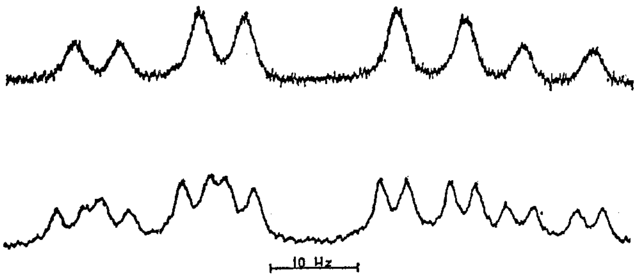

Figure 1.—Methylene region of phenylalanine. Upper trace is from the ordinary ^{14}N material, while the lower trace corresponds to the ^{15}N-labeled material. The spectra were measured at or near the isoelectric points and at different power and gain settings.

TABLE I

PROTON–PROTON AND PROTON–NITROGEN COUPLING CONSTANTS OF AMINO ACIDS[a]

Amino acid	Concn, *M*	J_{AX}[b]	J_{BX}[b]	J_{NA}[b]	J_{NB}[b]
Alanine (**3**, R = H)	0.43	7.0[c]		3.1[d]	
Phenylalanine (**3**, R = C_6H_5)	0.08	4.7[c]	7.9[c]	3.4[d]	2.9[d]
Aspartic acid (**3**, R = COOH)	0.05	3.1[d]	8.1[d]	3.0[c]	3.0[e]

[a] Measured at ambient probe temperatures, ~35° for alanine, ~19° for phenylalanine and aspartic acid. [b] In hertz. [c] ±0.1. [d] ±0.2. [e] ±0.3

rotamer **3a**, with the *trans* arrangement of the large R and COO^- groups, is predominant.[5,7] In accord with the above equations, the rotational isomer populations for phenylalanine are $p_a = 0.48$, $p_b = 0.19$, and $p_c = 0.33$ from which we can derive the *gauche* and *trans* ^{15}N–H couplings as $J_g^N = 1.8 \pm 0.8$ Hz and $J_t^N = 5.1 \pm 1.2$ Hz. The large probable errors are a consequence of the small difference between p_a and p_c.

Support for the derived values of J_g^N and J_t^N can be obtained in two ways. (1) Because alanine (**3**, R = H) has no preferred staggered conformation, the measured vicinal ^{15}N–H coupling constant must be a weighted average of the *trans* and *gauche* coupling constants, namely

$$J_{NH,vic} = \frac{1}{3}(2J_g^N + J_t^N) \qquad (10)$$

Substitution of the above values gives $J_{NH,vic} = 2.9$ Hz, in excellent agreement with the experimental value of 3.1 Hz.[10] (2) Using eq 3–5, the relative conformational populations of aspartic acid are $p_a = 0.50$, $p_b = 0.05$, and $p_c = 0.45$. These, in conjunction with equations 6–7, give calculated values of J_{NA} and J_{NB} as 3.5 ± 0.7 and 3.3 ± 1.5 Hz, which are in satisfactory agreement with the measured values.

The above treatment assumes that **3a** is the dominant conformation. If this is not assumed, and the assignments are reversed, then the alternative values of $J_g^N = 2.2$ Hz and $J_t^N = 5.8$ Hz result, which are within the probable error of the values derived above. Using these, a reasonable N–H coupling constant is derived for alanine, and values within the error limits of those given above are obtained for aspartic acid. Similarly, reversal' of the aspartic acid assignments allows calculation of values for J_{NA} and J_{NB} whose error limits span the experimental value. Thus, the particular assignment of the amino acid chemical shifts is not critical to the derivation of J_t^N and J_g^N.

TABLE II

ANGULAR DEPENDENCE OF VICINAL NITROGEN-PROTON COUPLING CONSTANTS

Angle, deg	J_{NH},[a] Hz	J_{NH},[b] Hz	J_{NH},[c] Hz
0	1.9, 3.8	4.3	
60	<0.4	0.3, 1.0	1.8
120	<0.4, 1.1		
180		6.9, 8.7, 9.7	5.1

[a] Reference 3. [b] Reference 4. [c] This work.

In Table II, J_t^N and J_g^N are compared with those already reported.[11] Although the numerical agreement is far from perfect, it is perhaps better than one might expect, given the large differences in the structures of the compounds from which the values are derived. In any case, the trends are such that, if we assume all of the J_{NH} values have the same sign, the couplings define a fairly shallow and somewhat skewed Karplus-type correlation between dihedral angle and coupling constant. The minimum in the curve is uncertain but appears to be between 80 and 120°.

Experimental Section

Enriched alanine and phenylalanine were obtained from Bio-Rad Laboratories, while the aspartic acid was a product of Merck Sharpe and Dohme of Canada. Spectra were taken at ambient probe temperatures on Varian HA-60, A56/60, and HR-220[12] spectrometers. Chemical shifts were measured by direct counting of the sweep oscillator frequency (for the HA-60) or by the usual audio side-band calibration method (for the A56/60 and HR-220 spectrometers).

Registry No.—**3** (R = H), 56-41-7; **3** (R = Ph), 63-91-2; **3** (R = CO_2H), 56-84-8.

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[10] The corresponding relationship should hold for the vicinal proton-proton coupling constant, but substitution for J_t^N and J_g^N gives 6.27 Hz,[4] compared with the experimental value of 7.0 Hz (Table I).

[11] The reported values for ^{14}N were corrected by $\gamma^{14}N/\gamma^{15}N = 0.713$ for this purpose.

[12] The HR-220 was purchased with the aid of National Science Foundation Grant No. GP 8450.

Charge-Transfer Energies of Benzylic Compounds with Tetracyanoethylene. A Convenient Method to Estimate the σ* Values

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Received December 29, 1969

Much literature on the charge-transfer complex has arisen in the past decade both from experimental and theoretical point of view.[2] A simple molecular orbital treatment based on the perturbation theory has been applied successfully to the charge-transfer spectra of alternant and nonalternant hydrocarbons,[3] where the

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[3] M. J. S. Dewar and A. R. Lepley, *J. Amer. Chem. Soc.*, **83**, 4560 (1961); A. R. Lepley, *ibid.*, **84**, 3577 (1962); K. Fukui, A. Imamura, T. Yonezawa, and C. Nagata, *Bull. Chem. Soc. Jap.*, **34**, 1076 (1961); **35**, 33 (1962).

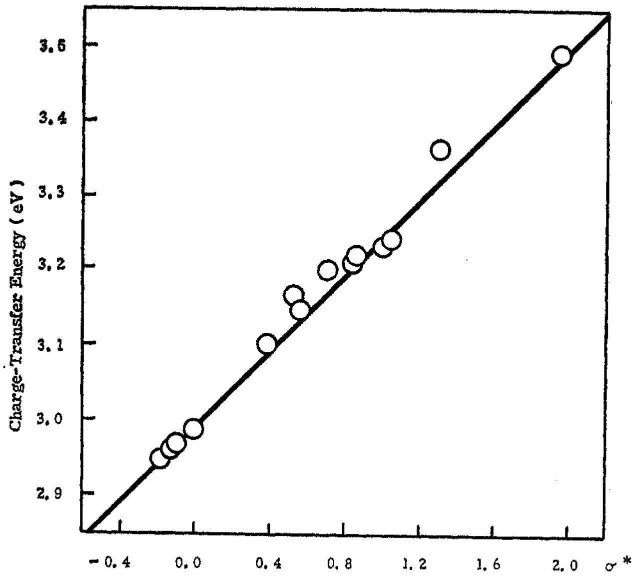

Figure 1.—Relationship between charge-transfer energies of $PhCH_2X$ and σ* of CH_2X.

energy required for the charge-transfer is simply related to the energy of the electronic transition from the highest occupied molecular orbital of the donor hydrocarbons into the lowest unoccupied molecular orbital of an interacting acceptor molecule.

Now a number of charge-transfer spectra of π complexes of benzylic compounds have been measured with tetracyanoethylene (TCNE) in dichloromethane at an ambient temperature, the results being listed in Table I.

TABLE I

CHARGE-TRANSFER ENERGIES OF BENZYLIC COMPOUNDS WITH TETRACYANOETHYLENE

Benzylic compd, XCH_2Ph	Registry no.	λ_{max} CT, nm	E_{CT}, eV	σ^* XCH_2
(Cl_2CHPh)	98-87-3	355	3.49	1.94
$NCCH_2Ph$	140-29-4	369	3.36	1.30
$ClCH_2Ph$	100-44-7	383	3.24	1.05
$BrCH_2Ph$	100-39-0	384	3.23	1.00
$CH_3CO_2CH_2Ph$	140-11-4	385	3.22	0.86
$PhOCH_2Ph$	946-80-5	390	3.18	0.85
$C_2H_5O_2CCH_2Ph$	101-97-3	388	3.20	0.71
$HOCH_2Ph$	100-51-6	393	3.15	0.555
CH_3OCH_2Ph	538-86-3	390	3.17	0.52
$ClCH_2CH_2Ph$	622-24-2	400	3.10	0.385
CH_3Ph	108-88-3	415	2.99	0
CH_3CH_2Ph	100-41-4	417	2.97	−0.1
n-C_4H_9Ph	104-51-8	419	2.96	−0.13
i-C_3H_7Ph	98-82-8	420	2.95	−0.19

The values of charge-transfer energies (E_{CT} in eV) are plotted against σ* as shown in Figure 1. A good linear relationship was obtained.

$$E_{\mathrm{CT}}\ (\mathrm{eV}) = 0.254\sigma^* + 2.99_9 \quad (r = 0.991)$$

Lepley[4] has demonstrated that the charge-transfer spectra of the π complexes of a number of methyl-substituted benzenes and naphthalenes with TCNE can be reasonably explained in terms of the first-order perturbation theory using only inductive effect models.[5] Therefore, in simple benzylic compounds, $PhCH_2X$, the charge-transfer energies can be related to parameters of inductive effect of XCH_2, *i.e.*, $\sigma^*_{XCH_2}$,[6] since in simple LCAO of $PhCH_2X$ only the atomic orbital at the point of XCH_2 attachment should be effected appreciably.

The present findings demonstrate not only the validity of using the inductive effect models to explain the charge-transfer spectra of simple hydrocarbons, but also potential utility of the relationship to evaluate the σ* value of XCH_2 group.

It should be noted, however, that there are apparent exceptions to the present relationship, for example, benzyltrimethylsilane ($\sigma^*_{Me_3SiCH_2} = -0.26$) afforded two well-resolved charge-transfer maxima at 491 and 415 nm as reported recently by Bock and Alt,[7] but the data deviated considerably from the above equation.

Recently, Traylor, *et al.*,[8] have measured charge-transfer absorptions in complexes of TCNE with substituted benzenes in dichloromethane. They have treated the data in a somewhat different manner, namely, in connection with the ability of substituents to stabilize carbonium ions The charge-transfer frequencies for the compounds, C_6H_5Y (Y = Me, PhCONH, MeO, MeCONH), correlate satisfactorily, although not perfectly, with σ_p^+. They have also shown that the benzyl–metal bonds such as in $PhCH_2SiMe_3$ and $PhCH_2HgCH_2Ph$ are highly hyperconjugated if a positive charge is in the ring and that the charge-transfer frequencies for these compounds are also correlated with σ_p^+.

However, the ionization energies or charge-transfer frequencies may be treated by the Hammett equation only in the case that the substituent causes rather a small perturbation on the benzene ring.[8] Actually, Traylor has measured the charge-transfer frequencies of various benzyl-X (X not a hyperconjugative) with TCNE and has plotted them against σ_I.[9]

In summary, the relationship found in the present investigation will be useful to estimate σ* values in the range of −0.2 ∼ +2.0. Applications of this relationship will be reported later.

Experimental Section

Materials.—Benzylic compounds purchased or prepared by known procedures were purified by distillation, purities being checked by glpc. TCNE was obtained from Eastman Organic Chemicals and was used without further purification.

Spectra.—Charge-transfer spectra were run on a Shimadzu Model SV-50A automatic recording spectrophotometer using 10-mm quartz cell. Dichloromethane was used as the solvent throughout the experiment, concentrations of TCNE and benzylic compounds being kept at 10^{-4}–10^{-3} and 10^{-2}–10^{-1} mol/l., respectively. The solutions were made up and mixed immediately before measurement. These solutions decolorized fairly rapidly, but were stable enough to record the charge-transfer maxima two or three times.

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[6] R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1965, Chapter 13.

[7] H. Bock and H. Alt, *Chem. Commun.*, 1299 (1967); *Angew. Chem.*, **79**, 934 (1967).

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[9] T. G. Traylor, private communication.

Registry No.—Tetracyanoethylene, 670-54-2.

Acknowledgment.—The author is grateful to Professor T. G. Traylor for making his results available prior to publication and for helpful discussions.

The Sodium Borohydride Reductions of Indolylethylpyridinium Bromides. Hexahydroindoloquinolizines

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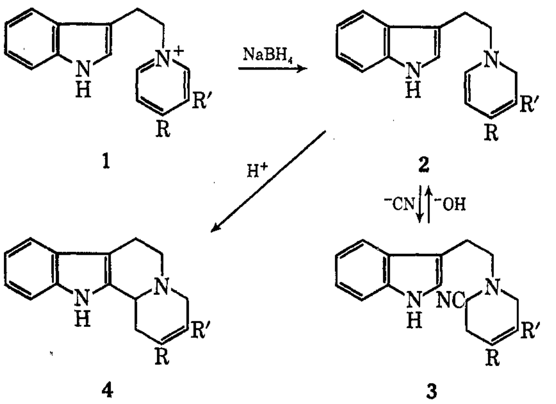
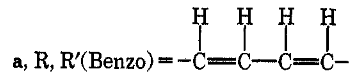
Sodium borohydride under ordinary conditions has not proved useful for the reduction of 1-(2-indol-3-ylethyl)pyridinium and the corresponding isoquinolinium salts to the dihydro bases **2**, intermediates for the synthesis of the quinolizines **4**.[1–4] The reduction to the tetrahydro bases which characterized this reagent was observed to a lesser extent with lithium aluminum hydride[1–5] and with lithium tri-*t*-butoxyaluminum hydride.[3] The results presented in this note show that control over the sodium borohydride reduction can be easily gained by using the alklai method of Panouse[6] together with the rapid removal of products from the reaction site. In addition, conversion of the dihydropyridines into nitriles in the reaction medium proved to be convenient and was usually desirable.[7a]

The advantages of using a nitrile in a sequence involving a 1,2-dihydropyridine lie in its stability relative to the parent diene and in the ease with which the nitrile reverts to the diene under basic and acidic conditions. Its availability, however, may be limited by the alkalinity of the parent sodium cyanide reduction system which may in itself be high enough to make the **2** $\rightleftarrows$ **3** equilibrium favor the diene. Lowering the alkalinity of the cyanide solution shifts the equilibrium toward the nitrile, but whether there is an accompanying increase in liability to further reduction is not presently known. Previous investigations have shown that annelations of the dienes require acid conditions, and in the present work the nitriles readily lost hydrogen cyanide in hot acid with closure to the quinolizine salts. Much milder conditions effect this ring closure when the dihydropyridine system is involved, so that the yield of quinolizine from a reduction mixture containing both **2** and **3** can in itself give no information on the relative amounts of the precursors.

A constant factor in all reductions and one of great importance is the two-phase liquid mixture of water, methanol, and ether which provided for a rapid separation of the initial reduction products from the foaming reaction mixture. By this means alone and without additional alkali a 66% yield of **2a** was obtained; in the presence of sodium hydroxide the recovery of this base rose to 89%. The dihydro base **2a** was also the main product from reductions in the more concentrated sodium cyanide solutions, and only in a moderately basic cyanide solution (partial neutralization with acid) did the nitrile form in appreciable amount in the reaction mixture. Not unexpectedly, **2a** was readily converted into **3a** (94%) in a similar cyanide solution. In contrast with the results obtained with the isoquinolinium salt, the water–methanol–ether mixture did not prevent reduction of the pyridinium bromide **1b** into its tetrahydro base in 78% yield; no quinolizine was obtained. The reduction of **1b** in sodium hydroxide followed by acid ring closure gave the hydrochloride of **4b** in 40% yield, and this was increased to 50% by the cyanide technique. Here noncrystalline products precluded assessment of the **2** $\rightleftarrows$ **3** interchange, but the ir absorption spectra indicated that this mixture was present in the crude oil.





a, R, R′(Benzo) = $-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-$

b, R = R′ = H

c, R = H; R′ = Me

d, R = H; R′ = Et

e, R = R′ = Me

f, R = Me; R′ = H

Among the variables to which little attention was given, but which made necessary a standardization of the synthetic procedure, are two which deserve special mention. The first of these is the alcohol used to dilute the aqueous solutions. Whether its contribution to the product yield stems from its role as a solvent or whether it also functions as a moderating nucleophile is a matter of conjecture. The second is the manner in which the acid annelation is conducted. Minor variations in solvent and acid sometimes had a marked effect on the yield of quinolizine salt. No attempt was made to identify a cause, but care was taken to duplicate conditions where comparisons were made.

Acid-induced elimination of hydrogen cyanide from related cyanotetrahydropyridines has been observed to be followed by a shift of the double bond into conjugation with the azomethine linkage. This isomerization has proved useful in controlling steric requirements of

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(7) (a) E. M. Fry, *J. Org. Chem.*, **29**, 1647 (1964); (b) E. M. Fry, *ibid.*, **28**, 1869 (1963).