[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BRANDEIS UNIVERSITY, WALTHAM 54, MASS.]

Bicyclic, Cyclic and Acyclic Azo Compounds. 2,3-Diazabicyclo[2,2,2]-2-octene, 3,6-Dimethyl-Δ^1-tetrahydropyridazine and Azoisopropane[1]

BY SAUL G. COHEN AND ROBERT ZAND

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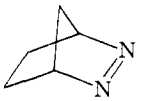
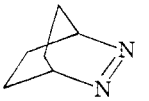
Decomposition of the azo compound 2,3-diazabicyclo[2,2,2]-2-octene (II) has been studied in the gas phase from 199.5 to 259.0°. The reaction shows first-order kinetics, $k_1 = 2.0 \times 10^{15}\, e^{-44,600/RT}$, $\Delta S^{\ddagger} = 10.5$ e.u. The data are compared with those of acyclic aliphatic azo compounds, and with the related compound, 2,3-diazabicyclo[2,2,1]-2-heptene (I). Compound II was prepared *via* Diels–Alder addition of diethyl azodicarboxylate to 1,3-cyclohexadiene; this reaction was accompanied by much allylic addition of the diene to the azo-ester. The cyclic analog of II, 3,6-dimethyl-Δ^1-tetrahydropyridazine (III), was prepared *via* addition of the azo-ester to 2,4-hexadiene; compound III tautomerized readily to the Δ^2-isomer, the hydrazone. Infrared absorption bands, assigned to the azo linkage, are found at 6.66 μ, compound I, and at 6.55 and 6.63 μ, compound II. Chemical shift values of 5.07 and 4.95 p.p.m. are assigned to the bridgehead protons of I and II, respectively.

As part of a study of the effects of structure on the kinetics of decomposition of azo compounds, it was of interest to examine some bridged bicyclic azo compounds and compare the results with those of structurally related cyclic and acyclic azo com-



I



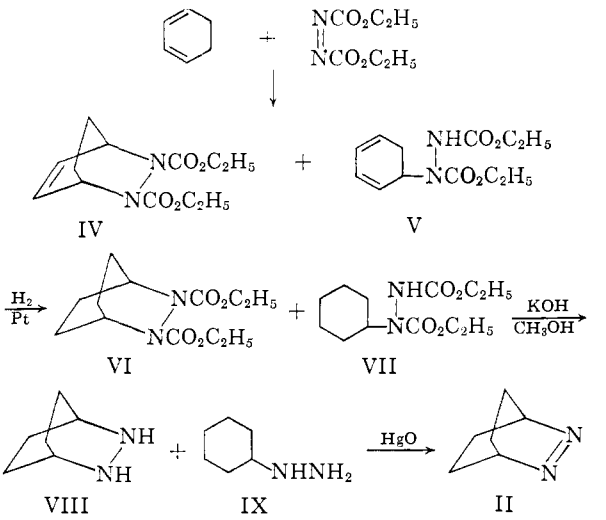
II

pounds. A study of 2,3-diazabicyclo[2,2,1]-2-heptene was recently described,[2] and we now report on the preparation and decomposition of a less strained homolog 2,3-diazabicyclo[2,2,2]-2-octene (II). Work on the preparation of the cyclic analog of II, 3,6-dimethyl-Δ^1-tetrahydropyridazine (III), will also be described.

Compound II.—Compound II was prepared by the sequence of reactions described in the literature,[3] analogous to those used[2,4] in the preparation of compound I: addition of diethyl azodicarboxylate to 1,3-cyclohexadiene, followed by hydrogenation of the adduct, saponification of the carbethoxy groups, decarboxylation, and oxidation of the hydrazo compound with mercuric oxide (Chart I).

The initial addition reaction was complex, leading to some diethyl hydrazodicarboxylate, and to a mixture of the desired 1,4-adduct IV and the product of allylic addition of cyclohexadiene to the azo-ester V. Allylic addition had not been reported in this reaction[3] but it has been described in the addition of many other olefins to the azo-ester.[5-10] This mixture was used as such in the next step. Treatment of the mixture with bromine led, surprisingly, to a high yield (57%) of diethyl hydrazodicarboxylate. Catalytic hydrogenation of the mixture of IV and V led to absorption of about 1.5 moles of hydrogen and to formation of diethyl

CHART I



hydrazodicarboxylate, and a mixture of compounds VI and VII. The sample of the hydrogenated product which was purified for elementary analysis proved not to be the bicyclic compound VI, but identical with an authentic sample of VII, which was subsequently prepared *via* radical-initiated allylic addition of cyclohexene to diethyl azodicarboxylate,[7] followed by catalytic hydrogenation. Saponification of the mixture of VI and VII led to a mixture of the bicyclic hydrazo compound VIII and cyclohexylhydrazine IX. The latter crystallized out slowly and was characterized as its hydrochloride and its phenylthiocarbamate, which was identical with that prepared from the authentic sample of VII. The mixture of hydrazines VIII and IX was satisfactory for oxidation to the bicyclic azo compound II, since the cyclohexylhydrazine appeared to be destroyed by oxidation, and the desired compound II was readily isolated and purified, m.p. 146–147°.

The ultraviolet absorption spectrum of compound II in isoöctane showed peaks at 378 mμ, ϵ 187; 365 mμ, ϵ 92; and at 342 mμ, ϵ 20. The spectrum in ethanol showed lower intensity and less detail, as we observed[2] for compound I. The absorption peak at 378 mμ was used to follow the kinetics of decomposition. The position of this maximum is displaced slightly from that of a six-membered cyclic *cis-azo* compound,[11] 387 mμ, while that of the

(1) We are pleased to acknowledge generous support of this work by the National Science Foundation, Grants G 4744 and G 14049.

(2) S. G. Cohen, R. Zand and C. Steel, *J. Am. Chem. Soc.*, **83**, 2895 (1961).

(3) J. Pirsch and J. Jorgel, *Ber.*, **68B**, 1324 (1935).

(4) O. Diels, J. H. Blom and W. Knoll, *Ann.*, **443**, 242 (1925).

(5) K. Alder, E. Pascher and E. Schmitz, *Ber.*, **76B**, 27 (1943).

(6) E. Muller and S. Peterson, *Angew. Chem.*, **63**, 18 (1951).

(7) R. Huisgen and F. Jakob, *Ann.*, **590**, 37 (1954).

(8) K. Alder, H. Niklas, R. Aumuller and B. Olsen, *ibid.*, **585**, 81 (1954).

(9) R. Huisgen and H. Pohl, *Ber.*, **93**, 527 (1960).

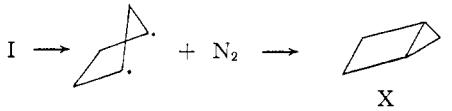
(10) R. Y. Levina, Y. S. Shabarov and M. G. Kuzmin, *Doklady Akad. Nauk. U.S.S.R.*, **131**, 1050 (1960).

more strained compound I, 341 mμ, is similar to that of acyclic *trans*-azo compounds.

The infrared spectra of compounds I and II and of their cuprous chloride complexes were of interest since assignment of an infrared frequency to the azo linkage has been difficult, and is reported in the 6.15–6.35 μ region.[12] The rigid bicyclic structure appears to lead to a distinct azo band. Compound I has a band at 6.65 μ, and II has bands at 6.55 and 6.63 μ (in KBr) which it may be reasonable to assign to the —N=N—stretching vibration. That these are at somewhat higher wave lengths than those suggested earlier for acyclic nonstrained systems is consistent with the observations that the —C=C—absorptions in norbornene and bicyclo-(2,2,2)-octene at 6.38 and 6.20 μ, respectively, are displaced to higher wave lengths as compared with the usual—C=C—absorption.[13] In the cuprous chloride complex of I the azo band seems to be displaced to 6.15 μ, while interpretation of the spectrum of the cuprous chloride complex of II is less clear.

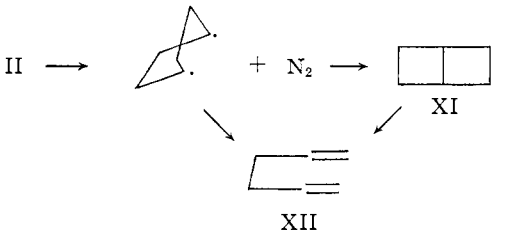
Proton magnetic resonance spectra of dilute solutions of I and II in carbon tetrachloride were obtained at 60 megacycles with a Varian model V-4300 C spectrometer. Resonance peak positions, determined by the side-band modulation technique, are reported in parts per million displacement to lower field from internal tetramethylsilane. The lowest field peaks in the spectra of I (5.07 p.p.m.) and of II (4.95 p.p.m.) are assigned to the bridgehead protons. The deshielding reflected in these values is due in part to the azo linkage and in part to the bicyclic structure. Full n.m.r. spectra of these and other azo compounds will be reported later.

The products of decomposition are of intrinsic interest and pertinent to discussion of the kinetic data. Symmetrical acyclic azo compounds R—N=N—R appear to decompose to three fragments, two R· radicals and nitrogen, by simultaneous rupture of both C–N bands.[14] Cyclic azo compounds may decompose similarly, with formation of two fragments, nitrogen and a biradical; when the latter is a 1,4-biradical it may apparently form a cyclobutane[15a,b] or decompose further to two molecules of olefin, as in the formation of styrene in the decomposition of 3,6-diphenyl-Δ^1-tetrahydropyridazine.[11] The bicyclic azo compound I forms nitrogen and a biradical which leads to bicyclo(2,1,0)-pentane[15c] in high yield.



X

Analogous products from II may be bicyclo(2,2,0)-hexane (XI) or 1,5-hexadiene (XII). Dilute solutions of II in isoöctane and in toluene were heated, as in the kinetic runs, at 240° for one hour, and four hours (approximately one and four half-lives), and were analyzed by vapor phase chromatography. The product was identified as 1,5-hexadiene (XII). In isoöctane, it appeared as a shoulder on the solvent peak, the resolution being improved when authentic 1,5-hexadiene was added. In toluene, resolution was excellent, the product appearing in a sharp band, distinct from that of the solvent and with retention time identical to that of 1,5-hexadiene in toluene in a blank run. When 1,5-hexadiene was added to the toluene solution of decomposed II, a single peak for this material was obtained. The alternative product, bicyclo(2,2,0)-hexane (XI), has been reported[16] in low yield from photolysis of bicyclo(3,2,0)-heptanone-3, as a compound which is rapidly converted to 1,5-hexadiene (XII) at 230°. Thus, isolation of XII from the decomposition of II does not of itself preclude the formation of XI as the initial product. V.P.C. analyses also showed that propene, cyclohexene, cyclohexane, benzene and 1,3-cyclohexadiene were not formed. The characteristic odor of biallyl was readily detected.



XII

The kinetics of decomposition of II were studied in the vapor phase at 199.5°, 216.0°, 240.0° and 259.0°. At each temperature 0.10-ml. samples of 0.19 mole/l. of II in isoöctane (*ca.* 2% solutions) were heated in 13–26 ml. evacuated ampoules, the total internal pressure being approximately 1–2 atmospheres. At 240° several variations were examined: one run was carried out at one-tenth the concentration of II; a second was run in toluene (0.13 mole/1.) instead of isoöctane to examine the effect of a possible chain inhibitor; in a third, the ampoules were packed with four feet of 3 mm. Pyrex tubing; in a fourth, the volume of isoöctane solution was reduced to 0.05 ml. and 0.01 ml. to examine the effect of reduced pressure. At each temperature in the standard runs 6 to 8 points were taken; the reactions were followed to 89% completion at 199.5°, and to 95–98% of reaction at the higher temperatures. At the lower concentration of II in isoöctane 3 points were taken to 91% reaction; two points were taken in each of the packing and pressure variations. Rate constants were calculated for each point and there were no discernible effects due to variations in concentration, solvent, pressure or surface area. The decompositions showed excellent first-order kinetics; plots of ln $(O.D._0/O.D._x)$ *vs.* time were linear, and from their slopes rate constants were calculated. Half-lives were 38.2 hr. at 199.5°, 7.8 hr. at 216.0°, 54.2 min. at 240.0°, and 11.4 min. at 259.0°. The data at 240° are summarized in Fig.

(11) S. G. Cohen, S. Hsiao, E. Saklad and C. H. Wang, *J. Am. Chem. Soc.*, **79**, 4400 (1957).

(12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1958, p. 272.

(13) R. C. Lord and R. W. Walker, *J. Am. Chem. Soc.*, **76**, 2523 (1954).

(14) S. G. Cohen and C. H. Wang, *ibid.*, **77**, 3628 (1955).

(15) (a) M. G. Kuzmin, Abstract, Ph.D. Thesis, State University of Moscow U.S.S.R., 1959; (b) C. G. Overberger, N. R. Byrd and R. B. Mesrobian, *J. Am. Chem. Soc.*, **78**, 1961 (1956); (c) R. Criegee and A. Rimmelen, *Ber.*, **90**, 414 (1957).

(16) S. Cremer and R. Srinivasan, *Tetrahedron Letters*, **No. 21**, 24 (1960).

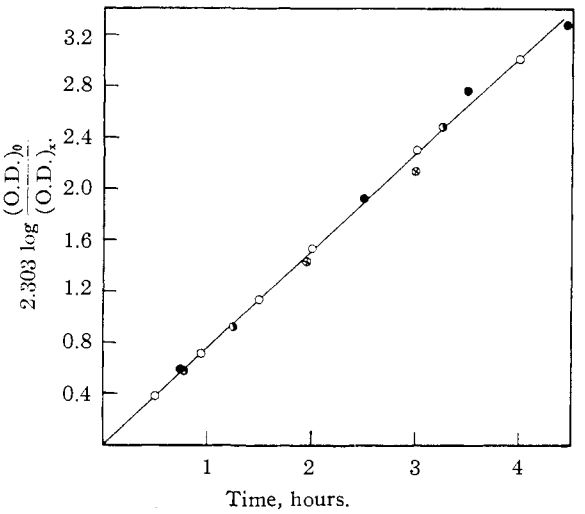


Fig. 1.—Decomposition of 2,3-diazabicyclo[2,2,2]-2-octene (II) at 240°, vapor phase: ○, initial concentration, 0.19 mole/l. in isoöctane; ◑, initial concentration, 0.019 mole/l. in isoöctane; ●, in the presence of toluene; ⊗, ampoules packed with Pyrex tubing to increase surface area.

1. A plot of log k *vs.* $1/T$ was linear (Fig. 2), and from it was calculated the activation energy; the entropy of activation and the pre-exponential factor A were calculated in the usual way. The kinetic data are summarized in Table I.

TABLE I

DECOMPOSITION OF 2,3-DIAZABICYCLO(2,2,2)-2-OCTENE(II)

T, °C.	199.5	216.0	240.0	259.0
$10^5 k$, sec.$^{-1}$	0.504[a] ± 0.008	2.48[a] ± 0.04	21.2[a] ± 0.2 21.2[b] ± .3	101[a] ± 1
E_A, kcal. mole^{-1}			44.6 ± .2	
$\Delta S^{\ddagger}$, cal. mole^{-1} deg.$^{-1}$			+10.5 ± .3	
log A			15.3 ± .1	

[a] Isoöctane. [b] Toluene.

The kinetic data for the bicyclic cis-azo compound are compared in Table II with those for the more highly strained bicyclic compound I and for some open chain aliphatic *trans*-azo compounds.

TABLE II

VAPOR PHASE DECOMPOSITION OF ALIPHATIC AZO COMPOUNDS

Compound	log A, sec.$^{-1}$	$\Delta S^{\ddagger}$, cal. mole^{-1} deg.$^{-1}$	E_A, kcal. mole^{-1}	k 250° sec.$^{-1}$
II	15.3	10.5	44.6	4.9×10^{-4}
I	14.9	8.7	37.3	1.9×10^{-1}
Azomethane[17]	15.7	12.2	51.2	2.2×10^{-6}
Azoethane[18]	15.8	12.2	48.5	2.9×10^{-5}
Azoisopropane[19a]	13.7	3.1	40.9	4.6×10^{-4}
2,2-Azoisobutane[19b]	15.3	15.2	42.8	2.8×10^{-2}

Compound II is much more stable than I, decomposing at about the same rate as I at 70° higher temperatures in the ranges studied; at 250°, I decomposes about 400 times faster than II. The difference in reactivity is due to the more favorable activation energy in the decomposition of I, 37.3 kcal. compared with 44.6 kcal. for II. This presumably arises from the more highly strained structure of I, and more than compensates for the slightly more favorable pre-exponential factor and entropy of activation in the decomposition of II. The higher entropy of activation in the decomposition of II gives support to the formation of 1,5-hexadiene (XII) as the initial product of decomposition, but the difference is small and the formation of the more restricted compound XI cannot be excluded. The entropies of activation of both I and II are high enough to indicate that two bonds are breaking simultaneously in the transition state.

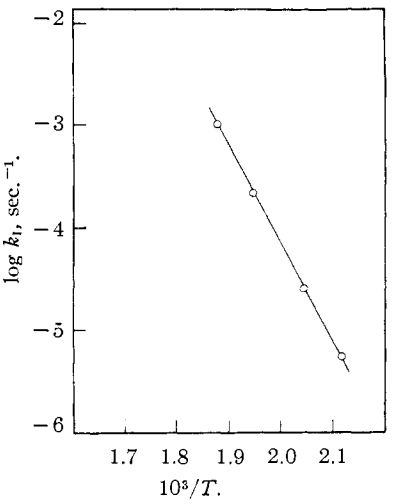


Fig. 2.—Thermal decomposition of 2,3-diazabicyclo[2,2,2]-2-octene (II).

The more favorable entropies of activation in the decomposition of open-chain aliphatic azo compounds (excepting azoisopropane) seem to reflect their decomposing directly into three fragments,[2,20] as compared with I and II which decompose into two. Compound II appears to decompose at about the same rate at 250° as its acyclic analog, azoisopropane, although one might expect the cyclic *cis*-azo compound to decompose more rapidly.[11] However, since the entropies and energies of activation differ for the two compounds, the coincidence of the rates is accidental. In addition it has been noted[2] that the entropy and energy of activation for the decomposition of azoisopropane seem exceptional.

A sample of azoisopropane was prepared and its decomposition was studied briefly at 276° in the vapor phase in the presence of isoöctane, as described above for the decomposition of II. Azoisopropane has a symmetrical absorption band, λ_{max} 358 mμ, ϵ 19, falling to zero at 295 mμ, and at 485 mμ. This absorption fell as the compound decomposed, but new more intense absorption appeared at about 260 mμ and at about 230 mμ.[21] Thus the decomposition appears to be accompanied by rearrangement to the isomeric hydrazone, which

(17) C. Steel and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 975 (1959).

(18) W. D. Clark, Ph.D. Dissertation, University of Oregon, Eugene, Ore., 1959, discussed in C. Steel and K. J. Laidler, *J. Chem. Phys.*, **34**, 1827 (1961).

(19) (a) H. C. Ramsperger, *J. Am. Chem. Soc.*, **50**, 714 (1928); (b) J. B. Levy and B. K. W. Copeland, *ibid.*, **82**, 5314 (1960).

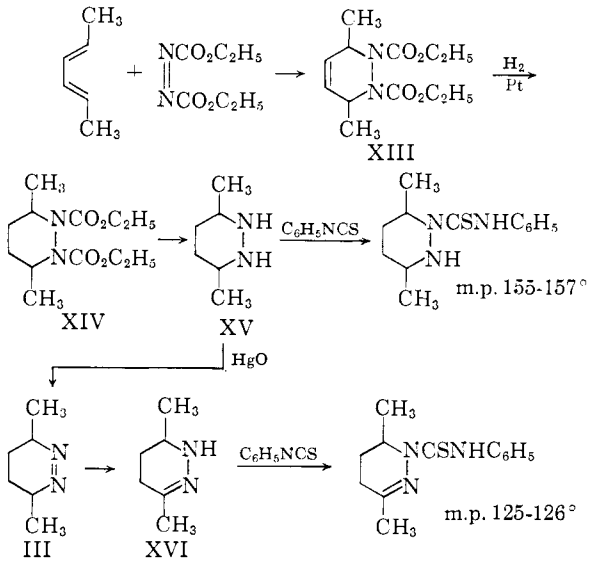
(20) C. Steel, *J. Chem. Phys.*, **31**, 899 (1959).

(21) Absorption bands in the 234–269 mμ region are reported for methyl- and dimethylhydrazones of aliphatic ketones; R. H. Wiley and G. Irick, *J. Org. Chem.*, **24**, 1925 (1959).

may not be stable at this temperature. The decomposition of azoisopropane, which merits more detailed study, is a complex process, accounting for the exceptional entropy and energy of activation (Table II).

Compound III.—Compound III, 3,6-dimethyl-Δ^1-tetrahydropyridazine, was prepared by the sequence of reactions analogous to those used in the preparation of 3,6-diphenyl-Δ^1-tetrahydropyridazine:[11] addition of diethyl azodicarboxylate to 2,4-hexadiene[22]; hydrogenation of the adduct; saponification of the carbethoxy groups and decarboxylation to the hexahydropyridazine, which was characterized as its phenyl thiocarbamate; and oxidation to III (Chart II).

CHART II



Oxidation of the hydrazo compound with mercuric oxide in petroleum ether proceeded readily leading to a solution which showed a characteristic azo absorption band at 382 mμ. However, when the solution was allowed to stand for several days and was then distilled, compound XVI was obtained with ultraviolet absorption similar to that of a hydrazone,[11] with peaks at 318 and 248 mμ in methanol. This compound was characterized as the phenyl thiocarbamate. The azo compound III was obtained when the product of oxidation of XV was distilled immediately at 0.25 mm., λ_{max} 382.5 mμ, ϵ 112. This slowly isomerized to XVI when stored at $-20°$. Isomerization is troublesome in study of aliphatic azo compounds containing the >CH—N=NC— grouping since the hydrazone is the more stable tautomer. Non-cyclic *trans*-azo compounds isomerize slowly enough so that their kinetics of decomposition may usually be studied. The analog of III, 3,6-diphenyl-Δ^1-tetrahydropyridazine, tautomerized extremely rapidly,[11] conjugation with the phenyl group apparently further stabilizing the hydrazone. The six-membered ring and *cis*-azo configuration in III also appears to facilitate the isomerization.

(22) P. Baranger, S. Levesalles and M. Vuidart, *Compt. rend.*, **236**, 1365 (1953).

Experimental[23]

1,3-Cyclohexadiene (Columbia Organic Chemicals Co. Inc.) was distilled immediately before use, b.p. 79–80°.

Diethyl hydrazodicarboxylate was prepared in 82% yield according to the published procedure,[24] m.p. 133–135°, reported m.p. 134–135°. Diethyl azodicarboxylate was prepared as described previously,[2] essentially according to the published procedure,[25] 89% yield, b.p. 90–95° (5 mm.).

2,3-Dicarbethoxy-2,3-diazabicyclo(2,2,2)-5-octene(IV) and 5 - (N,N' - Dicarbethoxyhydrazino) - 1,3 - cyclohexadiene (V).—1,3-Cyclohexadiene (56 g., 0.7 mole) was added in two portions to a solution of 112 g. (0.65 mole) of diethyl azodicarboxylate in 50 ml. of cyclohexane. There was a brief induction period followed by a strongly exothermic reaction which was moderated by cooling in ice. The mixture was allowed to stand at room temperature for 48 hr. A solid was collected: diethyl hydrazodicarboxylate 3.8 g. 3.4% yield, m.p. 131–134° mixed m.p. 132–134°. The solution was distilled, leading to the product mixture, IV and V, b.p. 135–140° (0.3–0.5 mm.), reported[3] 155° (1.5 mm.), 146 g. (0.58 mole), 89% yield. This crystallized on standing, m.p. 53.5–55.5°.

Anal. Calcd. for $C_{12}H_{18}O_4N_2$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.24; H, 7.17; N, 11.09.

A portion of this 2.6 g. (0.010 mole) was treated with a solution of bromine in carbon tetrachloride at 10°, forming diethyl hydrazodicarboxylate, 1.1 g. (0.0057 mole), 57% yield.

2,3-Dicarbethoxy-2,3-diazabicyclo(2,2,2)-octane (VI) and N,N'-Dicarbethoxyhydrazinocyclohexane (VII).—A solution of 51 g. (0.20 mole) of the adducts, above, in 100 ml. of ethanol was hydrogenated over 0.3 g. of platinum oxide, 0.3 mole of hydrogen being absorbed in 2 hours. The solution was filtered and concentrated, and the residue was crystallized from methanol, leading to diethyl hydrazodicarboxylate, 9.0 g. (0.051 mole), 25% yield. The residue was chromatographed on alumina containing 2% water, eluted with chloroform and concentrated, leading to the hydrogenated products, 39 g. (0.15 mole), 75% yield, an oil, which slowly crystallized, m.p. 61–63°. A sample was crystallized from and washed with cyclohexane, **N,N'-dicarbethoxyhydrazinocyclohexane.**

Anal. Calcd. for $C_{12}H_{22}O_4N_2$: C, 55.79; H, 8.58; N, 10.85. Found: C, 55.82; H, 8.46; N, 11.09.

2,3-Diazabicyclo(2,2,2)-octane (VIII) and Cyclohexylhydrazine (IX).—A solution of 36 g. (0.62 mole) of the mixed hydrogenated products, above, in 50 ml. of methanol was treated with a solution of 36 g. (0.62 mole) of potassium hydroxide in 150 ml. of methanol under reflux, in a nitrogen atmosphere, for 5 hours. The mixture was filtered, the filtrate was concentrated and the residue was extracted with ether. The extract was dried and concentrated leading to a yellow residue, 9.6 g. (0.084 mole), 55% yield. This was refrigerated leading slowly to a yellow oil and to crystals IX, 2.7 g., m.p. 43–50° dec.; reported[26] for cyclohexylhydrazine, m.p. 46–50°.

A solution of 0.3 g. of the solid IX in 10 ml. of ethanol was saturated with dry hydrogen chloride and diluted with ether, leading slowly to a small quantity of white crystals, m.p. 109–110°, from ethanol–ether; reported[25] for cyclohexylhydrazine hydrochloride, m.p. 107–110°.

A solution of 0.30 g. (0.0026 mole) of the solid in 3 ml. of ether was treated with 1.0 g. (0.0070 mole) of phenyl isothiocyanate, leading to the phenyl thiocarbamate of cyclohexylhydrazine, m.p. 146–147° from alcohol, reported[26] m.p. 147–148°, mixed m.p. with an authentic sample subsequently prepared, 146–147°.

Anal. Calcd. for $C_{13}H_{19}N_3S$: C, 62.61; H, 7.68; N, 16.85. Found: C, 62.34; H, 7.72; N, 17.02.

2,3-Diazabicyclo(2,2,2)-2-octene (II).—A solution of 2.0 g. (0.018 mole) of the yellow oil, above, in 20 ml. of *n*-hexane was treated in portions with a small excess of mercuric oxide. The oxidation was exothermic, and gas was evolved. The

(23) Melting points are uncorrected. Elementary analyses are by Dr. S. M. Nagy, Massachusetts Institute of Technology.

(24) N. Rabjohn, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 375.

(25) A. Rodgman and G. F. Wright, *J. Org. Chem.*, **18**, 468 (1953).

(26) H. H. Hawkins and H. L. Lochte, *J. Am. Chem. Soc.*, **46**, 450 (1929).

solution was filtered and concentrated and the residue was cooled, leading to the azo compound, 0.45 g. (0.0041 mole), 23% yield, m.p. 146–147° from *n*-hexane, reported[3] m.p. 141.4°.

Anal. Calcd. for $C_6H_{10}N_2$: C, 65.42; H, 9.15; N, 25.43. Found: C, 65.32; H, 9.46; N, 25.15.

Infrared spectra of compounds I and II and their cuprous chloride complexes were obtained in KBr pellets in a Perkin–Elmer model 21 spectrophotometer.

I: 3.33(m), 3.45(w), 6.66(m), 6.90(m), 7.65(w), 7.80(m), 7.95(m), 8.35(m), 8.53(w), 8.93(m), 9.65(w), 9.87(w), 10.23(w), 10.53(w), 11.30(m), 11.92(m), 12.18(m), 14.63(w), 14.97(w) μ.

II: 3.38(s), 3.45(m), 6.55(s), 6.63(m), 6.88(s), 7.22(w), 7.45(m), 7.56(s), 7.92(w), 8.08(m), 8.53(m), 8.80(w), 8.95(w), 9.05(m), 9.68(m), 9.75(m), 10.20(w), 11.10(m), 11.25(m), 12.15(w), 12.48(m), 15.18(w) μ.

I: Cu_2Cl_2:H_2O: 2.90(m), 3.40(m), 6.16(m), 6.92(s), 7.68 (w), 7.86(s), 8.00 (m), 8.28(w), 8.37(w), 8.58(w), 8.92(s), 9.68(w), 9.98(m), 10.16(w), 10.53(m), 10.63(m), 11.34(w), 11.58(w), 12.18(w), 12.75(w), 14.30(m) μ.

II: Cu_2Cl_2:H_2O: 2.90(m), 3.42(m), 6.13(w), 6.70(m), 6.82(m), 6.89(m), 7.41(w), 7.47(w), 7.56(m), 7.83(w), 7.98(m), 8.05(m), 8.55(w), 8.76(w), 9.05(m), 9.50(w), 9.78(w), 10.07(m), 11.28(w), 11.98(w), 12.10(w), 12.48(m) μ.

II: Cu_2Cl_2:H_2O.—Cuprous chloride was added to a stirred solution of II in water until formation of the red complex was completed. Stirring was continued for 0.5 hr., the complex was collected, washed with water, crystallized from aqueous ammonium chloride, washed with water and dried over P_2O_5; m.p. 238–243° dec.

Kinetics of decomposition of **II** were carried out as described previously[2] for I.

Analysis of Product.—Vapor phase chromatographic analysis was carried out on a Research Specialties Co. model 604 gas chromatograph, katharometer detector, Brown recorder. The solutions of II in isoöctane and toluene were identical with those in the kinetic runs and they were evacuated, sealed and heated in the same way. A 6-foot stainless steel column packed with 20% adipate resin (RC Polymeric BGA, Rubber Corp. of America) on Chromsorb W, (Johns–Manville), and helium carrier were used. Column temperatures were 65° (isoöctane) and 110° (toluene), detector 95°, vaporizer 230°. 1,5-Hexadiene for comparison was obtained from Matheson, Coleman and Bell.

Cyclohexylhydrazine (IX).—A solution of 0.2 g. of azo-bis-isobutyronitrile and 20 g. (0.115 mole) of diethyl azodicarboxylate in 40 g. (0.49 mole) of cyclohexene was boiled under reflux for 7 hours, concentrated and distilled in vacuum, leading to **3-(N,N'-dicarbethoxyhydrazino)-cyclohexene**, 22 g. (0.086 mole) 75% yield, b.p. 135–145° (0.1 mm.), m.p. 54–56°; reported[7] b.p. 130–145° (0.1 mm.), m.p. 55–56°. A solution of 20 g. (0.080 mole) of this in 100 ml. of ethanol was hydrogenated over 0.5 g. of platinum oxide. The solution was concentrated and distilled, leading to **N,N'-dicarbethoxyhydrazinocyclohexane**, 15 g. (0.058 mole), 72% yield, b.p. 145–155° (0.1 mm.), m.p. 61–64°, mixed m.p. with the analytical sample of the material isolated from hydrogenation of the adduct to cyclohexadiene, 61–64°; the infrared spectra of the two samples were identical. A solution of 10 g. (0.040 mole) of this product and 14.5 g. (0.26 mole) of potassium hydroxide in 100 ml. of methanol was boiled under reflux, under nitrogen, for 3.5 hr. Precipitated potassium carbonate was filtered and washed with methanol. The filtrate was concentrated and the residue was extracted with ether. The extract was dried and concentrated, leading to **cyclohexylhydrazine (IX)**, 3.5 g. (0.031 mole), 77% yield. A portion (1.14 g., 0.010 mole) was treated, in 10 ml. of ether, with 1.40 g. (0.010 mole) of phenyl isothiocyanate, leading to **cyclohexylhydrazine phenylthiocarbamate**, 1.2 g. (0.005 mole), 50% yield, m.p. 145–146°, reported[26] m.p. 147–148°.

1,2-Dicarbethoxy-3,6-dimethyl-Δ^4-tetrahydropyridazine (XIII).—Grignard reagent was prepared by addition of a solution of 305 g. (2.77 moles) of ethyl bromide in 100 ml. of ether to 64 g. (2.60 moles) of magnesium in 1200 ml. of ether. This was treated with a solution of 160 g. (2.82 moles) of crotonaldehyde in 150 ml. of ether, leading to 2-hexene-4-ol, 159 g. (1.59 moles), 70% yield, b.p. 57–58° (16 mm.), reported[27] b.p. 55° (15 mm.). 2-Hexene-4-ol, 76.5 g. (0.77 mole), was warmed with 5 ml. of 48% hydrogen bromide, distillate being collected at 85–95°. The organic phase of the distillate was separated and dried over sodium sulfate, **2,4-hexadiene**,[27] 34 g. (0.41 mole), 56% yield.

Diethyl azodicarboxylate, 47 g. (0.27 mole), was added slowly to a solution of 25 g. (0.30 mole) of 2,4-hexadiene in 25 ml. of benzene, a strongly exothermic reaction ensuing. The solution was allowed to stand for 36 hours, washed with sodium bisulfite and distilled, leading to XIII, 30 g. (0.12 mole), 43% yield, b.p. 85° (0.15 mm.), reported[22] b.p. 122° (0.4 mm.).

Anal. Calcd. for $C_{12}H_{20}O_4N_2$: N, 10.93. Found: N, 10.97.

1,2-Dicarbethoxy-3,6-dimethylhexahydropyridazine (XIV).—A solution of 27.3 g. (0.11 mole) of the adduct XIII in 75 ml. of 95% ethanol was hydrogenated over 0.3 g. of platinum oxide. The solution was filtered and distilled, leading to the saturated compound XIV, 19.0 g. (0.073 mole), 67% yield, b.p. 83–85° (0.05 mm.).

Anal. Calcd. for $C_{12}H_{22}O_4N_2$: C, 55.79; H, 8.58; N, 10.85. Found: C, 55.98; H, 8.54; N, 11.20.

3,6-Dimethylhexahydropyridazine (XV).—The hydrogenated product XIV, 15 g. (0.058 mole), was boiled under nitrogen for 2 hours in a solution of 13 g. (0.23 mole) of potassium hydroxide in 25 ml. of methanol. The mixture was concentrated, the residue was extracted with ether, and the extract was dried and distilled, leading to XV, 2.8 g. (0.024 mole), 41% yield, b.p. 65° (7 mm.). A portion, 1.1 g. (0.010 mole), was treated with 2.7 g. (0.020 mole) of phenyl isothiocyanate, leading to the monophenyl thiocarbamate, 2.1 g. (0.0084 mole), 84% yield, m.p. 155–157° from 95% ethanol.

Anal. Calcd. for $C_{13}H_{19}N_3S$: C, 62.61; H, 7.68; N, 16.85; S, 12.86. Found: C, 62.49; H, 7.74; N, 17.14; S, 12.86.

3,6-Dimethyl-Δ^2-tetrahydropyrdazine (XVI).—The hexahydropyridazine XV, 1.7 g. (0.015 mole), was dissolved in in 10 ml. of petroleum ether, b.p. 35°, and oxidized with 4.0 g. (0.018 mole) of mercuric oxide, leading to a solution showing a sharp band at 382.5 mμ. After standing for several days, the solution was distilled, leading to the hydrazone XVI, b.p. 65–67° (7 mm.), 0.62 g., 36% yield. This showed a shoulder at 385 mμ, a peak at 318 mμ, ϵ 254, and strong absorption at 248 mμ, ϵ 1302 (methanol).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 64.24; H, 10.78. Found: C, 64.12; H, 10.96.

A portion of this, 0.163 g. (1.45 mmole), was treated with 1 ml. of phenyl isothiocyanate and diluted with *n*-hexane, leading to the monophenyl thiocarbamate, 0.30 g. (1.21 mmole), 83% yield, m.p. 125–126°, from benzene–ether.

Anal. Calcd. for $C_{13}H_{17}N_3S$: C, 63.12; H, 6.93; N, 16.99; S, 12.96. Found: C, 62.99; H, 6.89; N, 17.10; S, 12.97.

The infrared spectrum of XVI was obtained in KBr: 2.78(w), 3.02(w), 3.45(s), 3.85(w), 4.10(w), 5.85(w), 6.08(w), 6.90(s), 7.04(m), 7.25(s), 7.45(m), 7.53(m), 810–8.35(m), 8.60(w), 8.86(m), 9.07(w), 9.55(m), 9.92(w), 10.15(m), 10.54(w), 10.90(w) μ.

3,6-Dimethyl-Δ^1-tetrahydropyridazine (III).—The hydrogenated adduct XIV, 40 g. (0.155 mole), in 50 ml. of methanol, was boiled under nitrogen for 1.25 hr. in a solution of 35 g. (0.62 mole) of potassium hydroxide in 100 ml. of methanol. The mixture was filtered, washed with 100 ml. of methanol and concentrated under nitrogen. The residue was extracted with ether, the extract was dried and concentrated, leading to slightly colored oil, 23 g. A 10-g. portion of this was extracted with 300 ml. of pentane; the pentane solution was treated with a mixture of 25 g. (0.11 mole) of mercuric oxide and 25 g. of sodium sulfate for 1 hour. The mixture was filtered and washed with pentane, the filtrate was distilled immediately under nitrogen, leading to the azo compound III, 5.21 g. (0.046 mole), 70% yield, b.p. 27° (0.25 mm.), λ_{max} 382.5 mμ, ϵ 112 (isoöctane), falling to zero at 310 and at 430 mμ. On standing at −20° for 52 days, the absorption at 382 decreased, ϵ 20; this fell to a shallow minimum at 357 mμ, ϵ 16, and rose to a strong maximum at 235 mμ, ϵ 2530 (isoöctane).

(27) R. Adams and T. A. Geissman, *J. Am. Chem. Soc.*, **61**, 2083 (1939).

The infrared spectrum of III was taken in chloroform: 2.96(w), 3.37(s), 4.05(w), 5.80(w), 6.05(w), 6.22(w), 6.86 (m), 7.00(w), 7.22(m), 7.42(w), 7.48(w), 8.05–8.30(w), 8.83(w), 9.18(w), 9.53(w), 9.90(w), 10.14(w), 10.50(w), 10.75–10.90(w) μ.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE RICE UNIVERSITY, HOUSTON, TEX.]

On the Solvent Dependence of Substituent Effects on Reactivities

BY C. D. RITCHIE AND E. S. LEWIS

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A solvent dependence of substituent effects on chemical reactivities has been noted in several recent studies. In the cases studied to date, the solvent dependence may be rationalized by assuming that solvents exert a differentiating effect on the direct interactions of substituents and reaction sites. The present study was undertaken to determine if solvent dependences exist in a case where direct interactions of the above type are not possible. For this purpose, we have measured the relative acidities of a series of 4-substituted bicyclo[2,2,2]octane-1-carboxylic acids in a variety of solvents. The linear free energy equations fail to correlate the data in dimethyl sulfoxide and 90% dimethyl sulfoxide. Although electrostatic models also fail to correlate all of the data, we find that Westheimer and Kirkwood's ellipsoidal cavity model does give fair agreement with experiment for the trimethylammonio substituted acid. It does not appear possible at the present time to attribute the solvent dependence of substituent effects to any detailed mechanism. The present results do clearly show, however, that factors other than direct interaction of substituent and reaction site are of importance.

Introduction

Over the past few years, evidence has accumulated which indicates that substituent effects are not generally independent of solvent. Jaffé[1] noted that the Hammett substituent constant for the hydroxyl group appears to be strongly solvent dependent, and attributed this to hydrogen bonding effects. Several workers have noted that the relative effects of alkyl groups on aromatic reactivities are solvent dependent, and have offered a variety of rationalizations for the phenomena.[2]

In attempting to separate polar from resonance effects in aromatic reactivities, Taft[3] found that the contribution of the resonance effects of substituents appears to depend on the solvent.

On other bases, Gutbezahl and Grunwald[4] postulated a solvent dependence for the substituent effect of the nitro group.

For aliphatic reactivities, Romberg and Cruse[5] have reported that trichloroacetic acid is a weaker acid than chloroacetic acid in acetonitrile. Grunwald's[6] n-value tabulation also reveals that the relative acidities of aliphatic acids in various ethanol–water mixtures cannot satisfy linear equations. A possible explanation of these solvent dependences may be based on solvent effects on conformations of the acids.[6]

Although other effects have been postulated in rationalizing the above phenomena, clear evidence that solvent dependences exist in the absence of direct interaction of substituent and reaction site has not been offered. In order to provide this evidence, we have measured the relative acidities of a series of 4-substituted bicyclo[2,2,2]octane-1-carboxylic acids in methanol, ethanol, acetone, dimethyl sulfoxide and mixtures of these with water. This series resembles aromatic systems in avoiding conformational problems and the aliphatic systems in avoiding resonance effects.

Methods and Results

The series of acids was prepared following the procedures of Roberts and Moreland.[7] In addition to the acids studied by these authors, we have measured the relative acidities of the carboxyl, carboxylate and trimethylammonio substituted acids. The solvents used were methanol, ethanol, acetone, dimethyl sulfoxide and mixtures of these with water.

An indicator method, using either p-nitrophenol or 5-nitrosalicylaldehyde, was employed for all measurements except those in 100% dimethyl sulfoxide. In this solvent, it was necessary to use a potentiometric method, described in detail in the Experimental section. All results are shown in Table I as the equilibrium constant for reaction A.

$$X\text{-}C_8H_{12}COOH + p\text{-}O_2NC_6H_4O^- = X\text{-}C_8H_{12}COO^- + p\text{-}O_2NC_6H_4OH \quad (A)$$

In those cases where log K is reported as greater than one, 5-nitrosalicylaldehyde was actually used as the indicator. Since there was substantial overlap in the two indicators, it was possible to calculate the constants for reaction A, and these values are reported in the table. Similarly, the overlap between the indicator and potentiometric method with the bromo-, cyano- and carboxy-substituted acids allowed the calculation of the equilibrium constant for reaction A.

At least four measurements of each equilibrium constant were made, using different ratios of indicator salt to acid. These measurements generally gave agreement within 10% of the mean value. When the equilibrium constant was very different from unity, deviations as large as 20% were ob-

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