

Properties and Reactions of Alkyl Free Radicals in Solution.
Part VIII. The Reducing Action of Some Water-soluble Radicals.*

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4 : 4'-Azobis-4-cyanopentanoic acid has been prepared and separated into its *meso*- and racemic isomers. When heated in aqueous solution each isomer gives in about 20% yield a mixture in equal proportions of the *meso*- and the racemic form of 4 : 5-dicyano-4 : 5-dimethyloctane-1 : 8-dioic acid.

The free radicals produced from this acid, from 4 : 4'-azobis-4-cyanoheptane-1 : 7-dioic acid, and from two of the azo-compounds previously studied (Part II, *J.*, 1951, 1851) have been found to reduce a number of inorganic reagents and also certain oxidation-reduction indicators. It is concluded that for these radicals E_{-e} , for the reaction $R\cdot \rightleftharpoons R^+ + e$, must be slightly less than $+0.4$ v.

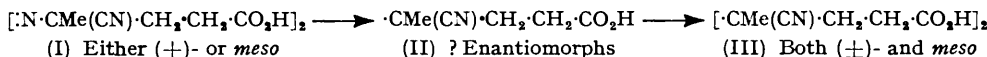
THE magnitudes of the two redox potentials, E_{+e} and E_{-e} , of free radicals, for electron gain and electron loss respectively, have been shown to be of significance in the elucidation of the mechanisms of both oxidation and reduction processes (Mackinnon and Waters, *J.*, 1953, 323; Drummond and Waters, *J.*, 1954, 2456). Though redox potentials of such transient entities as organic free radicals can be assessed approximately by relation to the properties of inorganic ions in aqueous solution, as yet suitable active radicals have rarely

* Part VII, *J.*, 1954, 1920.

been prepared in water except as transient intermediates in sequences of electron-transfer reactions which are difficult to analyse into their component stages.

Whilst many types of free radicals have been made by the homolysis of azo- and diazo-compounds (cf. *Ann. Reports*, 1952, **49**, 115—121) little attention seems to have been paid to the practicability of synthesising aliphatic azo-compounds which, by virtue of acidic or basic substituents, could be made to generate in aqueous solution organic free radicals of one known structure only. We are now engaged in exploring this approach to the assessment of free-radical reactivity.

One water-soluble aliphatic azo-compound, 4 : 4'-azobis-4-cyanopentanoic acid (I), has evidently been prepared by Madison Hunt (U.S.P., 2,471,959/1949) and by Lewis and Matheson (*J. Amer. Chem. Soc.*, 1949, **71**, 747) from lævulic acid, but no details concerning this substance, other than a rate of decomposition, have been reported. This azo-acid contains two identical asymmetric centres and should therefore exist in *meso*-, racemic,



and optically active forms. We have prepared it and have been able to separate the *meso*- and the racemic form by taking advantage of their difference in solubility in both water and aqueous methanol but have failed to identify them by achieving the resolution of one—the need to work only in cool solutions adds great difficulties to available techniques of optical resolution. Aqueous solutions of the isomeric free acids, and also their solutions in alkali, decompose when warmed, to give free radicals that can catalyse the polymerisations of vinyl cyanide, vinyl acetate, and methyl methacrylate (cf. Hunt, *loc. cit.*). Also the acids have been shown to catalyse the side-chain chlorination of toluene by sulphuryl chloride (cf. Part II, *J.*, 1951, 1851). The decompositions of each of the isomers (I) in water at about 90° gave about 22% of mixtures of 4 : 5-dicyano-4 : 5-dimethyloctane-1 : 8-dioic acids (III), from which *meso*- and (\pm)-isomers were successfully separated. Overberger and Berenbaum (*J. Amer. Chem. Soc.*, 1951, **73**, 4883) have claimed that a similar separation of the *meso*- and the (\pm)-form of $\alpha\beta$ -diisobutyl- $\alpha\beta$ -dimethylsuccinonitrile from the decompositions of both the pure *meso*- and the pure (\pm)-form of $\alpha\alpha'$ -azobis- $\alpha\gamma$ -dimethylvaleronitrile indicates that the free radicals $\text{CRR}'(\text{CN})\cdot$ have a planar structure, but this argument is not valid, for if the homolyses of both the *meso*- and the (\pm)-form of the azo-nitriles liberated enantiomorphous (+)- and (−)-radicals then at all times during the decomposition both these would be present in equivalent amounts from each starting material and would, by random combination, necessarily yield 50% each of the *meso*- and the (\pm)-dimer of type (III).

The major product of the decomposition of the acid (I) was a very soluble gum which immediately reduced cold permanganate. This unsaturation indicates that the gum consists mainly of the products of disproportionation of the radicals (II). It is not a product of their reaction with water since a decomposition of the acid (I) in chlorobenzene yielded a similar gum and an even smaller percentage of dimers (III).

A more symmetrical water-soluble azo-compound, 4 : 4'-azobis-4-cyanoheptanedioic acid, has also been prepared from γ -oxopimelic acid. Its decomposition in water yields only 10% of the radical dimer, 4 : 5-di-(2-carboxyethyl)-4 : 5-dicyano-octanedioic acid. Since dialkylazonitriles yield 50—80% of dimers it appears that the presence of carboxyl substituents in free alkyl radicals reduces their tendency to dimerise.

Cold aqueous solutions of the aliphatic azo-compounds mentioned above show no reducing properties, but when these solutions are heated, under nitrogen or carbon dioxide on a boiling-water bath, many substances can be reduced as the organic free radicals are generated. Similar experiments have been carried out with $\alpha\alpha'$ -azobisisobutyronitrile and $\alpha\alpha'$ -azobis- α -methylbutyronitrile in dilute aqueous alcohol (Table I). Corresponding tests have also been carried out with representative oxidation-reduction indicators of known E_0' . These gave less convincing evidence of the ease with which free alkyl radicals can lose electrons, for the indigosulphonates and the quinonoid indophenol dyes were irreversibly decolorised, presumably by addition of radicals to their quinonoid systems (cf. Parts I and V, *J.*, 1950, 1764; 1952, 4666; Part VII, *loc. cit.*).

Table 1 indicates that for the four radicals tested the value of E_{-e} (for the reaction $R\cdot \rightleftharpoons R^+ + e$) must be slightly less than +0.4 v, the standard hydrogen electrode being

TABLE 1. Reactions of inorganic oxidising agents with aliphatic free radicals.

Reagent	Standard redox potential, E_0 (v)	Reactions with radicals *			
		A	B	C	D
Acid permanganate	1.5	Reduced to Mn^{2+}	—	—	—
Acid dichromate	1.3	Reduced to Cr^{3+}	—	—	—
Bromine water	1.06	Decolorised	—	See Part II (J., 1951, 1851)	—
Ammoniacal silver nitrate	(0.8)	Reduced to silver	—	Reduced	—
Selenious acid	0.74	pH 2, red. to Se	pH 2, red. : not reduced	pH 7, Not reduced	—
Ferric chloride (acid)	0.74	Red. to Fe^{2+}	Slight reduction	Slight reduction	—
Mercuric chloride (pH 7)	0.6	Reduced to mercurous chloride			
Iodine	0.54	Decolorised rapidly	—	See Part II	—
Potassium ferricyanide (pH 7)	0.49	Ferrocyanide formed	—	—	Slow reduction
Ammonium vanadate (pH 7)	0.4	Red. through $(VO_2)^{2+}$ to V^{3+}	Red. to V^{3+}	Reduced to V^{3+} at pH 2, but not reduced at pH 7	—
Fehling's solution	—	$Cu_2O \downarrow$	$Cu_2O \downarrow$	Very slight reduction	—
Stannic chloride	(0.13)	Not reduced	—	—	—
Folin's phenol reagent (pH 7) (molybdate)	—	Slight reduction	—	Slight reduction	—
				At pH 1, no reduction	

* Radicals used: A, $\cdot CMe(CN)\cdot CH_2\cdot CH_2\cdot CO_2H$ in H_2O . B, $\cdot C(CN)(CH_2\cdot CH_2\cdot CO_2H)_2$ in H_2O . C, $\cdot CMe_2\cdot CN$ in aq. alcohols. D, $\cdot CMeEt\cdot CN$ in aq. alcohols

the reference zero. Table 2 indicates that the corresponding value of E' at pH 7 is 0.0 to -0.1 v, and since $E'_0 = 0.0$ corresponds to $E_0 = +0.42$ for reactions involving hydrogen transfer the two sets of observations are concordant. The free radicals $CRR'(CN)\cdot$ do not reduce tetrazolium salts and are therefore less powerful reducing agents than the radicals

TABLE 2. Reactions of aliphatic free radicals with oxidation-reduction indicators.

Indicator	Redox potential E'_0 (v) (at pH 7)	Reactions with radicals *			
		A	B	C	D
Phenolindo-2 : 6-dichlorophenol	+0.0226	Irreversibly decolorised			
Phenol-indophenol	+0.220	" "			
2-Chlorophenol-indophenol	+0.200	" "			
Lauth's violet	+0.056	Reversibly decolorised			
Methylene-blue	+0.011	Reversibly decolorised (slight action only)			
Potassium indigotetrasulphonate	-0.046	Irreversibly decolorised			
Potassium indigodisulphonate	-0.123	" "			
2 : 3 : 5-Triphenyltetrazolium chloride	—	Not attacked	—	—	—

* See footnote to Table 1.

$CHMe(OH)\cdot$ and $CMe_2(OH)\cdot$ formed from ethanol and propan-2-ol by Fenton's reagent (Mackinnon and Waters, *loc. cit.*). This difference was expected since the electron-withdrawing CN groups of these radicals should diminish their tendency to suffer further electron loss.

EXPERIMENTAL

4 : 4'-Azobis-4-cyanopentanoic Acids.—To sodium cyanide (49 g.) and hydrazine sulphate (65 g.) in water (500 ml.) at 50° was added during 30 min. with rapid stirring a neutralised solution of lævulic acid (116 g.) in water (200 ml.). The solution was stirred at 45—50° for a further 3 hr. and then allowed to cool. It was then made just acid to litmus, cooled in ice, stirred rapidly, treated dropwise with bromine until the latter just remained in excess, and stirred for a further 30 min. The excess of bromine was destroyed with sodium hydrogen sulphite, and the white solid which had separated (73 g.) was collected and washed once with

ice-water. It had m. p. 115—127° and was a mixture of *meso*- and (\pm)-isomers (Found : equiv., 138. Calc. for $C_{12}H_{16}O_4N_4$: equiv., 140).

A portion of the dry acid was shaken with 25 ml. of water; after 1 hr. the saturated solution was filtered, the solid residue was shaken with a further 25 ml. of water, and this whole procedure was repeated a number of times. Each portion of aqueous extract was titrated with alkali. Plotting of the successive titres indicated that the acid was a mixture of two components, the more soluble (48% of the whole) having a solubility of 2.75 g./l. and the less soluble 0.47 g./l. at room temperature. A similar determination in 10% methanol indicated that the more soluble isomer might be dissolved completely from 1 g. of mixed acids by 60 ml. of this solvent. By a separation in this way the less soluble *acid*, after crystallisation from warm water, was obtained as needles, m. p. 128° (decomp.) (Found : C, 51.3; H, 5.9; N, 20.0. $C_{12}H_{16}O_4N_4$ requires C, 51.4; H, 5.7; N, 20.0%). The more soluble *isomer*, recovered by careful evaporation of the solvent under diminished pressure and crystallisation from small volumes of warm water, had m. p. 110—111° (decomp.) (Found : C, 50.8; H, 5.8; N, 19.4%). Attempted resolution of the more soluble isomer by brucine in acetone gave impure resinous salts, of which the most and the least soluble fraction had α_D -47° and -57° respectively, but the regenerated free acids had no detectable activity. The brucine salts of the more soluble acid could be obtained only as resins the specific rotations of which were almost identical for all fractions. The use of strychnine was even less successful.

Decomposition of the 4 : 4'-Azobis-4-cyanopentanoic Acids.—The more soluble acid (5 g.) in water (200 ml.) was heated on a steam-bath until evolution of nitrogen had ceased (5 hr.). On cooling, 0.6 g. of a brownish solid, m. p. 195—207°, was deposited. Partial evaporation gave 0.4 g. of a white solid, m. p. 173—179°, and complete evaporation of the remainder a brown gum, of which 1 g. proved to be insoluble in dry acetone and could be separated as a powder, m. p. 120—175°. The acetone-soluble part of the gum immediately reduced cold permanganate; attempts to prepare crystalline solids from it failed. From the solid of high m. p. repeated crystallisation from ethanol gave the less soluble isomer of 4 : 5-dicyano-4 : 5-dimethyloctane-1 : 8-dioic acid in needles, m. p. 207—208° (Found : C, 57.3; H, 6.1; N, 10.8%; *M*, 272. $C_{12}H_{16}O_4N_2$ requires C, 57.2; H, 6.4; N, 11.1%; *M*, 252). From the powder of lower m. p. repeated crystallisation from water gave the more soluble *isomer*, m. p. 182—183° (Found : C, 56.9; H, 6.4; N, 11.2%; *M*, 280). Both isomers were also obtained in similar yields (10—14%) by decomposing the less soluble azo-acid in water. The total yield of 4 : 5-dicyano-4 : 5-dimethyloctane-1 : 8-dioic acids obtained by decomposition in water of a larger bulk of the mixed azo-acids was 22%. Decomposition in chlorobenzene solution at 100° gave only 13% of these isomers, again in nearly equal proportions.

4 : 4'-Azobis-(4-cyanoheptanedioic) Acid.— γ -Oxopimelic acid (Marckwald, *Ber.*, 1887, 20, 2813) (35 g., 0.2 mole) neutralised with sodium carbonate solution (200 c.c.) was added slowly to a stirred mixture of sodium cyanide (0.2 mole) and hydrazine sulphate (0.1 mole) in water (200 c.c.) at 45°. Stirring was continued at this temperature for 3 hr. after the addition. After a further 24 hr. the solution was acidified, cooled to 0°, and oxidised with bromine as described above. The white powder which was deposited was collected (15.5 g., 39%) and crystallised from warm aqueous ethanol; it had m. p. 133—135° (decomp.) (Found : C, 48.5; H, 5.3; N, 14.0. $C_{16}H_{20}O_8N_4$ requires C, 48.5; H, 5.1; N, 14.1%). This *acid* (20 g.) was decomposed in boiling water (200 c.c.); the resulting solution after evaporation to half its bulk deposited 1.8 g. (10%) of 4 : 5-di-(2-carboxyethyl)-4 : 5-dicyano-octanedioic acid, m. p. 252—254° (from aqueous methanol) (Found : C, 52.6; H, 5.5; N, 7.3. $C_{16}H_{20}O_8N_2$ requires C, 52.3; H, 5.5; N, 7.6%). The remainder of the decomposition product was a very soluble unsaturated gum.

Decompositions of the Azo-compounds in the Presence of Oxidising Agents.—(a) With inorganic oxidising agents the tests were carried out by heating the azo-compound (0.1 g.) in water (20 ml.) with 0.5 equiv. of reagent for 30 min. on a boiling-water bath and treating similarly a control tube containing the oxidising agent and distilled water. When the reduced product might be affected by air, then nitrogen or carbon dioxide was bubbled continuously through both tubes.

(b) With organic oxidation-reduction indicators the pH of the solutions was always adjusted to 7.0 by a phosphate buffer, and a stream of nitrogen was bubbled through the apparatus to exclude air. Tests were carried out by adding 5 ml. of a 0.2% solution of the indicator in water to 0.1 g. of the azo-compound in 25 ml. of aqueous solution. This mixture was heated under reflux as before, together with a control tube containing indicator and buffer solution only. Since the azo-compounds *C* and *D* were insoluble in water a little ethanol or propan-2-ol was added to promote dissolution (this did not appear to affect the results, for similar, but less reliable, results were obtained with dispersions of the molten azo-compounds in hot water).

The results are given in the Tables. The reversibility of the reduction was tested by exposing the cooled decolorised solutions to air. Only with methylene-blue and thionine did the original colour of the dye reappear.

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