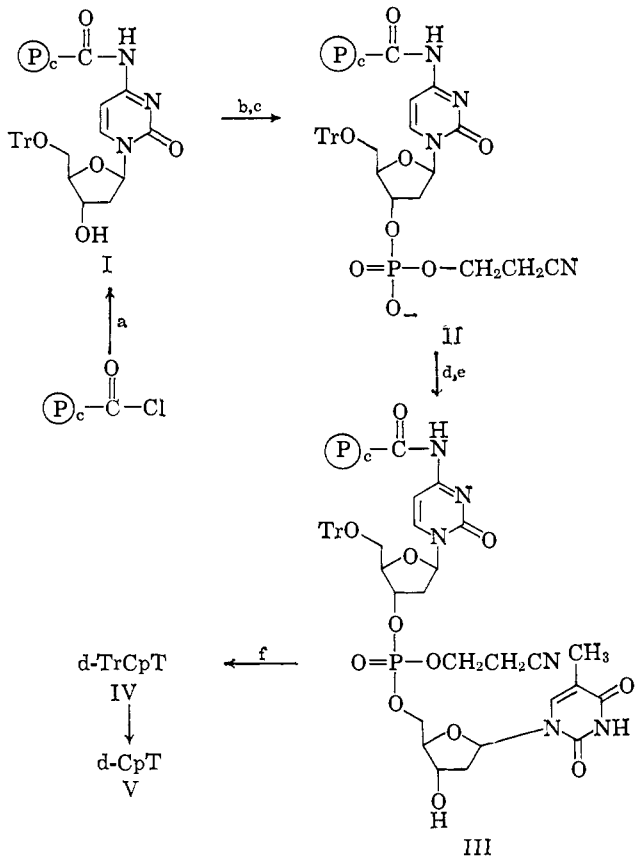
Chart I



in 40 ml. of pyridine. After 2 days the solid was separated and washed carefully. Nucleotidic material was cleaved from the support by four successive 3-hr. treatments with 40-ml. portions of 0.2 *M* sodium hydroxide (f) in 1:1 dioxane–ethanol. The resulting alkaline solution was neutralized with Dowex-50 resin (pyridinium form), concentrated, and chromatographed on DEAE-cellulose with a linear gradient of triethylammonium bicarbonate. From 1.215 g. of III was obtained 1340 $O.D._{267}$[8] units of 5′-O-trityldeoxycytidylylthymidine (IV), which was isolated as the triethylammonium salt (101 mg.) by concentration and lyophilization; R_f 0.78[9]; electrophoretic mobility relative to deoxycytidine 5′-phosphate at pH 10.8, 0.32; λ_{max} 267 mμ, λ_{min} 244 mμ. Some 5′-O-trityldeoxycytidine (32 mg.), deoxycytidine (10 mg.), thymidine (16 mg.), and a trace of a compound corresponding to trityldeoxycytidine 3′-phosphate were also obtained.

Detritylation of IV with 80% aqueous acetic acid afforded deoxycytidylylthymidine (V), which was isolated as the ammonium salt; R_f 0.33; electrophoretic mobility relative to deoxycytidine 5′-phosphate at pH 10.8, 0.58; ultraviolet at pH 6.9, λ_{max} 267 mμ, λ_{min} 240 mμ.; at pH 2.15, λ_{max} 275 mμ, λ_{min} 239 mμ. In the presence of phosphodiesterase from Russel's viper venom[10] IV hydrolyzed completely to thymidine 5′-phosphate (R_f 0.16) and 5′-O-trityldeoxycytidine (R_f 0.85). With spleen phosphodiesterase[11] V was hydrolyzed extensively (~95%) to deoxycytidine 3′-phosphate (R_f 0.13) and thymidine (R_f 0.70).

(8) T. M. Jacob and H. G. Khorana, *J. Am. Chem. Soc.*, **87**, 372 (1965).
(9) The paper chromatograms were all run on Whatman 3MM paper with isopropyl alcohol–ammonium hydroxide–water (7:1:2).
(10) Calbiochem, Los Angeles, Calif.
(11) Nutritional Biochemical Corp., Cleveland, Ohio.

In addition to the polymer support aspect, this synthetic route has two other novel features: (1) mesitylenesulfonyl chloride was used to activate a phosphodiester rather than a phosphomonoester and (2) a nucleoside with both the 3′- and 5′-hydroxyl groups free was employed. As a check on the selectivity of the condensation step (e), deoxycytidylyl-(3′→5′)-thymidine was prepared independently by using 3′-O-2,4-dinitrobenzenesulfenylthymidine[1] in place of thymidine in the synthetic sequence. Following the condensation step and prior to cleavage (f), the dinitrobenzenesulfenyl group was removed by treating the insoluble polymer with excess thiophenol in pyridine at room temperature. The dinucleotide obtained had the same physical and chromatographic properties as V prepared directly from thymidine, and it behaved the same on enzymatic degradation, indicating that step (e) with thymidine involves attack at the 5′-hydroxyl. The selectivity probably depends upon the fact that the hydroxyl group must approach a relatively hindered phosphorus in the condensation step.

Following the general procedure outlined in the flow sheet, the 5′-O-trityl derivatives of deoxycytidylyldeoxycytidine, deoxycytidylylthymidylyldeoxyadenosine, and deoxycytidylylthymidylylthymidine have been prepared.

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Electron Spin Resonance of Tropenyl Radical[1]

Sir:

There is considerable current experimental[2,3] and theoretical[4] interest in the highly symmetrical π-electron radicals such as $C_5H_5\cdot$, $C_6H_6^{\pm}$, $C_6(CH_3)_6^{+}$, $C_7H_7\cdot$, and $C_8H_8^{\mp}$, especially with regard to the removal of spatial degeneracy in these species. We have prepared the tropenyl (cycloheptatrienyl) radical ($C_7H_7\cdot$) in solution by homolytic thermal cleavage of bitropenyl[5,6] and have investigated its electron spin resonance spectrum.[7] There have been only a few previous e.s.r. investigations[8] in which well-character-

(1) This research was supported by the Department of the Army through the U. S. Army Research Office (Durham) (Grants DA-ARO-(D)-31-124-G-254 and -G-362).
(2) (a) R. W. Fessenden and S. Ogawa, *J. Am. Chem. Soc.*, **86**, 3591 (1964); (b) T. R. Tuttle and S. I. Weissman, *ibid.*, **80**, 5342 (1958); (c) M. K. Carter and G. Vincow, *Bull. Am. Phys. Soc.*, **10**, 374 (1965); (d) A. Carrington and I. C. P. Smith, *Mol. Phys.*, **7**, 99 (1963–1964); (e) H. L. Strauss, T. J. Katz, and G. K. Fraenkel, *J. Am. Chem. Soc.*, **85**, 2360 (1963).
(3) (a) H. J. Silverstone, D. E. Wood, and H. M. McConnell, *J. Chem. Phys.*, **41**, 2311 (1964); (b) R. G. Lawler, J. R. Bolton, G. K. Fraenkel, and T. H. Brown, *J. Am. Chem. Soc.*, **86**, 520 (1964); (c) T. R. Tuttle, Jr., *ibid.*, **84**, 1492, 2839 (1962); (d) J. R. Bolton, A. Carrington, A. Forman, and L. E. Orgel, *Mol. Phys.*, **5**, 43 (1962); (e) A. Carrington and P. F. Todd, *ibid.*, **7**, 533 (1963–1964).
(4) (a) H. M. McConnell and A. D. McLachlan, *J. Chem. Phys.*, **34**, 1 (1961); (b) H. M. McConnell, *ibid.*, **34**, 13 (1961); (c) A. D. McLachlan and L. C. Snyder, *ibid.*, **36**, 1159 (1962); (d) T. H. Brown and M. Karplus, *ibid.*, **39**, 1115 (1963).
(5) A. G. Harrison, L. R. Honnen, H. J. Dauben, Jr., and F. P. Lossing, *J. Am. Chem. Soc.*, **82**, 5593 (1960).
(6) Homolysis studied mass spectrometrically by Lossing and coworkers.
(7) H. J. Dauben, Jr., Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 1963, p. 7S.
(8) D. M. Gardner and G. K. Fraenkel, *J. Am. Chem. Soc.*, **78**, 3279 (1956); M. R. Das, A. V. Patankar, and B. Venkataraman, *Proc. Indian Acad. Sci.*, **53**, 273 (1961); L. H. Piette, F. A. Johnson, K. A. Booman, and C. B. Colburn, *J. Chem. Phys.*, **35**, 1481 (1961).

ized radicals were produced by thermal cleavage at *elevated temperatures;* this study is the first in which the C–C bond is involved.

The principal spectral results obtained are a *temperature dependence* of the proton hyperfine splitting, and the carbon-13 splitting and its *temperature dependence*. This is the first report of a temperature variation for a C-13 hyperfine splitting.

Samples of bitropenyl (neat) have been degassed and sealed under nitrogen. An e.s.r. signal, which increases in intensity with increasing temperature, has been detected over the range 80–210°. It consists of eight equally spaced components, of width $\Delta H_{\text{m.s.}} = 0.19 \pm 0.01$ gauss, the relative intensities of which are consistent with hyperfine interaction from seven equivalent protons. This resonance is ascribed to the tropenyl radical.

The proton hyperfine splitting[9,10] *varies substantially with temperature*, decreasing from 3.75 ± 0.015 gauss[11] at 96° to 3.62 ± 0.015 gauss at 196°, a 3.5% change over 100°. The splitting constant variation over the interval 80–196° can be represented within experimental uncertainty by a linear dependence obtained from an unweighted least-squares analysis of 92 splittings from the same number of spectra: $|a^{H}(t°)| = -1.33 \times 10^{-3}t + 3.87$ gauss. Standard deviations of the slope and intercept are 4.2×10^{-5} and 6.2×10^{-3}, respectively.

In order to extend the range of observation of this effect we have performed the *in situ photochemical* cleavage of bitropenyl in cyclohexane and in *n*-heptane solutions. The tropenyl radical has been detected over a range of temperatures down to room temperature. To the best of our knowledge this is the first e.s.r. detection of a radical in solution produced by steady-state photochemical cleavage of a carbon–carbon bond. At 20° the average splitting is 3.865 ± 0.015 gauss. A least-squares analysis of the splitting data obtained photochemically in the range 20–80° results in a slightly *higher magnitude* for the slope than in the range 80–196°. Refinements of the experiments and extension of the investigations to lower temperatures are in progress in order to determine the *shape* of the temperature-dependence curve.

The $C_7H_7\cdot$ splitting at 20° is in good agreement with that measured[2d] in an aqueous medium at room temperature, 3.91 ± 0.02 gauss. Further, the splitting reported for tropenyl radical at −50 to −90° in hydrocarbon solvents, 3.95 ± 0.01 gauss,[2a] is approximately that predicted by the temperature-dependence relationship obtained in this work.

Fessenden and Ogawa[2a] have recently communicated that the proton splitting in $C_6H_6^{-\cdot}$ increases by 2.5% as the temperature is reduced from about −60 to −130°. We have confirmed this very interesting effect for "spatially degenerate" radicals and have found a comparable percentage temperature coefficient. The temperature dependence of the proton splitting in $C_7H_7\cdot$ (and in $C_6H_6^{-\cdot}$) most likely arises from population of low-lying excited vibronic states. A calculation of the vibronic wave functions of $C_7H_7\cdot$ using the dynamical Jahn–Teller theory is required but is a formidable task, as evidenced by the efforts of McConnell and McLachlan[4a] on $C_6H_6^{-\cdot}$. The detailed effect of the time-dependent solvent perturbation must also be treated. Further, it is clear that the effect of averaging the contact interaction over the molecular vibrations must be considered, as have Schrader and Karplus[12] for $CH_3\cdot$.

The temperature effect is in the *direction* predicted by considering simple C–H vibrational excitation. The ratio of "aromatic" proton to deuteron splitting is about 1% lower than the magnetic moment ratio.[13] This can be interpreted as signifying a decrease in the magnitude of the splitting with increase in vibrational amplitude. The splitting in a vibrationally excited state would therefore be smaller than in the zero-point state, and the averaged value decrease as temperature is increased.

The carbon-13 hyperfine constant for $C_7H_7\cdot$ has been measured and observed to *increase* with increasing temperature. At 139° the splitting,[9,10] corrected for overlap, is 2.24 ± 0.025 gauss[11] and at 188°, 2.31 ± 0.02 gauss; the variation is 3% in a 50° interval. A linear fit of the splitting *vs.* temperature (81 points) has been obtained using the unweighted least-squares method and is $|a^{C}| = 1.48 \times 10^{-3}t + 2.02$ gauss. Standard deviations of the slope and intercept are 1.2×10^{-4} and 1.9×10^{-2}, respectively.

The C-13 splitting bears comparison with the corresponding data for $C_6H_6^{-\cdot}$ (2.8 ± 0.1 gauss)[14] and $C_8H_8^{-\cdot}$ (1.28 ± 0.05 gauss).[15] Although quantitative agreement with experiment has been obtained for a number of less-symmetrical radicals[16,17] using the parameters of the Karplus–Fraenkel theory of C-13 splittings,[16] the agreement is poor for the "spatially degenerate" radicals. For $C_6H_6^{-\cdot}$ the computed splitting is 1.3 gauss and for $C_8H_8^{-\cdot}$, in which case the theory has been extended[15] to allow for changes in orbital hybridization, the magnitude of the theoretical value is less than 0.97 gauss. In part these discrepancies are due to a temperature dependence as observed for $C_7H_7\cdot$ in this work; quantitative elucidation for the series, $C_6H_6^{-\cdot}$, $C_7H_7\cdot$, $C_8H_8^{-\cdot}$, constitutes an important theoretical problem.

Although the case of $C_7H_7\cdot$ is far more complex, it is of interest that an increasing C-13 splitting with increasing temperature can be predicted for methyl radical from the calculation of Schrader and Karplus,[12] and is consistent with the greater splitting for $C^{13}H_3\cdot$ as compared with $C^{13}D_3\cdot$.[12] The C-13 splitting is found to depend strongly on vibrational amplitude due mainly to the admixture of 2s character into the "p-type" orbital with near-unit spin polarization; the effect is held to be somewhat damped due to incomplete orbital following.[12] A greater percentage change of splitting as a function of temperature is indicated for C-13 than for proton splittings, as is found in our

(9) Splittings have been measured relative to those of naphthacene monopositive ion ($a^{H}_{a} = 5.06$, $a^{H}_{b} = 1.684 \pm 0.008$, $a^{H}_{c} = 1.020 \pm 0.007$ gauss): J. S. Hyde, private communication, and ref. 10. Uncertainties in the splittings of the standard should be combined with those mentioned in the text as a measure of the total limits of error.

(10) J. S. Hyde and H. W. Brown, *J. Chem. Phys.*, **37**, 368 (1962).

(11) Maximum limits of error.

(12) D. M. Schrader and M. Karplus, *J. Chem. Phys.*, **40**, 1593 (1964).

(13) R. W. Fessenden and R. H. Shuler, *ibid.*, **39**, 2147 (1963).

(14) J. R. Bolton, *Mol. Phys.*, **6**, 219 (1963).

(15) H. L. Strauss and G. K. Fraenkel, *J. Chem. Phys.*, **35**, 1738 (1961).

(16) M. Karplus and G. K. Fraenkel, *ibid.*, **35**, 1312 (1961).

(17) J. R. Bolton and G. K. Fraenkel, *ibid.*, **40**, 3307 (1964).

measurements on $C_7H_7\cdot$. A positive temperature coefficient has also been recently found in the related case of nitrogen-14 splittings for the N,N'-dihydro-1,4-diazine cation and similar radicals.[18]

Further work in progress includes calculation of the enthalpy of cleavage of bitropenyl from the temperature dependence of the e.s.r. intensity, investigations of alkyl- and aryl-substituted tropenyl radicals, and studies of the chemical and physical properties of the tropenyl radical.

Acknowledgment. We wish to thank Professor Ernest R. Davidson for many helpful discussions.

(18) M. R. Das and G. K. Fraenkel, *J. Chem. Phys.*, **42**, 792 (1965).
(19) Alfred P. Sloan Foundation Research Fellow.

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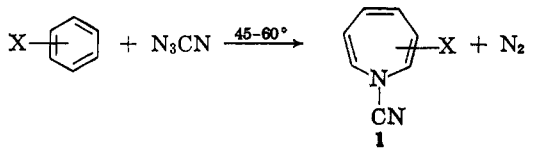
N-Cyanoazepines from Cyanonitrene and Aromatic Compounds

Sir:

Cyanonitrene,[1,2] formed by thermolysis of cyanogen azide at 45–60°, reacts with aromatic compounds to give N-cyanoazepines (**1**)[3] (X = H, CH_3, *p*-$(CH_3)_2$, CO_2CH_3, Cl, F, 6F, CF_3, CCl_3) in high yield. The physical properties of the parent compound **1** (X = H, 70% yield) are similar to those of N-carboethoxyazepine,[4–8] but some of its chemical properties are significantly different. N-Cyanoazepine (**1**, X = H) is a mobile, red oil (b.p. 48° (0.2 mm); $n^{25}D$ 1.5520; $\lambda_{max}^{CCl_4}$ 2.27 (=CH), 4.50 (C≡N), and 6.03, 6.13 μ (-CH=CH-); $\lambda_{max}^{isooctane}$ 330 (ε 437) and 202 mμ (ε 25,500); H n.m.r. complex pattern at τ 3.83–3.93 (2 H) and multilined pattern at τ 4.40–4.49 (4 H)). *Anal.* Found: C, 71.14; H, 5.25; N, 23.66; mol. wt. 118 (mass spectrometric).

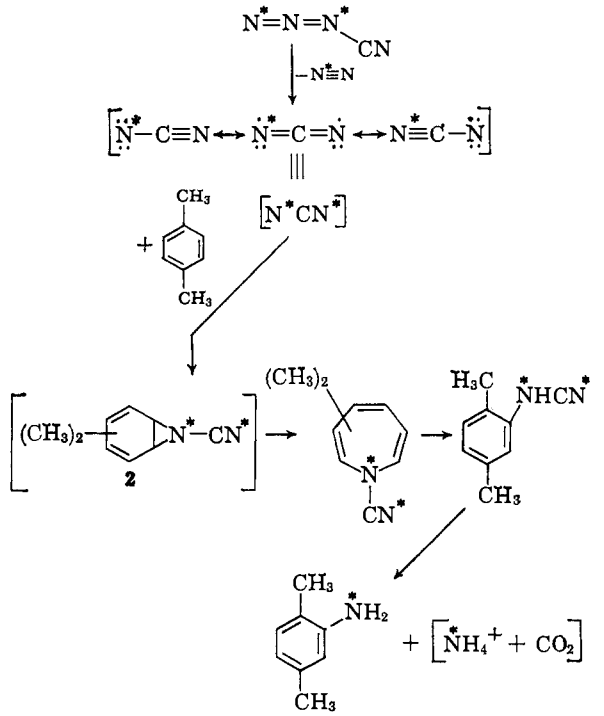


1

At room temperature **1** (X = H) spontaneously dimerizes to a white crystalline solid (m.p. 220–221°) but is stable when sealed in glass and stored at −78°. In dilute acid it is rearranged to phenylcyanamide and hydrolyzed to phenylurea in quantitative yield. In basic hydrogen peroxide it is hydrolyzed without rearrangement to give yellow crystalline N-carbamylazepine (m.p. 118.5–119.5°).

(1) F. D. Marsh and M. E. Hermes, *J. Am. Chem. Soc.*, **87**, 1819 (1965).
(2) A. Anastassiou, H. E. Simmons, and F. D. Marsh, *ibid.*, **87**, 2296 (1965).
(3) *Chemical Abstracts* nomenclature for the parent compound 1 (X = H) is 1H-azepine-1-carbonitrile.
(4) K. Hafner and C. König, *Angew. Chem.*, **75**, 89 (1963).
(5) K. Hafner, *ibid.*, **75**, 1049 (1963).
(6) K. Hafner, D. Zinser, and K. L. Moritz, *Tetrahedron Letters*, **26**, 1733 (1964).
(7) R. J. Cotter and W. F. Beach, *J. Org. Chem.*, **29**, 751 (1964).
(8) W. Lwowski, T. J. Maricich, and T. W. Mattingly, Jr., *J. Am. Chem. Soc.*, **85**, 1200 (1963).

N-Cyanoazepine appears to be formed from a symmetrical intermediate believed to be cyanonitrene as illustrated by the following experiment. Cyanogen azide with azido nitrogens 1 and 3 labeled (N^{15}) was allowed to react with *p*-xylene to give two isomeric dimethyl-N-cyanoazepines (84%), which rearranged subsequently to 2,5-dimethylphenylcyanamide (100%) containing 51.5% of the original N^{15}. Hydrolysis of the cyanamide gave 2,5-dimethylaniline (70%) containing 25.5% of the original N^{15}. Scrambling of nitrogen atoms in the intermediate cyanonitrene can account for this observation. Presumably, the 7-azanorcaradiene (**2**) is an intermediate. An alternative mechanism, involving an unstable N-cyanotriazoline intermediate,[9] is eliminated since addition of labeled cyanogen azide to olefins occurs without scrambling of the label.[2] Although the ground state of NCN is $^3\Sigma_g^-$,[10] the species produced in the low temperature thermolysis of cyanogen azide may be an excited singlet state because of spin conservation. Experiments to test this point are in progress (A. G. Anastassiou).



Monosubstituted benzenes react with cyanogen azide to give three isomeric N-cyanoazepines. Substituents have a marked influence on the stability and reactions of the products. Electron-withdrawing substituents such as F, CCl_3, or CF_3 stabilize the seven-membered ring, and these products show less tendency to rearrange to cyanamides but dimerize when heated. Mixtures of the three isomeric methyl-N-cyanoazepines rearrange at room temperature to *ortho*- and *para*-substituted phenylcyanamides in 2:1 ratio. The isomeric chloro-N-cyanoazepines gave comparable results. Acid-catalyzed hydrolysis of the mixture of isomeric fluoro-N-cyanoazepines from fluorobenzene gave *o*- and *p*-fluorophenylureas in 1:1 ratio containing less than 0.5% *meta* isomer. The absence of *meta*

(9) F. D. Marsh and M. E. Hermes, *ibid.*, **86**, 4506 (1964).
(10) G. Herzberg and D. N. Travis, *Can. J. Phys.*, **42**, 1658 (1964); G. J. Pontrelli and A. G. Anastassiou, *J. Chem. Phys.*, **42**, 3735 (1965).