[7] *W. P. Jencks*, 'Catalysis in Chemistry and Enzymology', McGraw-Hill Book Co., New York, N.Y. 1969, p. 116.
[8] *H. R. Bosshard*, unpublished experiments.
[9] *N. Kundu, S. Roy & F. Maenza*, Eur. J. Biochem. *28*, 311 (1972).
[10] *A. Patchornik & S. Ehrlich-Rogozinski*, Anal. Chemistry *31*, 985 (1959).
[11] *S. Ehrlich-Rogozinski & H. R. Bosshard*, Anal. Chemistry, in press.
[12] *J. S. Fritz*, Anal. Chemistry *22*, 1028 (1950).
[13] *D. Ben-Ishai & A. Berger*, J. biol. Chemistry *17*, 1564 (1952).
[14] *E. D. Nicolaides, M. K. Craft & H. A. DeWald*, J. med. Chemistry *6*, 524 (1963).

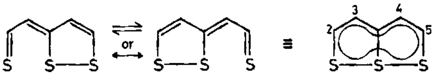
190. Conformational Study by ESR. of Some Alkyl Substituted 6a-Thiathiophthene Radical Anions

by **Fabian Gerson**[1], **Josef Heinzer**[2] and **Madeleine Stavaux**[3]
Physikalisch-Chemisches Institut der Universität, 4056 Basel, Switzerland
Laboratorium für Organische Chemie der Eidg. Techn. Hochschule, 8006 Zürich, Switzerland, and
Ecole Nationale Supérieure de Chimie, 14000–Caen, France

(17. V. 73)

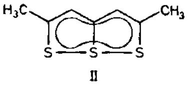
Summary. ESR. data are reported for the radical anions ($\mathrm{II}^{\ominus}$ to $\mathrm{VI}^{\ominus}$) of five alkyl substituted *6a-thiathiophthenes*. Rates and activation parameters for the inversion of the 3,4-trimethylene chain in $\mathrm{IV}^{\ominus}$, $\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$ have been obtained by means of an iterative least squares computer program ESRCEX. Preferential conformations of the alkyl substituents are discussed in terms of the $\langle\cos^2\theta\rangle$ dependence of the β-proton coupling constants and with the aid of molecular models. Experimental evidence strongly suggests that the partial rotation of the ethyl and isopropyl groups in $\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$ is correlated with the inversion of the 3,4-trimethylene chain.

A few years ago, the ESR. data were reported [1] for the radical anions of several symmetrically substituted derivatives of *6a-thiathiophthene* (I) [2]. In the temperature range of investigation (−60 to +20°), the radical anions were found to retain the mirror plane passing through the C–S bond.

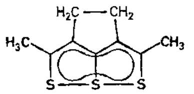


I

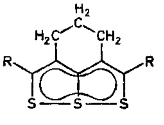
In the present paper, we deal in more detail with two of the radical anions considered in the previous paper ($\mathrm{II}^{\ominus}$ and $\mathrm{V}^{\ominus}$) [1] and extend the study to three other alkyl substituted derivatives ($\mathrm{III}^{\ominus}$, $\mathrm{IV}^{\ominus}$ and $\mathrm{VI}^{\ominus}$). The ESR. spectra of $\mathrm{IV}^{\ominus}$, $\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$ display marked temperature dependence due to inversion of the 3,4-trimethylene chain and restricted rotation ofthe 2,5-alkyl groups ($\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$).



II



III



IV $R=CH_3$
V $R=CH_2CH_3$
VI $R=CH(CH_3)_2$

---

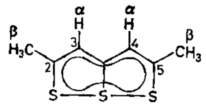
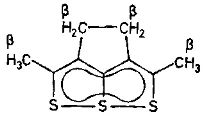
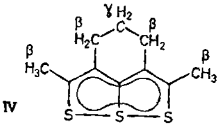
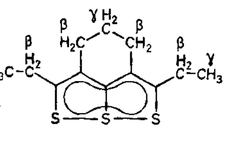
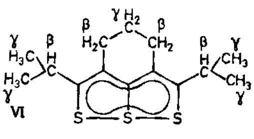
[1] Universität Basel.
[2] Eidg. Technische Hochschule, Zürich.
[3] Ecole Nationale, Caen.

Experimental Part. The synthesis of the five alkyl substituted 6a-thiathiophthenes II to VI has been described elsewhere [3]. The radical anions $II^{\ominus}$ to $VI^{\ominus}$ were generated by electrolytic reduction in N,N-dimethylformamide (DMF) with tetraethylammonium-perchlorate as the supporting salt. The stability of the radical anions increases in the sequence $II^{\ominus} < III^{\ominus}$, $IV^{\ominus} < V^{\ominus} < VI^{\ominus}$, *i.e.*, it is enhanced by large alkyl substituents. Whereas the half-life of $II^{\ominus}$ is only a few minutes at + 20°, the radical anion $VI^{\ominus}$ does not decay noticeably at this temperature, even over a period of several hours.

The temperature dependent spectra of $IV^{\ominus}$, $V^{\ominus}$ and $VI^{\ominus}$ were fitted with the aid of an iterative least squares program ESRCEX developed by one of us [4]. This program optimizes both the hyperfine coupling constants and the rates of conformational interconversions.

Results. – In Table 1, the proton coupling constants (a_{H_μ}) are given for the radical anions $II^{\ominus}$ to $VI^{\ominus}$ at –60 and +20°. Their assignment is straightforward in the case of $II^{\ominus}$, $III^{\ominus}$ and $IV^{\ominus}$. It is also unambiguous for $V^{\ominus}$ and $VI^{\ominus}$, since there is only one choice which leads to a meaningful interpretation of the ESR. spectra at varying temperature.

Table 1. *Proton coupling constants* (a_{H_μ} in Gauss) *for the radical anions* $II^{\ominus}$ *to* $VI^{\ominus}$. Experimental error: ± 2% for $a_{H_\mu} < 1$ Gauss, and ± 1% for larger values.

Radical anion of	–60°	+20°	Nr. of protons	Assignment to position
 II	6.36	6.35	six	β, methyl
	2.19	2.17	two	α
 III	6.58	6.55	six	β, methyl
	2.61	2.52	four	β, dimethylene
 IV	6.60	6.51	six	β, methyl
	3.03	2.11	two	β, trimethylene [a]
	1.23	2.11	two	β, trimethylene [b]
	0.52	0.32	one	γ, trimethylene
	0.13	0.32	one	γ, trimethylene
	4.08	4.00	two	β, ethyl
 V	3.56	4.00	two	β, ethyl
	2.95	2.05	two	β, trimethylene [a]
	1.19	2.05	two	β, trimethylene [b]
	0.52	0.31	one	γ, trimethylene
	0.11	0.31	one	γ, trimethylene
	<0.1	<0.1	six	γ, ethyl
	1.77	1.93	two	β, isopropyl
 VI	2.95	2.06	two	β, trimethylene [a]
	1.20	2.06	two	β, trimethylene [b]
	0.52	0.31	one	γ, trimethylene
	0.12	0.31	one	γ, trimethylene
	<0.1	<0.1	twelve	γ, isopropyl

[a] Axial position at –60°.

[b] Equatorial position at –60°.

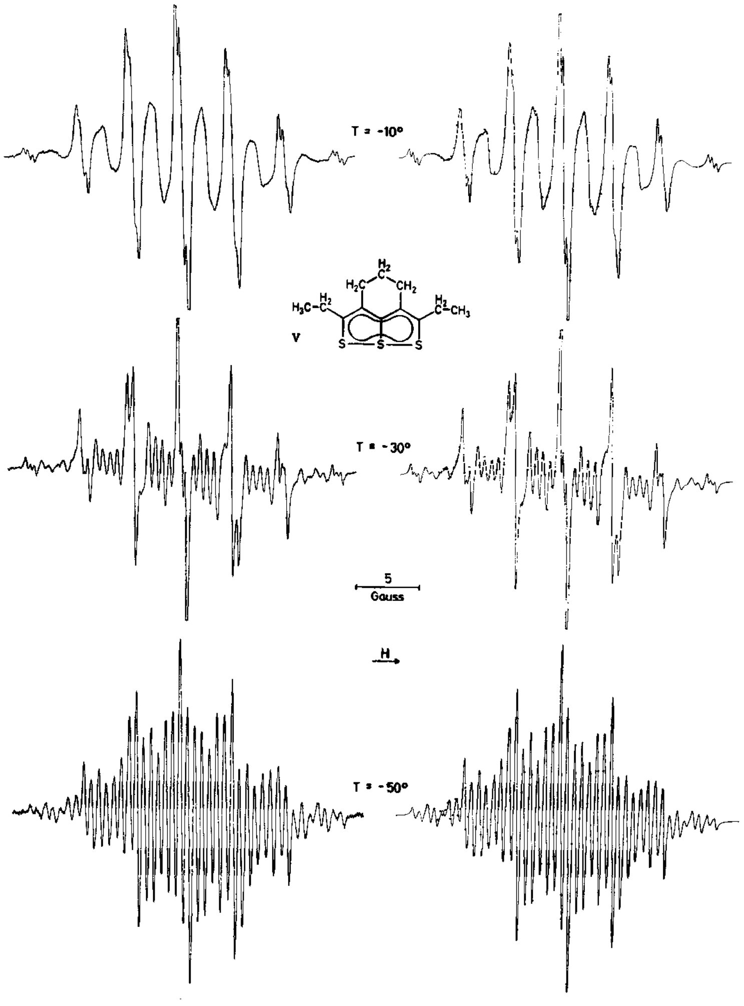


Fig. 1. *ESR. spectra of the radical anion $V^{\ominus}$ at variable temperature.* Left: Experimental spectra. Solvent: DMF; counterion: $(C_2H_5)_4N^{\oplus}$. Right: Spectra simulated with the aid of the following proton coupling constants (a_{H_μ} in Gauss), line-widths (l. w. in Gauss) and inversion rates (K in Hz):

Temp.	a_{H_μ} (two protons)	a_{H_μ} (one proton)	l.w.	K
−10°	4.22; 3.70; 2.93; 1.18	0.52; 0.11[a])	0.20	$1.47 \cdot 10^6$
−30°	4.17; 3.64; 2.94; 1.18	0.52; 0.11[a])	0.20	$5.18 \cdot 10^5$
−50°	4.10; 3.59; 2.94; 1.19	0.52; 0.11[a])	0.18	$1.40 \cdot 10^5$

[a]) This splitting, which is required by the least squares fit, was not resolved.

With regard to the temperature dependence of their $a^{\beta}_{H\mu}$ values, the β-protons can be classified as follows:

(1) Protons of the two 2,5-methyl groups in $\mathrm{II}^{\ominus}$, $\mathrm{III}^{\ominus}$ and $\mathrm{IV}^{\ominus}$, and of the 3,4-dimethylene chain in $\mathrm{III}^{\ominus}$. Their coupling constants depend only slightly on temperature.

(2) Protons of the inverting 3,4-trimethylene chain in $\mathrm{IV}^{\ominus}$, $\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$. Since the range, in which the pertinent hyperfine lines coalesce, lies between –30 and –10°, coupling constants of the axial and equatorial protons are distinguishable at –60, but become averaged at +20°. Their mean values do not markedly depend on temperature.

(3) Protons of the two 2,5-ethyl groups in $\mathrm{V}^{\ominus}$. The two protons of one substituent have different coupling constants at –60, but equal ones at +20°; the averaging process occurs in the coalescence range mentioned above. Moreover, there is a distinct increase in the mean $a^{\beta}_{H\mu}$ value at higher temperature.

(4) Protons of the two 2,5-isopropyl groups in $\mathrm{VI}^{\ominus}$. Their coupling constant also exhibits an appreciable increase on going from –60 to +20°.

The impressive agreement between the observed spectra and those simulated with the aid of our ESRCEX program [4] is demonstrated by Fig. 1 which shows the two derivative curves of $\mathrm{V}^{\ominus}$ at –10, –30 and –50°. *It is essential to note that partial rotation of the 2,5-ethyl substituents had to be accounted for*, in addition to the inversion of the 3,4-trimethylene chain, *and that excellent fit could be achieved by setting the rotational frequency equal to the rate K of the chain inversion.*

The rates K increase from 10^5 at –60 to $4 \cdot 10^6$ Hz at +20°. In the coalescence range they amount to $5 \cdot 10^5$–10^6 Hz (*cf.* caption to Fig. 1).

Fig. 2 presents the plots of $\ln\left(\frac{h}{kT}K\right)$ *vs.* $\frac{1}{T}$ for $\mathrm{IV}^{\ominus}$, $\mathrm{V}^{\ominus}$ and $\mathrm{VI}^{\ominus}$, whereas Table 2 lists the activation parameters $\log A'$, E_A, $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$ which are related to K by the *Arrhenius* and the *Eyring* [5] equations

$$\ln\frac{K}{A} = -\frac{E_A}{RT} \qquad (1)$$

and

$$\ln\left(\frac{h}{kT}K\right) = -\frac{\Delta G^{\neq}}{RT} = -\frac{\Delta H^{\neq}}{RT} + \frac{\Delta S^{\neq}}{R}. \qquad (2)$$

All notations have their conventional meanings. A′ is the dimensionless value of A (in Hz).

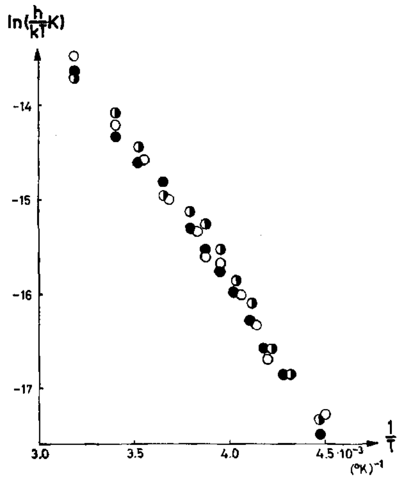


Fig. 2. *Plot of ln* (h/kT K) vs. 1/T *for the radical anions* $\mathit{IV}^{\ominus}$ (○), $\mathit{V}^{\ominus}$ (◑) *and* $\mathit{VI}^{\ominus}$ (●).

Table 2. *Activation parameters of ring inversion for the radical anions* $IV^{\ominus}$, $V^{\ominus}$ *and* $VI^{\ominus}$

Radical anion	log A′	E_A (kcal/mol)	$\Delta H^{\neq}$ (kcal/mol)	$\Delta S^{\neq}$ (e.u.)	$\Delta G^{\neq}$ (kcal/mol)
$IV^{\ominus}$	11.5	6.4	5.9	−8	8.3
$V^{\ominus}$	11.4	6.3	5.8	−8	8.2
$VI^{\ominus}$	11.2	6.2	5.6	−9	8.4
exp. error	±0.3	±0.4	±0.4	±2	±0.5

Discussion. – *Preferential conformations.* The experimental data given in Table 1 indicate that the π-spin populations at the carbon centers $\mu = 2,5$ and $3,4$ are nearly equal throughout the series, and thus the observed differences in the β-proton coupling constants $a^{\beta}_{H\mu}$ must be due to conformational effects.

The relationship [6]

$$a^{\beta}_{H\mu} = B \cdot \varrho_{\mu} \cdot \langle \cos^2\theta \rangle \tag{3}$$

connects the coupling constant of a β-proton in an alkyl substituent with the π-spin population ϱ_{μ} at the substituted carbon center μ. The dihedral angle θ, depicted in Fig. 3, is formed by the $2p_z$-axis of the center μ and the projection of the C(alkyl)–H(β) bond on the plane perpendicular to the C(μ)–C(alkyl) linkage. For freely rotating methyl substituents $\langle \cos^2\theta \rangle$ is 0.5. The parameter B is usually given a value of ca +40 Gauss in the case of radical anions [7–8].

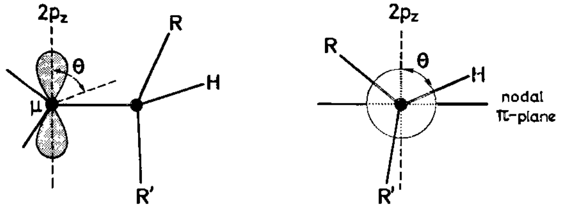


Fig. 3. *Schematic representations of an alkyl substituent at a carbon* π*-center* μ

For an estimation of the angles θ in the 2,5- and 3,4-alkyl substituents, the π-spin populations $\varrho_{2,5}$ and $\varrho_{3,4}$ at the substituted centers μ had to be determined. The value $|\varrho_{2,5}| = 0.33$ was calculated from the coupling constants of the methyl β-protons in $III^{\ominus}$ and $IV^{\ominus}$ by means of equation (3) ($\langle \cos^2\theta = 0.5 \rangle$) and $|B| = 40$ Gauss, whereas $|\varrho_{3,4}| = 0.08$ resulted from the coupling constant of the α-protons ($a^{\alpha}_{H\mu}$) in $II^{\ominus}$ with the use of the *McConnell* [9] relation

$$a^{\alpha}_{H\mu} = Q \cdot \varrho_{\mu} \tag{4}$$

and $|Q| = 27$ Gauss. Insertion of these π-spin populations into equation (3), along with the values $a^{\beta}_{H\mu}$ observed for the alkyl substituents other than methyl (Table 1; −60°), yields the dihedral angles listed in Table 3.

Clearly, the angles θ obtained in this way should be applied with some reservation, in view of the approximate nature of equation (3) and the uncertainties in $|\varrho_{2,5}|$, $|\varrho_{3,4}|$ and $|B|$. Nevertheless, they offer an insight into the preferential conformations of the

Table 3. *Dihedral angles* θ (in degrees) *of the alkyl substituents in the radical anions* $II^{\ominus}$ *to* $VI^{\ominus}$. Temperature: $-60°$. Abbreviations: Me = methyl; Et = ethyl; iPr = isopropyl; ax = axial; eq = equatorial; ab = above and bel = below the nodal π-plane.

Radical anion	2,5-alkyl groups	3,4-di- or trimethylene chain
$II^{\ominus}$	$(\theta_{Me} = 44)$	–
$III^{\ominus}$	$(\theta_{Me} = 45)$	$\theta_{ab} = 25$; $\theta_{bel} = 155$
$IV^{\ominus}$	$(\theta_{Me} = 45)$	$\theta_{ax} = 13$; $\theta_{eq} = 128$
$V^{\ominus}$	$\theta_{Et,1} = 59$; $\theta_{Et,2} = -56$	$\theta_{ax} = 16$; $\theta_{eq} = 128$
$VI^{\ominus}$	$\theta_{iPr} = 69$	$\theta_{ax} = 16$; $\theta_{eq} = 128$

2,5- and 3,4-alkyl substituents. With regard to the 2,5-ethyl and isopropyl groups in $V^{\ominus}$ and $VI^{\ominus}$, the values θ_{Et} and θ_{iPr} confirm the observation of previous workers [10] that the rotation of these substituents about the C(μ)–C(alkyl) bond is restricted, even in non-viscous solvents. The β-protons preferentially assume positions near the nodal π-plane, and this conformational preference is accentuated on passing from ethyl to isopropyl (*e.g.*, $\theta_{Et} = 56$ and $\theta_{iPr} = 64°$ in the radical anions of ethyl- and isopropylbenzene, respectively [11]). The angles θ_{ax} and θ_{eq} found for the 3,4-trimethylene chain in $IV^{\ominus}$, $V^{\ominus}$ and $VI^{\ominus}$ are also compatible with the generally accepted geometry of such a substituent, and the same is true for the corresponding values θ_{ab} and θ_{bel} $(= 180° - \theta_{ab})$ of the 3,4-dimethylene chain in $III^{\ominus}$. It is noteworthy that the latter values point to a slight, but significant increase in the H(β)–C(alkyl)–H(β) angle relative to the open-chain analogues.

Temperature dependence. The conformational behaviour of the 3,4- di- and trimethylene chains on raising the temperature (no marked effect for $III^{\ominus}$, enhanced rate of the chain inversion in $IV^{\ominus}$, $V^{\ominus}$ and $VI^{\ominus}$) meets the expectation and requires only a few comments. It is evident from the plot in Fig. 2 and the values in Table 2 that all activation parameters for the chain inversion in the three radical anions are equal within the experimental error. They supplement the scarce data reported for similar ESR. studies [12].

Less obvious is the effect of raising the temperature on the conformations of the 2,5-alkyl substituents in $V^{\ominus}$ and $VI^{\ominus}$. Fig. 4 depicts the preferential conformations of these substituents as required by the angles θ_{Et} and θ_{iPr} (Table 3) and indicated by consideration of molecular models[4]). For each substituent, there exist two such conformations which are symmetric with regard to the nodal π-plane and which can interconvert by a partial rotation about the C(μ)–C(alkyl) bond (Fig. 4). It is an enhancement in the frequency of this rotation at higher temperature which leads to the averaging of the β-proton coupling constants for the ethyl substituents in $V^{\ominus}$. *The findings that the rotational frequency should be equal to the rate constant K of the chain inversion in the coalescence range* (see Results) *strongly suggest a correlation of the two conformational interconversions.* Indeed, molecular models[4]) indicate that the partial rotation of the 2,5-alkyl substituents in $V^{\ominus}$ and $VI^{\ominus}$ is least sterically hindered when the trimethylene chain assumes a planar conformation, *i.e.*, when it is in the transition state of the chain inversion. Since the activation barriers usually found for a restricted

---

[4]) The models, which take into account the x-ray data [13], show that the 2,5-ethyl and isopropyl substituents should keep their methyl groups away from the 3,4-trimethylene chain.

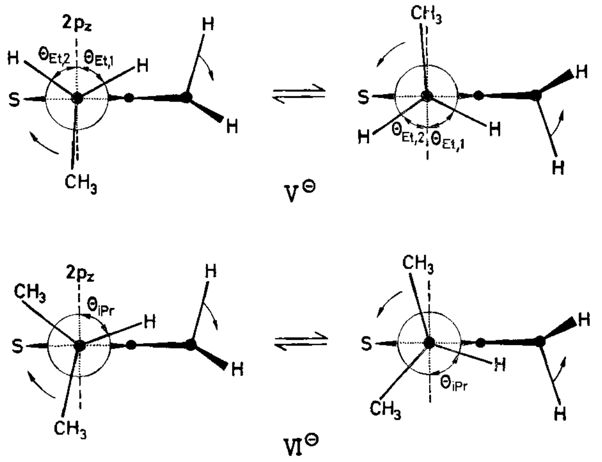


Fig. 4. *Preferential conformations of the 2,5-alkyl substituents in* $V^{\ominus}$ *and* $VI^{\ominus}$

rotation of the alkyl groups [14] are substantially lower than the analogous energies for the inversion of the trimethylene chain (Table 2), the rotational frequencies in $V^{\ominus}$ and $VI^{\ominus}$ should accomodate themselves to the inversion rates K and not *vice versa*. This conclusion is in accordance with the experimental rates K which are almost insensitive to the nature of the 2,5-alkyl groups in the radical anions (Fig. 2).

An additional effect of raising the temperature consists of a slight decrease in the angles θ_{Et} and θ_{iPr} which is reflected by an overall increase in the β-proton coupling constants for the 2,5-ethyl and isopropyl substituents (*cf.* Table 1 and caption to Fig. 1). Rationalization of this effect must be preceded by an explanatory remark. It should be borne in mind, that the angles θ_{Et} and θ_{iPr} of the 2,5-alkyl groups are not as well defined as the analogous values θ_{ab}, θ_{bel}, θ_{ax} and θ_{eq} of the 3,4-di- and trimethylene chains. Whereas the latter values characterize distinct conformations, the former can result from rotational time-averaging over several orientations separated by very low energy barriers. This implies that the angles θ_{Et} and θ_{iPr} given in Table 3 represent the preferential conformations of the 2,5-alkyl groups only to a first approximation, since they may contain small contributions of energetically less favourable orientations. The slight decrease in θ_{Et} and θ_{iPr} at higher temperature thus signifies that such orientations become somewhat more populated at the expense of the preferential conformation.

We thank Dr. *D. Leaver*, University of Edinburgh, for a sample of the compound III, Prof. *R. Gleiter*, Technische Hochschule Darmstadt, for his interest in this work, and the Rechenzentrum of the Eidg. Techn. Hochschule, Zürich, for an allowance of computer time. Support of the *Schweiz. Nationalfonds* (Project Nr. SR 2.477.71) is also gratefully acknowledged.

REFERENCES

[1] *F. Gerson, R. Gleiter, J. Heinzer & H. Behringer*, Angew. Chem. *82*, 294 (1970); Angew. Chem. Int. Ed. *9*, 306 (1970).

[2] For reviews see: *E. Klingsberg*, Quart. Rev. *23*, 537 (1969); *N. Lozac'h*, Adv. Heterocyclic Chem. *13*, 161 (1971).

[3] *F. Arndt, P. Nachtwey & J. Pusch*, Ber. deutsch. chem. Ges. *58*, 1633 (1925); *E. I. G. Brown, D. Leaver & D. M. McKinnon*, J. chem. Soc. (C), *1970*, 1202; *H. Behringer, M. Ruff & R. Wiedenmann*, Chem. Ber. *97*, 1732 (1964); *A. Josse & M. Stavaux*, unpublished work.

[4] *J. Heinzer*, J. Magn. Resonance, in print; see also Mol. Physics *22*, 167 (1971) and Computer Program ESREXN, QCPE 209 (1972).

[5] *S. Glasstone, K. Laidler & H. Eyring*, 'The Theory of Rate Processes', McGraw-Hill, New York, 1941.

[6] *C. Heller & H. M. McConnell*, J. chem. Physics *32*, 1535 (1960); *A. Horsfield, J. R. Morton & D. H. Whiffen*, Mol. Physics *4*, 425 (1961).

[7] *G. A. Russell*, Semidione Radical Anions, in Radical Ions (E. T. Kaiser and L. Kevan, ed.), Interscience Publishers, New York, 1967, pp. 110–112.

[8] *F. Gerson*, 'High Resolution ESR. Spectroscopy', J. Wiley and Sons Ltd. New York, and Verlag Chemie, Weinheim, 1970; p. 44.

[9] *H. M. McConnell*, J. chem. Physics *24*, 632 (1956).

[10] For a review see: *D. H. Geske*, 'Conformation and Structure as Studied by Electron Spin Resonance Spectroscopy', in 'Progress Phys.-Org. Chemistry' (A. Streitweiser, Jr., and R. W. Taft, eds), *4*, 175–189 (1967).

[11] *F. Gerson, G. Moshuk & M. Schwyzer*, Helv. *54*, 361 (1971).

[12] *G. A. Russell, G. R. Underwood & D. C. Lini*, J. Amer. chem. Soc. *89*, 6636 (1967); *R. F. C. Claridge, B. M. Peake & R. M. Golding*, J. Magn. Resonance *6*, 29 (1972); *F. W. Pijpers, M. R. Arick, B. M. P. Hendriks & E. de Boer*, Mol. Physics *22*, 781 (1971).

[13] *F. Leung & S. C. Nyburg*, Chem. Commun. (London) *1969*, 137; *A. Hordvik & K. Julshamn*, Acta Chem. Scand. *26*, 343 (1972); *B. Birkness, A. Hordvik & L. F. Saethre*, *ibid. 26*, 2140 (1972).

[14] *E. L. Eliel, N. L. Allinger, S. J. Anyal & G. A. Morrison*, 'Conformational Analysis', Interscience Division of J. Wiley and Sons Ltd., New York 1965; pp. 20 and 140.

---

191. Photosynthese von Dihydroazepinonen aus 2-Alkyl-indazolen

von **W. Heinzelmann** und **M. Märky**

Physikalisch-Chemisches Institut der Universität Zürich

(28. V. 73)

Summary. N(2)-alkylated indazoles are known to undergo two different photoreactions, namely i) rearrangement into benzimidazoles in organic solvents and neutral aqueous solution, and ii) solvolysis yielding *o*-amino-benzaldehydes or acetophenones, in strongly acidic solution.

In diluted acidic solution (pH 3–4) both of these reactions are suppressed and a new photoreaction takes place, leading to two isomeric dihydroazepinones.

Irradiation of 2,3-dimethyl-indazole in diluted sulfuric acid (pH = 3.8) yields 7-acetyl-1,3-dihydro-2*H*-azepin-2-one and 3-acetyl-1,3-dihydro-2*H*-azepin-2-one.

2-Alkyl-indazole lagern photochemisch in den meisten organischen Lösungsmitteln praktisch quantitativ in die entsprechenden 1-Alkyl-benzimidazole um [1–2] [5–7].