Notes

Preparation and Stereochemistry of 4-Aryl-3-butenylamines. A Novel Synthesis of an Oxazolo[2,3-*a*]isoindole

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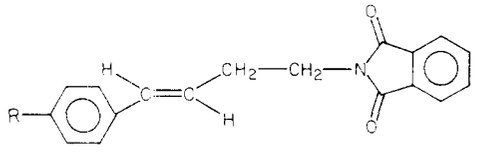
Because of their structural similarities to 2-phenylethylamine, 4-aryl-3-butenylamines are possible adrenergic agents. Potentially, they may also be cyclized to 2-arylpyrrolidines (structurally similar to nornicotine), as shown by the recent cyclization of 4-(3-pyridyl)-3-butenylamine.[1]

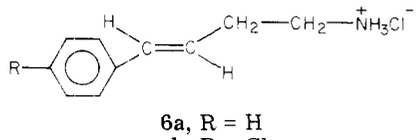
By treatment of a series of aromatic aldehydes **1a–f** with 3-(phthalimidopropylidene)triphenylphosphorane (**2**) and hydrazinolysis of the products **3a–f**, we have utilized a combination of the Wittig reaction and the Gabriel synthesis to prepare a number of *cis*-4-aryl-3-butenylamine hydrochlorides in moderate to good yields. The reaction sequence is shown in Scheme I.

The first step of the sequence was accomplished in tetrahydrofuran as the solvent, using potassium *tert*-butoxide to obtain the phosphorane (**2**) from the corresponding phosphonium bromide salt. We were unable to isolate any product when the phosphonium salt was treated with sodium hydride in dimethyl sulfoxide solution.

In Table I are listed the yields and melting points of the *N*-(4-aryl-3-butenyl)phthalimides (**3a–f**).

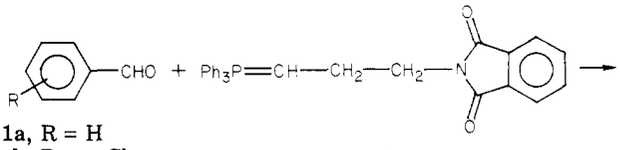
The IR spectra of **3a–f** were of limited value in assigning configurations. A lack of strong bands between 960 and 980 cm^{-1} (trans olefinic proton region) implied cis orientation, but the complexity of the spectra between 665 and 730 cm^{-1} (cis olefinic proton region) made confirmation difficult. Configurations were determined by comparison of the ^1H NMR spectra of **3a–f** with the spectra of **5a** and **5b**, two known trans compounds prepared by an independent method.[2] The olefinic protons of each of the structures **3a–f** displayed typical first-order splitting patterns: a doublet (H-4) and two overlapping triplets (H-3). Coupling constants ($J_{3,4}$) were 11.6–12.0 Hz, values which are borderline between those normally assigned to cis and trans configurations (cis, 6–12 Hz; trans, 12–18 Hz).[3] However, the corresponding protons of the trans structures **5a** and **5b** displayed second-order splitting patterns with coupling constants ($J_{3,4}$) of 15.0 and 16.0 Hz, respectively, indicating, by contrast, that **3a–f** are cis compounds.[4,5]





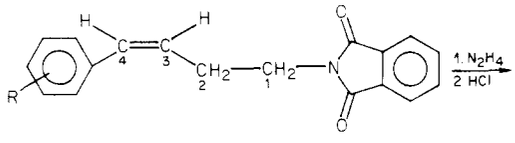
6a, R = H
b, R = Cl

Scheme I

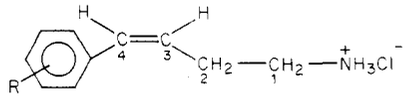


1a, R = H
b, R = *p*-Cl
c, R = *p*-CH_3
d, R = *p*-OCH_3
e, R = *p*-NO_2
f, R = *m*-NO_2

2



3a–f



4a–f

Table I. *N*-(4-Aryl-3-butenyl)phthalimides and 4-Aryl-3-butenylamine Hydrochlorides

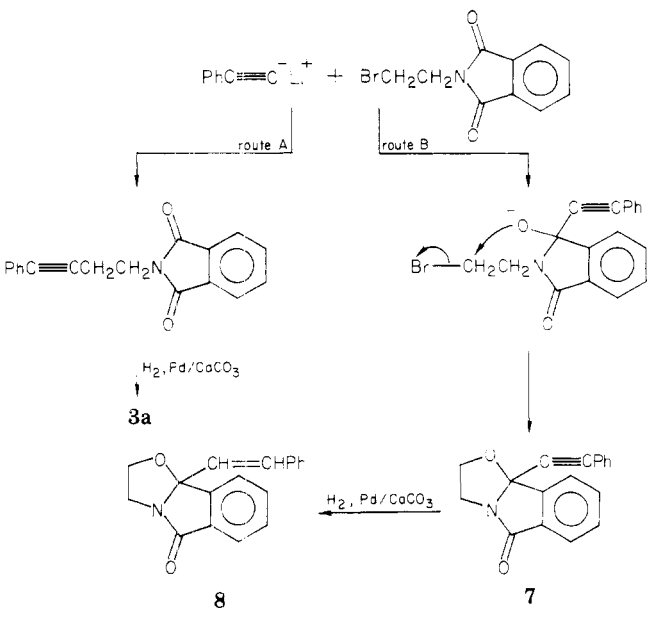
compd[a]	% yield	mp, °C
3a[b]	59	61.5–62
3b[b]	57	102–103
3c[b]	56	118–119
3d[b]	56	104.5–105.5
3e[b]	72	122–124
3f[b]	57	107.5–108
5a[b]	51	144–146
5b[b]	32	130–131.5
4a[c]	85	135–136
4b[d]	91	147.5–149
4c[d]	95	140.5–142
4d[d]	92	113.5–115
4e[e]	82	154–155
4f[f]	83	128–129
6a		214–220[g]
6b	41	205–210

[a] Satisfactory analytical data (±0.3% for C, H, N) were obtained for all new compounds. [b] Recrystallized from 95% ethanol. [c] Recrystallized from acetone–ethanol (95:5). [d] Recrystallized from acetone. [e] Recrystallized from ethyl acetate. [f] Recrystallized from acetone–ethyl acetate. [g] Lit.[2] mp 219–220 °C. ^1H NMR of **6a** (D_2O, Me_4Si external standard) δ 2.89 (m, 2, H-2), 3.47 (m, 2, H-1), 6.46 (2 t, 1, H-3), 6.95 (d, 1, H-4), 7.70 (m, 5, Ar) ($J_{3,4}$ = 16.0 Hz).

(1) W. C. Frank, Y. C. Kim, and R. F. Heck, *J. Org. Chem.*, 43, 2947 (1978).
(2) N. K. Kachetov and N. V. Dudykina, *Zh. Obshch. Khim.*, 28, 2399 (1958).
(3) R. M. Silverstein, G. C. Bassler, and T. C. Morrill, "Spectrometric Identification of Organic Compounds", 3rd ed., Wiley, New York, 1974, p 226.

0022-3263/80/1945-4049$01.00/0

Scheme II



The chemical shifts of H-3 in **3a–f** tend to confirm this configurational assignment. By application of the formula of Pascual, Meier, and Simon[6] (eq 1), the calculated

$$\delta = 5.28 + \Sigma_i Z_i \text{ for the structure } \begin{matrix} R_{cis} & & H \\ & C{=}C & \\ R_{trans} & & R_{gem} \end{matrix} \quad (1)$$

chemical shift[7] for H-3 in a cis position to another proton is δ 5.62; in a trans position it is δ 6.09. There is close agreement between our measured values for H-3 (ranging from δ 5.60 to 5.74) in compounds **3a–d** and the calculated value for H-3 in a cis configuration. The observed chemical shifts for H-3 in the nitro derivatives **3e** and **3f** are somewhat farther downfield (δ 5.93 and 5.90, respectively), perhaps due to strong electron withdrawal by the nitro group. The trans structures **5a** and **5b** also exhibit chemical shifts for H-3 (δ 6.15 and 6.22, respectively) which are in close agreement with the calculated value.

Treatment of the phthalimide derivatives with hydrazine yielded primary amines isolated as the hydrochloride salts, **4a–f**. Table I lists yields and melting points for the products obtained. Assuming that no configurational change occurs during hydrazinolysis, all of the products would have cis configurations. It should also be noted that **4a–f** show coupling constants ($J_{3,4}$) of 11.8–12.0 Hz whereas the coupling constants ($J_{3,4}$) of two of the corresponding known trans amine hydrochlorides, **6a** and **6b**, show coupling constants ($J_{3,4}$) of 16.0 Hz.

In an attempt to prepare **3a** by an alternate method (Scheme II, route A) entailing reduction of the corresponding alkyne, *N*-(2-bromoethyl)phthalimide was treated with lithium phenylacetylide. However, the reaction led to 2,3-dihydro-9b-(phenylethynyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**7**), formed by attack of the carbanion at an imide carbonyl group followed by ring closure (Scheme II, route B). Evidence for the structure of **7** is furnished by IR, ^{1}H NMR, and ^{13}C NMR spectra (see Experimental Section). The structural assignment was corroborated by a partial hydrogenation of **7** over Lindlar's catalyst. The ^{1}H NMR spectrum of the resulting alkene displayed two doublets in the ethylenic proton region, indicating clearly that the protons are coupled only to each other. This is a feature of structure **8**, the expected hydrogenation product of **7**. A cis configuration for **8** is indicated by its method of preparation and the ethylenic proton coupling constant (12.2 Hz).

The oxazolo[2,3-*a*]isoindole system has been reported only occasionally in the literature[8] and this method of synthesis appears to be novel. Work on the preparation of other heterocycles by this method is in progress.

Experimental Section

Melting points were determined in capillary tubes with a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Pascher and Pascher, Microanalytische Laboratories, Bonn, West Germany, Galbraith Laboratories, Inc., Knoxville, TN, and Industrial Testing Laboratories, Inc., St. Louis, MO. The ^{1}H NMR spectra were determined on a Perkin-Elmer R12A spectrometer and ^{13}C NMR were determined on a Bruker WH 90 FT NMR spectrometer. Infrared spectra were obtained on a Beckman IR-20A.

Triphenyl(3-phthalimidopropyl)phosphonium bromide. To a solution of 26.8 g (0.100 mol) of *N*-(3-bromopropyl)-phthalimide in 150 mL of xylene was added 26.3 g (0.100 mol) of triphenylphosphine. The mixture was heated under reflux for 44 h to yield a white solid. After being collected by filtration and washed with ether, the product weighed 49.3 g (93%). Drying in vacuo at 135 °C yielded an analytically pure sample: mp 242–244 °C; ^{1}H NMR ($CDCl_3$) δ 7.69 (m, 19, aromatic), 3.85 (m, 4, CH_2P and CH_2N), 2.12 (m, 2, $CH_2CH_2CH_2$); IR (KBr) 1770 and 1700 cm^{-1} (C=O), 1430 (P-phenyl).

Anal. Calcd for $C_{29}H_{25}BrNO_2P$: C, 65.67; H, 4.75; N, 2.64. Found: C, 65.82; H, 4.93; N, 2.62.

This product has been previously reported by Baker and Jordaan[9] who utilized benzene as a solvent and listed a melting point of 158–160 °C. In our hands, preparation in benzene yielded a product of the same melting point (242–244 °C) as that obtained in xylene. IR and ^{1}H NMR spectra and a mixture melting point showed the products from the two different solvents to be identical. Formation in benzene was much slower; after a 42-h reflux period our yield was only 29%.

General Method for Preparation of *cis*-*N*-(4-Aryl-3-butenyl)phthalimides (3a–f). The procedure for the synthesis of *cis*-*N*-[4-(*p*-nitrophenyl)-3-butenyl]phthalimide (**3e**) illustrates the method of preparation of compounds **3a–f**. A dry three-necked flask was equipped with a solid addition port, a nitrogen inlet, and a condenser fitted with a take-off attachment to allow evacuation of the system. In the flask was placed 3.0 g (0.020 mol) of *p*-nitrobenzaldehyde (dried over P_2O_5), 10.6 g (0.020 mol) of triphenyl(3-phthalimidopropyl)phosphonium bromide and 150 mL of dry THF. Potassium *tert*-butoxide (2.24 g, 0.0200 mol) was placed in the solid addition port. The system was evacuated, flushed with dry nitrogen several times, then cooled in an ice bath,

(4) We note that our ethylenic proton coupling constants are in close agreement with those displayed by *cis*- and *trans*-4-phenyl-3-buten-1-ol and its *p*-chloro derivative as reported by A. R. Hands and A. J. H. Mercer, *J. Chem. Soc. C*, 2448 (1968).

(5) We were unable to isolate any *trans*-*N*-(4-aryl-3-butenyl)phthalimide from any of our Wittig reaction mixtures, indicating that the trans products were either absent or present in only minor amounts. M. Schlosser, G. Muller, and K. F. Kristmann, *Angew. Chem., Int. Ed. Engl.*, **5**, 667 (1966), have found that alkylidenetriphenylphosphoranes which do not have stabilizing α substituents tend, in general, toward cis olefination. For a review of the stereochemistry of the Wittig reaction see M. Schlosser, *Top. Stereochem.*, **5**, 1 (1970).

(6) C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, **49**, 164 (1966); see also ref 3, p 223.

(7) In the selection of substituent constants from tabulated values (ref 6), the following increments were utilized: 0.44 (the R_{gem} constant for simple alkyl groups) for the phthalimidoethyl group in **3a–f** and **5a** and **5b**, −0.10 (the R_{trans} constant for aromatic groups) for all of the aryl groups in **3a–f**, 0.37 (the R_{cis} constant for aromatic groups) for both aryl groups in **5a** and **5b**, and 0.0 (the constant for H in any position).

(8) (a) P. Aeberli and W. J. Houlihan, *J. Org. Chem.*, **34**, 165 (1969); (b) W. J. Houlihan, U.S. Patent 3 334 113 and divisions thereof; *Chem. Abstr.*, **68**, 59600 (1968); (c) Y. Sato, H. Nakai, M. Kawaniski, K. Yuichi, *Chem. Pharm. Bull.*, **25**, 1164 (1973); (d) T. S. Sulkowski, U.S. Patent 3 336 306; *Chem. Abstr.*, **68**, 69007 (1968); (e) J. Honzyl, *Chem. Listy*, **49**, 1671 (1955); *Chem. Abstr.*, **50**, 5621 (1955); (f) P. Freytag, *Chem. Ber.*, **48**, 648 (1915); *Chem. Abstr.*, **9**, 1915 (1915).

(9) B. R. Baker and J. H. Jordaan, *J. Heterocycl. Chem.*, **3**, 319 (1966).

and stirred under a nitrogen flow for 15 min. The potassium *tert*-butoxide was added in one portion. The mixture became purple. After being stirred for 15 min, the mixture was warmed to room temperature, stirred for an additional hour, and then heated under reflux for 3 h. The mixture became deep red. The suspension was filtered and the solvent removed from the filtrate. The remaining solid was recrystallized from 95% ethanol to yield 4.6 g of yellow needles.

When, on occasion, difficulty was encountered in inducing the product to crystallize, chromatography on silica gel with 95:5 benzene–ethyl acetate was utilized, resulting in a solid product.

^{1}H NMR spectra for **3a–f** were determined in $CDCl_3$. All showed the same pattern. Chemical shift ranges, signal splitting, and integration were as follows: δ 2.70–2.76 (q, 2, H-2), 3.80–3.87 (t, 2, H-1), 5.60–5.74 except for **3e**, 5.93, and **3f**, 5.90 (2 overlapping t, 1, H-3), 6.45–6.63 (d, 1, H-4); $J_{3,4}$ range for **3a–f**, 11.6–12.0 Hz; aromatic signals all showed appropriate integrations; additional signals for **3c** δ 2.28 (s, 3, CH_3), for **3d** δ 3.77 (s, 3, OCH_3).

General Method for Preparation of *cis*-4-Aryl-3-butenylamine Hydrochlorides (4a–f). The procedure for removal of the phthaloyl group from **3a** to form *cis*-4-phenyl-3-butenylamine hydrochloride (**4a**) illustrates the method of preparation of compounds **4a–f**. A 1.0-g (3.5 mmol) quantity of **3a** and 0.15 mL (4.4 mmol) of hydrazine (95+%) were placed in 40 mL of 95% ethanol. The mixture was heated under reflux. The starting material initially dissolved on heating, but after 30 min a solid began to form. After 1 h, heating was discontinued and the solvent removed from the suspension. An IR spectrum indicated that the remaining solid was the phthalhydrazide salt of the amine. It was placed in 20 mL of 95% ethanol and 1 mL of 6 N HCl was added. After being heated under reflux for 1 h, the mixture was cooled and the precipitated phthalhydrazide removed by filtration. The filtrate was evaporated to dryness, leaving a solid which was recrystallized from acetone to yield 0.56 g of white crystals, mp 128–134 °C. An analytical sample was prepared by recrystallization from acetone–ethanol (95:5). IR (KBr) spectra of **4a–f** were all consistent with amine hydrochloride structures.

^{1}H NMR spectra for **4a–f** were determined in D_2O with Me_4Si as an external standard. All showed the same pattern. Chemical shift ranges, signal splitting, and integration were as follows: δ 3.10–3.19 (m, 2, H-2), 3.51–3.66 (m, 2, H-1), 6.10–6.44 (2 t, 1, H-3), 7.00–7.19 (d, 2, H-4); $J_{3,4}$ range for **4a–f**, 11.8–12.0 Hz; aromatic signals all showed appropriate integrations; additional signals for **4c** δ 2.65 (s, 3, CH_3), for **4d** δ 4.30 (s, 3, OCH_3).

***trans*-*N*-(4-Phenyl-3-butenyl)phthalimide (5a).** *trans*-4-Phenyl-3-butenylamine hydrochloride (**6a**), prepared from *trans*-cinnamaldehyde by the method of Kachetov and Dudykina,[2] was phthaloylated by the procedure of Bose, Greer, and Price.[10] A 0.92-g (5.0 mmol) quantity of **6a**, 0.74 g (5.0 mmol) of phthalic anhydride, and 1.3 mL of triethylamine were placed in 100 mL of toluene and the mixture was heated under reflux for 3 h as the water evolved was collected in a Dean–Stark water separator. The mixture was filtered and the filtrate heated under reflux for an additional 0.5 h before the solvent was removed. There remained a tan solid which, on recrystallization from 95% ethanol, yielded 0.71 g of white crystals: IR (KBr) 1770 and 1700 (C=O), 970 (*trans*-ethylenic protons) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.57 (q, 2, H-2), 3.83 (t, 2, H-1), 6.15 [second-order splitting, δ determined from ABX_2 formula (m, 1, H-3)], 6.43 [second-order splitting (m, 1, H-4)], 7.29 (s, 5, Ph), 7.77 (m, 4, Phth) ($J_{3,4}$ = 15.0 Hz).

***trans*-*p*-Chlorocinnamaldehyde.** The procedure used for this preparation was based on the method of Faust and Sahyun[11] for the preparation of *o*-chlorocinnamaldehyde. The crude products of three runs, each obtained from 70.4 g (0.500 mol) of *p*-chlorobenzaldehyde, 100 mL of absolute ethanol, 3.2 g of KOH, and 14.0 g (0.32 mol) of acetaldehyde were combined. Distillation and subsequent recrystallization from ether/petroleum ether yielded 30.3 g (0.19 mol, 20%) of white crystals: mp 61–63 °C (lit.[12] mp 62–62.5 °C); IR (KBr) 2850 (CH in CHO), 1700 (C=O), 973 (*trans*-ethylenic protons), 805 (*p*-disubstituted Ar) cm^{-1} [no bands occur in the 675–730-cm^{-1} region (*cis*-ethylenic protons)].

1-Nitro-4-(*p*-chlorophenyl)-1,3-butadiene. This compound was prepared by the method of Kachetov and Dudykina.[2] From 20.0 g (0.122 mol) of *trans*-*p*-chlorocinnamaldehyde was obtained, after recrystallization from methanol, 10.6 g (0.0506 mol, 41.5%) of light yellow crystals, mp 108–110 °C. The compound darkens on exposure to light; IR (KBr) 1510 and 1340 (NO_2), 835 (*p*-disubstituted Ar) cm^{-1}.

Anal. Calcd for $C_{10}H_8ClNO_2$: C, 57.29; H, 3.84; N, 6.68. Found: C, 57.50; H, 3.85; N, 6.62.

***trans*-4-(*p*-Chlorophenyl)-3-butenylamine Hydrochloride (6b).** This compound was prepared by the method of Kachetov and Dudykina.[2] When 3.75 g (17.7 mmol) of 1-nitro-4-(*p*-chlorophenyl)-1,3-butadiene dissolved in 100 mL of ether was added to 3.49 g of $LiAlH_4$ in 100 mL of ether an oil was obtained which, on distillation at 0.005 mm, yielded four fractions of clear, colorless liquid: (1) bp 83–87 °C, (2) bp 87–89 °C, (3) bp 89–94 °C, (4) bp 94–100 °C. Each fraction was dissolved in ether and treated separately with dry HCl gas to yield the corresponding fractions of hydrochloride salts: (1) 570 mg, (2) 600 mg, (3) 324 mg, (4) 80 mg [total 1.57 g (40.8%)].

The crude fractions contain an impurity, probably 4-(*p*-chlorophenyl)butylamine hydrochloride, in successively decreasing concentration as shown by a diminishing peak at δ 2.0 in the ^{1}H NMR spectra. The combined fractions are sufficiently pure for utilization in the next synthetic step. An analytical sample, mp 205–210 °C, was prepared by recrystallization from methanol/ether: IR (KBr) 3000, 1610, 1500 (NH_3^+), 970 (*trans*-ethylenic protons), 840 (*p*-disubstituted Ar) cm^{-1}; ^{1}H NMR (D_2O, Me_4Si external standard) δ 2.93 (m, 2, H-2), 3.46 (m, 2, H-1), 6.43 (2 t, 1, H-3), 6.88 (d, 1, H-4), 7.77 (m, 4, Ar) ($J_{3,4}$ = 16.0 Hz).

***trans*-*N*-[4-(*p*-Chlorophenyl)-3-butenyl]phthalimide (5b).** This was prepared in the same manner as **5a**. From 1.02 g (4.7 mmol) of *trans*-4-(*p*-chlorophenyl)-3-butenylamine hydrochloride was obtained 0.47 g (1.5 mmol), mp 122–128 °C. Recrystallization from 95% ethanol yielded an analytical sample: mp 130–131.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.65 (q, 2, H-2), 3.88 (t, 2, H-1), 6.22 [second-order splitting, δ determined from ABX_2 formula (m, 1, H-3)], 6.46 [second-order splitting (m, 1, H-4)], 7.23 (s, 4, Ph), 7.78 (m, 4, *o*-disubstituted Ar) ($J_{3,4}$ = 16.0 Hz).

2,3-Dihydro-9b-(phenylethynyl)oxazolo[2,3-*a*]isoindol-5-(9b*H*)-one (7). In a 250-mL round-bottomed three-necked flask fitted with reflux condenser, an argon inlet tube, and a syringe stopper was placed a solution of 4.7 g (0.046 mol) of phenylacetylene and 75 mL of dry THF. The mixture was cooled in an ice bath and stirred under an argon flow as 30.3 mL of a 1.7 M solution of *n*-butyllithium in hexane was added dropwise via syringe over a period of 20 min. A solution of 12.7 g (0.050 mol) of *N*-(2-bromoethyl)phthalimide in 50 mL of dry THF was then added via syringe over a period of 15 min. The mixture was stirred for 1 h at 0 °C and an additional hour at room temperature. The solvent was removed, leaving a brown oil which failed to crystallize on cooling. It was added to 350 mL of cold water and shaken for 20 min with intermittent ice cooling. On refrigeration of the aqueous mixture the oil settled and solidified. On collection by filtration and recrystallization from 95% ethanol 7.6 g (60%) of fine white crystals was obtained: mp 69.5–71.5 °C; IR (KBr) 3080, 2980, 2900, 2110 (C≡C), 1725 (C=O), 1330, 1155, 1105, 1085, 1050, 1015, 978, 760, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20–8.00 (m, 9, Ar), 3.80–4.75 (unsymmetrical m, downfield inclination,[13] 4, aliphatic); ^{13}C NMR ($CDCl_3$) δ 42.05 (CH_2N), 70.2 (CH_2–O), 83.8 and 86.3 (C≡C), 92.4 (quaternary C), 121.5, 122.9, 123.6, 124.3, 128.4, 129.2, 130.9, 131.3, 132.0, 132.8, 133.5, 144.1 (Ar), 172.5 (C=O).

Anal. Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.33; H, 4.89; N, 4.97.

***cis*-2,3-Dihydro-9b-(phenylethenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (8).** A 1.37-g (5.00 mmol) quantity of **7** was placed in a flask charged with 5 mL of 95% ethanol, 1.0 mL of quinoline, and 0.10 g of Lindlar's catalyst.[14] The mixture was hydrogenated at atmospheric pressure until 5 mmol of hydrogen had been absorbed (ca. 4 h). The mixture was filtered and the

(10) A. K. Bose, F. Greer, and C. Price, *J. Org. Chem.*, **23**, 1335 (1958).
(11) J. A. Faust and M. Sahyun, U.S. Patent 3 094 561; *Chem. Abstr.*, **59**, 11330 (1963).
(12) F. Strauss, *Justus Liebigs Ann. Chem.*, **393**, 235 (1912).
(13) See ref 8a. One of the two protons in the CH_2NCO group appears to lie in the plane of the lactam oxygen atom and, as a result, gives a low-field signal.
(14) H. Lindlar and R. Dubois, "Organic Syntheses", Wiley, New York, 1973, Collect. Vol. 5, p 880.

solvent removed from the filtrate to yield an oil which crystallized on the addition of 3 mL of 95% ethanol, wt 1.04 g (3.75 mmol, 75%), mp 94–96 °C. Recrystallization from 95% ethanol yielded an analytical sample: mp 95–96 °C; IR (KBr) 3010, 2960, 2940, 2880, 1720 (C=O), 1470, 1350, 1098, 1050, 1026, 1018, 980, 765, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.9–7.3 (m, 4, *o*-disubstituted Ar), 7.20 (s, 5, Ph), 6.81 (d, 1, =CHPh, J= 12.2 Hz), 5.92 (d, 1, =CHC, J = 12.2 Hz), 4.18–3.63 (m, 3, OCH_2CH_AN),[13] 3.50–2.88 (m, 1, CH_BN).[13]

Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.23; H, 5.54; N, 5.04.

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Registry No. **1a**, 100-52-7; **1b**, 104-88-1; **1c**, 104-87-0; **1d**, 123-11-5; **1e**, 555-16-8; **1f**, 99-61-6; **3a**, 74591-93-8; **3b**, 74591-94-9; **3c**, 74591-95-0; **3d**, 74591-96-1; **3e**, 74591-97-2; **3f**, 74591-98-3; **4a**, 74591-99-4; **4b**, 74592-00-0; **4c**, 74592-01-1; **4d**, 74592-02-2; **4e**, 74609-62-4; **4f**, 74592-03-3; **5a**, 74592-04-4; **5b**, 74592-05-5; **6a**, 74592-06-6; **6b**, 74592-07-7; **7**, 74592-08-8; **8**, 74592-09-9; *N*-(3-bromopropyl)phthalimide, 5460-29-7; triphenyl(3-phthalimidopropyl)phosphonium bromide, 7743-29-5; phenylacetylene, 536-74-3; *N*-(2-bromoethyl)-phthalimide, 574-98-1; *trans*-*p*-chlorocinnamaldehyde, 1075-77-0; 1-nitro-4-(*p*-chlorophenyl)-1,2-butadiene, 74592-10-2.

Neopentyl *p*-Toluenesulfonate Solvolysis. A Study of Response to Solvent Ionizing Strength

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Much experimental and theoretical evidence has been collected to support the contention that cyclopropylcarbinyl derivatives solvolyze with σ-participation, leading to the formation of a set of rapidly equilibrating nonclassical cationic intermediates.[2,3] Although controversy continues to surround the precise nature of these cationic intermediates,[2c,3c] the present understanding[3,4] indicates that, unlike the neophyl system,[5] delocalization of charge in the carbocation-like transition state takes place not by bridging[6] but via a greatly enhanced hyperconjugative interaction between the 2p (C^+) orbital and the exocyclic ring orbitals.[3c,7]

Recently,[4a] we proposed an experimental procedure for distinguishing between delocalization of charge by enhanced hyperconjugation and delocalization of charge by bridging. The procedure adopted was an extension of the test used by Winstein to establish the existence of discrete k_Δ and k_s pathways in the solvolysis of 2-phenyl-1-ethyl-OTs,[5] *n*-Pr-OTs,[8] and related systems.[9] Specifically, the rates of solvolysis of cyclopropylcarbinyl-OPms were plotted against the solvolysis rates (k_t) of neophyl-OTs.

It was found that such a plot yielded not a quantitative correlation, as reported by Winstein for substrates solvolyzing by the k_Δ pathway,[5,8,9] but instead yielded a dispersion with lines of different slopes for ethanol/water on the one hand and the carboxylic acids formic and acetic on the other. On the basis of the mechanistic significance assigned to k_t for neophyl-OTs (delocalization of charge in a carbocation-like transition state by bridging) and the predominantly k_Δ process followed in the solvolysis of cyclopropylcarbinyl-OPms,[4a] we ascribed the dispersion to the special properties (delocalization of charge by enhanced hyperconjugation) of the cyclopropylcarbinyl system.

While differences in leaving-group solvation and ion return were deduced to be unlikely explanations for the observed data,[4a] the possibility remains that the dispersion could be due to a different response to medium effects by a phenyl and an alkyl neighboring group.[10] Therefore, an important addition to the previous study is its extension to a primary alkyl substrate whose solvolysis is assisted exclusively by neighboring alkyl participation.

In solvolysis reactions, neopentyl-OTs is a rather good model for a primary alkyl substrate solvolyzing via the k_Δ pathway.[12] Although it is thought that it solvolyzes with alkyl participation without nucleophilic solvent participation,[12,13] the rates of solvolysis of neopentyl-OTs in both ethanol/water and carboxylic acid solvents have not been analyzed for correlation with those of neophyl-OTs. In this paper we report the results of such an analysis which further support the use of the proposed experimental procedure as a probe for distinguishing between delocalization of charge by enhanced hyperconjugation and delocalization of charge by bridging in solvolytic transition states.

In the course of this study we also confirmed the earlier conclusion that the solvent dispersion was not due to differences in leaving-group solvation.

The first-order rate constants for solvolysis of neopentyl

(1) Taken in part from the M.S. thesis submitted to Louisiana Tech University, 1980.

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(9) A. Diaz and S. Winstein, *J. Am. Chem. Soc.*, **91**, 4300 (1969).

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