and 37:63 (δ_{NCH_2} 4.42 and 4.47 ppm) mixtures of diastereomeric salts obtained, respectively, from quaternizations of tropinone (**3a**) with benzyl brosylate and *N*-benzylnortropinone (**3c**)[17] with methyl brosylate gave the same 72:28 mixture, the predominant isomer being the major product of the benzylation. Essentially the same product ratio was obtained on addition of *N*-methylbenzylamine hydrochloride to 2,6-cycloheptadienone. If one allows that the *N*-benzyltropinonium salt with the benzyl group equatorial is the more stable, these results indicate that quaternizations of tropinone with benzyl brosylate and *N*-benzylnortropinone with methyl brosylate also occur predominantly by equatorial attack. As reactions of benzyl brosylate with tropine (**1a**), pseudotropine (**2a**), and tropane (**4a**) give product ratios (90:10) similar to that obtained with tropinone (**3a**), and, in view of the similar stereochemistry seen in alkoxycarbonylmethylations, deuteriomethylations, or ethylations of the four bases, it seems likely that the benzylations of **1a**, **2a**, and **4a** also occur mainly by equatorial attack.

Experimental Section[18]

Amines and quaternizing agents used were either obtained commercially or prepared following well-described procedures. Unless noted otherwise, quaternary salts were prepared at 30° from equimolar amounts of amine and quaternizing agent. Preparative runs were carried out in acetonitrile with initial concentrations of 0.2–0.5 *M*; for other runs, initial concentrations were 0.07–0.10 *M*.

Nmr spectra were determined with a Varian A-60A system of 10–20% solutions of the quaternary salts in deuterium oxide, dimethyl-d_6 sulfoxide, or equal volumes of these solvents containing 1% 3-trimethylsilyl-1-propanesulfonic acid sodium salt. Several reactions in acetonitrile containing 1% TMS were also followed directly by nmr. The ratio of the diastereomeric salts was taken as equal to the intensity ratio of the bands due to the *N*-methyl protons and, when possible, the *N*-benzyl protons. At least eight determinations of product compositions from reactions with high ($\gtrsim$7:1) and moderate ($\sim$3:1) degrees of stereoselectivity gave average deviations of 3 and 2%, respectively. Chemical shifts of the bands used for analysis were not changed significantly (±2 cps) when the anion was changed from bromide to chloride or iodide; change of anion from bromide to brosylate resulted in similar upfield shifts of these bands (*cf.* ref 10b and 10c). Assignment of bands in the nmr spectra of salts other than bromides was confirmed by examination of the spectra of mixtures of these salts and the corresponding bromides.

Ruthenium oxide solutions were prepared as described by House and Tefertiller,[14] and oxidations were carried out with approximately 200 mg of mixed quaternary salts. Yields of crude products, which were analyzed by nmr, ranged from 92–99%.

The *N*-benzyltropinonium brosylates and *N*-deuteriomethyl benzenesulfonates, as 0.3–0.5 *M* solutions, were equilibrated in 12–96 hr at 39° in 0.15 *M* solutions of pyridine in either acetonitrile-d_3 or deuterium oxide. Attempts to equilibrate the *N*-ethoxycarbonylmethyltropinonium bromides with pyridine in acetonitrile-d_3 were complicated by rapid saponification, as indicated by the appearance in the nmr spectrum of the upfield bands due to ethanol.

N-Benzyltropinonium chloride was prepared in 67% yield by allowing a mixture prepared from 206 mg (1.9 mmol) of 2,6-cycloheptadienone, 300 mg (1.9 mmol) of *N*-methylbenzylamine hydrochloride, 20 μl of *N*-methylbenzylamine, and 1 ml of methanol to stand at room temperature for 58 hr.

Registry No.—**1a**, 120-29-6; **2a**, 135-97-7; **3a**, 532-24-1; **2a** reaction product with ethyl bromide, 32515-65-7.

---

[18] For details of most of the work summarized here, see C. C. Thut, Ph.D. thesis, University of California, Davis, 1970.

A Nuclear Magnetic Resonance Study of 2,4-Dinitrohalobenzenes and 2,4-Dinitrohalonaphthalenes

JOHN D. REINHEIMER* AND A. H. KAPPELMAN[1]

Severance Chemical Laboratory, The College of Wooster, Wooster, Ohio 44691

Received July 6, 1971

The three spin system of trisubstituted benzenes has been extensively studied,[2] but little data on substituted naphthalenes have appeared. The spectra of 2,4-dinitrohalobenzenes are simple first-order spectra which may be compared to the classic data of the halobenzenes. We anticipated finding more complex ABCD spectra for the 2,4-dinitrohalonaphthalenes and looked for similar comparisons with the halobenzene spectra.

Experimental Section

The 2,4-dinitrohalobenzenes were samples prepared for previous work.[3] Similarly, the preparation and purification of the 2,4-dinitrohalonaphthalenes are described.[4] The nmr spectra of the 2,4-dinitrohalobenzene series were observed with a Varian T-60, in 10% solution (acetone solvent) with TMS as an internal standard. The T-60 was calibrated against the Jungnickel[5] standard solution. The naphthalene series spectra were observed on a Varian HA-100.[6] The naphthalene samples were run in degassed dioxane solution; the solutions were less than 10% by weight. The chemical shifts and coupling constants were calculated on a control Data Corp. computer, CDC-6400 with the LAOCN3 program, as modified by J. T. Gerig.[7]

Results and Discussion

The calculated chemical shifts and coupling constants are presented in Tables I, II, and III. Comparison of our data with that of Smith and Ihrig indicates that there is reasonable agreement (Table III). We believe that the maximum error in absolute chemical shift will be ±1 Hz. The benzene series gave first-order spectra, but the napthalene series gave complex spectra.

TABLE I

CHEMICAL SHIFTS FOR 1-X-2,4-DINITRONAPHTHALENES IN DIOXANE

Proton no.	Chemical shift from dioxane at 100 Mc, Hz		
	X = Cl	X = Br	X = I
3	512.60 ± 0.00	504.7 ± 0.00	493.3 ± 0.00
5	494.80 ± 0.02	419.35 ± 0.02	483.21 ± 0.02
6	436.23 ± 0.03	433.23 ± 0.02	428.77 ± 0.03
7	431.97 ± 0.03	429.98 ± 0.02	424.09 ± 0.03
8	506.67 ± 0.02	503.07 ± 0.02	496.10 ± 0.02

---

[1] Taken (in part) from the Senior Independent Study Thesis of A. H. Kappelman, The College of Wooster, 1970.

[2] L. M. Jackman and S. Sternhell, "Applications of NMR Spectroscopy to Organic Chemistry," Pergamon Press, Elmsford, N. Y., 1969, pp 94, 173, 205, 306.

[3] J. D. Reinheimer, R. C. Taylor, and P. E. Rohrbaugh, *J. Amer. Chem. Soc.*, **83**, 835 (1961).

[4] R. C. Krauss and J. D. Reinheimer, *Can. J. Chem.*, **45**, 77 (1967).

[5] J. L. Jungnickel, *Anal. Chem.*, **35**, 1985 (1963).

[6] We gratefully acknowledge the support of Dr. Brian Kieth and Dr. Henry Sable of Case Western Reserve for these spectra.

[7] LAOCN3, A. A. Bothner-By and S. M. Castellano, as modified by J. T. Gerig, personal communication.

TABLE II

COUPLING CONSTANTS FOR THE 1-X-2,4-DINITRONAPHTHALENES IN DIOXANE

J	X = Cl	X = Br	X = I
3,5	0	0	0
5,6	8.64 ± 0.04	8.49 ± 0.03	8.56 ± 0.04
5,7	1.17 ± 0.04	1.29 ± 0.03	1.05 ± 0.04
5,8	0.75 ± 0.03	0.57 ± 0.02	0.58 ± 0.03
6,7	7.16 ± 0.03	6.91 ± 0.02	6.93 ± 0.03
6,8	1.20 ± 0.04	1.12 ± 0.04	0.98 ± 0.04
7,8	8.59 ± 0.04	8.66 ± 0.04	8.56 ± 0.04

TABLE III

CHEMICAL SHIFTS AND COUPLING CONSTANTS FOR 1-X-2,4-DINITROBENZENES IN ACETONE

Substituent	Chemical shift			Coupling constant		
	ν_3	ν_5	ν_6	$J_{3,5}$	$J_{3,6}$	$J_{5,6}$
F[a]	530.2	515.7	466.1	3.0	0.2	9.3
Cl	530.8	512.6	483.4	2.49	0.10	8.85
Cl[b]	529.8	512.3	483.2	2.70	0.36	8.81
Br	527.9	506.6	494.0	2.63	0.26	8.76
I	523.5	495.4	510.7	2.54	0.02	8.80

[a] T. Schaefer, *Can. J. Chem.*, **40,** 431 (1962). [b] S. L. Smith and A. M. Ihrig, *J. Mol. Spectrosc.*, **22,** 241 (1967).

With the data of Spiesecki and Schneider,[8] a plot was made of the chemical shift of the halobenzene protons *vs.* the Pauling electronegativity of the halogen. The same type plot for the chemical shifts of the 2,4-dinitrohalobenzenes shows striking similarities. The H_3 and H_5 in the 2,4-dinitrohalobenzenes series are qualitatively similar to the meta protons of the halobenzene series; H_6 corresponds to the ortho protons in the halobenzenes. The two nitro groups affect the magnitude of the chemical shift, but the nature of the halogen still controls the relative chemical shift within the series.

The 2,4-dinitrohalonaphthalenes gave a much more complex spectra than the benzene series. H_3 appears as an intense singlet with a complex ABCD spectrum for the other protons, H_5, H_6, H_7, and H_8. Since the α protons of naphthalene have a greater chemical shift than β, the assignment of H_5 and H_8 to the downfield portion of the spectra is obvious. Since there is *no* coupling between the substituted and unsubstituted rings, the correct assignment of *one* of the protons (H_5 or H_8) is essential. From this one correct assignment, all other shifts and coupling constants are calculated *via* LAOCN3. The assignment of H_8 to the lower field is based on the data of Wells.[9] The effect of the nitro groups on H_5, H_6, H_7, and H_8 can be calculated.[9] These calculations indicate that $\nu_8 = 510$, $\nu_5 = 503$, $\nu_6 = 499$, and $\nu_7 = 437$ Hz. In other words, the order is $H_8 > H_5 > H_6 > H_7$. The data of Table I follow this pattern. If one draws resonance structures of the 1-halo-2,4-dinitronaphthalenes, both the 2- and the 4-nitro groups show resonance forms with + charges on the 6 and 8 positions. If electronegativity is the major factor in chemical shifts, these two protons should be downfield with respect to protons 5 and 7. The above argument has the implicit assumption that the halogens do not greatly affect the shift, and that their effect is a perturbation on the major effect of the nitro groups. Is this assumption correct or can we arrive at a satisfactory assignment on other bases? An alternative method is to apply the chemical shift changes of halogens in the ortho, meta, and para positions in benzene to the naphthalene series. If H_8 is regarded as meta to the halogen and H_5 as para, we arrive at the following qualitative result:

1-chloro	$\nu_8 = 510$ (for NO_2 groups)	(−2)	(*m*-Cl)	= 508 Hz
	$\nu_5 = 503$ (for NO_2 groups)	(−8)	(*p*-Cl)	= 495 Hz
1-bromo	$\nu_8 = 510$	(−6)	(*m*-Br)	= 504 Hz
	$\nu_5 = 503$	(−2)	(*p*-Br)	= 501 Hz
1-iodo	$\nu_8 = 510$	(−15)	(*m*-I)	= 495 Hz
	$\nu_5 = 503$	(−3)	(*p*-I)	= 500 Hz

These assumptions give the same qualitative order as the previous assumptions for the chloro and bromo compounds, but not for iodo. The iodine atom is large, and the peri positions of naphthalene are closer than the meta positions of the benzene. It is probable that the contributions of both the *m*-Br (−6) and the *m*-I (−15) are too negative; their real contribution would be more toward the ortho halogens, which are positive. This approach, though somewhat argumentative, supports the first. The peri effect has been discussed by Zweig, Lancaster, and Neglia.[10] The effect of a peri substituent is to shift that proton downfield; the low-field proton is always at the α position peri to the substituent. In our compounds, H_8 is the α and peri position and should be the low-field proton. Hence, the assignments $\nu_8 > \nu_5$ and $\nu_6 > \nu_7$ were accepted.

Comparison of the 2,4-dinitrohalonaphthalene series with the benzene series shows the meta pattern is followed. In each case, the chemical shift of the chloro compound is slightly greater than the bromo, which, in turn, is considerably greater than the iodo compounds.

Coupling constants do not vary much with respect to change in halogen. The ortho coupling constants, $J_{5,6}$ and $J_{7,8}$, are about equal (8.5 Hz) and greater than $J_{6,7}$ (7.0 Hz). The meta coupling constants, $J_{5,7}$ and $J_{6,7}$, show no pronounced trends and have the value of (1.0–1.3) Hz. The para coupling constants range from 0.75 to 0.6 Hz.

Registry No.—1-Cl-2,4-Dinitronaphthalene, 2401-85-6; 1-Br-2,4-dinitronaphthalene, 2401-86-7; 1-I-2,4-dinitronaphthalene, 4112-02-1; 1-Cl-2,4-dinitrobenzene, 97-00-7; 1-Br-2,4-dinitrobenzene, 584-48-5; 1-I-2,4-dinitrobenzene, 709-49-9.

---

[8] H. Spiesecki and W. G. Schneider, *J. Chem. Phys.*, **35**, 731 (1961).

[9] R. P. Wells, *J. Chem. Soc.*, 1967 (1963).

[10] A. Zweig, J. E. Lancaster, and M. T. Neglia, *Tetrahedron*, **23**, 2577 (1967).

Stepwise Synthesis of Oligopeptides with N-Carboxy-α-Amino Acid Anhydrides. IV. Glycine NCA

RYOICHI KATAKAI* AND MASANAO OYA

Department of Industrial Chemistry, College of Technology, University of Gunma, Kiryu-shi, Japan

KEIKICHI UNO AND YOSHIO IWAKURA

Department of Synthetic Chemistry, Faculty of Engineering, The University of Tokyo, Tokyo, Japan

Received July 6, 1971

A successful procedure for peptide synthesis using the controlled reaction of *N*-carboxy α-amino acid anhydrides (NCA's) in an aqueous system has been