}^{25°} = 1.3 \pm 0.3\ M^{-1}\ \text{sec}^{-1}$ with an activation energy, E_{ex}, of 7 ± 2 kcal/mol from 7 to 37°.

The rate constant for this exchange is very much less and the activation energy is considerably greater than has been found for other hydrogen atom transfers between like oxy radicals[11] and other nearly thermoneutral hydrogen transfers between dissimilar oxy radicals.[14] Hydrogen bond formation probably plays an important role in all these reactions.

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[1] Issued as NRCC No. 13025.

[2] J. L. Brokenshire, G. D. Mendenhall, and K. U. Ingold, *J. Amer. Chem. Soc.*, **93**, 5278 (1971).

[3] J. L. Brokenshire, J. R. Roberts, and K. U. Ingold, *ibid.*, **94**, 7040 (1972).

[4] When generated from **2c**-H and peroxide by photolysis, **2c** [$a_N = 30$ G, $a_H = 5.5$ G (1 H)] is stable for several hours at similar concentrations.

[5] We noted, qualitatively, a reversible decrease in K_{eq} on heating to 50°.

[6] Although intermolecular H bonding of **2a**-H may reduce the rate of the **1**–**2a**-H reaction, such an effect with **2c**-H is much too small to explain the large value of $K_{eq}^{25°}$. Thus, the free OH stretching bands of **2c**-H and **1**-H, recorded as 0.01 *M* solutions in CCl_4, are superimposable, yet in this solvent $K_{eq}^{25°} \approx 10^3$.

[7] In the absence of oxygen the unstable di-*tert*-butylketiminyl radical is obtained [$a_N = 28.9$ G, $a_H = 2.8$ G (18 H)].

[8] This is the first dialkyliminoxy to be labeled with ^{17}O although $MeCOC({=}N{-}^{17}O\cdot)Me$ has been prepared previously[9] by reaction of 2-butanone with labeled NO_2 (from $NO + {}^{34}O_2$). However, the NO_2 procedure is limited to compounds of the type $RCOCH_2R'$ and only half the ^{17}O present in the oxygen is incorporated in the radical.

[9] B. C. Gilbert and W. M. Gulick, Jr., *J. Phys. Chem.*, **73**, 2448 (1969).

[10] For comparison,[9] $a(^{17}O) = 22.75$ G for $MeCOC({=}N{-}^{17}O\cdot)Me$.

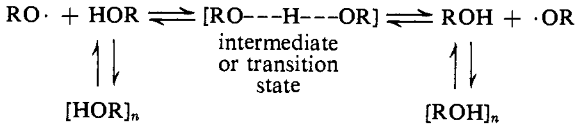
[11] For example, at room temperature in CCl_4: $k_{ex} \sim 200\ M^{-1}\ \text{sec}^{-1}$ for 2,4,6-tri-*tert*-butylphenoxy;[12,13] $k_{ex} \sim 160\ M^{-1}\ \text{sec}^{-1}$ for di-*tert*-butyl nitroxide;[12] $k_{ex} > 5 \times 10^6\ M^{-1}\ \text{sec}^{-1}$ for diphenyl nitroxide.[12] For these reactions E_{ex} is 0–4 kcal/mol.

[12] R. W. Kreilick and S. I. Weissman, *J. Amer. Chem. Soc.*, **84**, 306 (1962); **88**, 2645 (1966).

[13] M. R. Arick and S. I. Weissman, *ibid.*, **90**, 1654 (1968).

[14] At ambient temperatures k_{ex} values are in the range 10^3–10^6 $M^{-1}\ \text{sec}^{-1}$ for the reactants $ROO\cdot + R'OOH$,[15] $ROO\cdot + ArOH$,[16,17] $ArO\cdot + ROOH$,[17,18] and $ArO\cdot + Ar'OH$.[19] Activation energies are very low for thermoneutral and exothermic reactions but increase (and k_{ex} becomes smaller) when the exchange is endothermic.

[15] J. A. Howard, W. J. Schwalm, and K. U. Ingold, *Advan. Chem. Ser.*, No. **75**, 6 (1968).



$$\begin{array}{ccccc} RO\cdot + HOR & \rightleftharpoons & [RO{-}{-}{-}H{-}{-}{-}OR] & \rightleftharpoons & ROH + \cdot OR \\ \upharpoonleft\downharpoonright & & \text{intermediate or transition state} & & \upharpoonleft\downharpoonright \\ [HOR]_n & & & & [ROH]_n \end{array}$$

We infer that iminoxy radicals form hydrogen bonds more reluctantly than nitroxides[20] (or peroxy radicals[21]) from the observations that the a_N value of **1** in isopentane is within 1% of its value in ethanol and that the visible spectra of **1** in cyclohexane and in ethanol are virtually identical. Substantial changes of these properties in nitroxides have been associated with the formation of hydrogen bonds.[22,23] Reluctance to form a hydrogen-bonded intermediate probably explains the high activation energy and low rate constant for the **1** + **1**-H reaction.

The large value of $K_{eq}^{25°}$ for the **1** + **2c**-H system cannot be accounted for on this basis. We believe that it is due mainly to severe intramolecular repulsive interactions (principally R_1–R_2 and R_2–O) in the oxime **1**-H that are lessened by a more relaxed geometry in **1**. Evidence supporting this suggestion will be presented later.

The present results appear to be relevant to the potential use of stable iminoxy radicals as spin labels[24,25] and in other studies of local molecular environment.[26–28]

Acknowledgment. We gratefully acknowledge receipt of a generous sample of di-*tert*-butylketimine from Dr. H. D. Hartzler (Du Pont).

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(19) L. R. Mahoney and M. A. DaRooge, *ibid.*, **92**, 890 (1970); **94**, 7002 (1972).

(20) Iminoxy radicals ($a_N \sim$ 30 G) have greater s character in the radical orbital at N than do aliphatic nitroxides ($a_N \sim$ 14–19 G) and would therefore be expected to be less basic.

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(29) NRCC Postdoctoral Fellow, 1971–1973.

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Received September 22, 1972

Synthesis of Corticosteroids from Marine Sources

Sir:

Corticosteroids are generally synthesized either from plant sapogenins (*e.g.*, diosgenin, hecogenin) or from bile acids. The recent reports[1] of the occurrence of 5α-pregn-9(11)-ene-3β,6α-diol-20-one (**1**) in starfish raised the intriguing question whether corticosteroids might become available from marine sources. Since it has been shown that 11β-hydroxyprogesterone (**2**) and 11-oxoprogesterone (**3**) can be converted to corticosterone[2] as well as to cortisone[2] and cortisol[3] and since **2** can be prepared conveniently from pregna-4,9(11)-diene-3,20-dione (**4**),[4,5] the latter compound is the key missing link in a potentially practical synthesis of corticosteroids from a marine source. We record herewith the completion of the missing steps.

Examination of the literature[6–10] suggested that selective oxidation of the diequatorial diol system in **1** would not be feasible. The availability[1] of the fully oxidized triketone **5** suggested that selectivity at C-3 might be achieved at this stage.[8,11–13] *p*-Toluenesulfonic acid catalyzed reaction of the trione **5** with methanol at reflux for 1 hr furnished the oily 3,3-dimethoxy-5α-pregn-9(11)-ene-6,20-dione (**7**) [M^+ 374 (87%), *m/e* 342 ($M^+ - CH_3OH$), 257 (ring D cleavage + CH_3OH) 143, and a base peak at 101[14] ($MeOC(={}^+OMe)CH{=}CH_2$); nmr (60 MHz, $CDCl_3$) C-18 CH_3, 0.60 (s, 3 H), C-19 CH_3, 0.91 (s, 3 H), C-21 CH_3, 2.15 (s, 3 H), 3-OCH_3 3.13, 3.23 (s, 3 H each), and an olefinic proton 5.60 (c, 1 H)]. The work of Wheeler and Mateos[15] suggested that the 6-oxo group should be reduced 60 times faster than the 20-oxo functionality. Indeed, in 2-propanol solvent at room temperature, nmr studies[16] indicated that C-20 is not reduced during a 2–3-hr period by a 3–6 molar excess of sodium borohydride and the predominant product is 3,3-dimethoxy-6β-hydroxy-5α-pregn-9(11)-en-20-one (**8**). Hydrolysis (*p*-TsOH–acetone) of crude **8** furnished crystalline **10** [mp 223–226° (needles from benzene); ir ($CHCl_3$) 3500 (OH), 1700 cm^{-1} (>C=O); nmr ($CDCl_3$, 60 MHz) C-18 CH_3, 0.63 (s, 3 H), C-19 CH_3, 1.35 (s, 3 H), C-21 CH_3, 2.13 (s, 3 H), 6β-carbinol methine, 3.90 (c, 1 H, $^1/_2$ peak-height width, 8 Hz), and an olefinic proton, 5.42 (c, 1 H); mass spectrum M^+ 330, *m/e* 312 ($M^+ - H_2O$), 269 ($312 - C_2H_3O$), 255 ($312 - C_3H_5O$), 242 (ring A cleavage from 312), 227 (ring D cleavage + H_2O), and 85 [$CH_3CO(CH_2)_3$], all spectral properties consistent with the structure]. Dehydration of a mixture of **8** and **9** ($POCl_3$–Py), cleavage of the ketal, and migration of the double bond ($\Delta^5 \rightarrow \Delta^4$) furnished $\Delta^{9(11)}$-progesterone (**11**) [30–35% overall yield based on triketone **5**, mp 115–118°, mmp 115–120°; gc, ir, nmr, and mass

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