TABLE VI

SOLVENT EFFECT ON PROTON SHIFTS OF SUBSTITUTED PYRAZINES

Substituent	H_o	H_m	H_p	H_{CH_3}	Solvent
CH_3	1.52	1.52	1.60	7.47	Neat
CH_3	1.63	1.65	1.68	7.50	CCl_4
CH_3	1.60	1.58	1.62	7.49	$HCCl_3$
CH_3	1.71	1.73	1.75	7.53	CS_2
CH_3	1.50	1.54	1.60	7.50	DMSO
CH_3	1.50	1.54	1.60	7.44	MeOH
Cl	1.25	1.37	1.50		CCl_4
Cl	1.25	1.36	1.50		DMSO

chemical shift of the ring protons of pyrazines parallel changes in substituents. The double linearity of the meta correlation seems to reinforce the view that selective "second-order" mesomeric interaction between some substituents and the meta position is operative.

Experimental Section

2-Pyrazinamide was commercially obtained (Eastman), mp 189-90°.

2-Pyrazinecarboxylic acid was prepared by a basic hydrolysis of 2-pyrazinamide, mp 222-223° dec.

Methyl pyrazinoate[11] was prepared by a sulfuric acid-absolute methanol esterification of 2-pyrazinecarboxylic acid (67% crude) yield). Sublimation at 85° (2.5 mm) gave pure product, mp 57-58°.

2-Hydroxypyrazine was prepared by the method of Yafuso,[12] mp 187-188°.

2-Chloropyrazine[13] was obtained from J. Moshera.

Pyrazinaldehyde was prepared by the method of Rutner and Spoerri,[14] bp 57° (6 mm).

2-Cyanopyrazine,[15] bp 87° (6 mm), was obtained from J. Moshera.

2-Methoxpyrazine, bp 68° (28 mm), was prepared by the method of Albert and Phillips.[13]

2-Fluoropyrazine,[16] bp 107-108°, was obtained from H. Rutner.

2-Iodopyrazine,[17] bp 109-110° (34 mm), was obtained from H. Hertz.

2-Methylpyrazine was commercially obtained (K and K).

Physical Measurements.—All pyrazine nuclear magnetic resonance spectra were run at 37° on a Varian A-60 spectrometer operating at 60 MHz. The peak areas were integrated. Spinning of the samples was always employed. The samples were run five times, once relative to tetramethylsilane as the internal standard, in dimethyl sulfoxide at a rate of 500 cps, and four times relative to benzene as the internal standard in dimethyl sulfoxide, scanning the sample both upfield and downfield.

The least-squares correlations were obtained on a IBM 7040 computer using a program obtained from the Brooklyn Polytechnic Computer Center, and repeated at the computer facility of the Hebrew University.

Acknowledgment.—The authors wish to thank Mr. H. Talz, who ran the nmr spectra, and Mr. J. Moshera for some of the syntheses. Thanks are also due to Dr. A. Meyer for his help in obtaining the use of the computer facility at the Hebrew University.

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[11] W. F. Newell, private communication, 1965.

[12] M. Yafuso, B. S. Thesis, Polytechnic Institute of Brooklyn, June 1964.

[13] A. Albert and J. N. Philips, *J. Chem. Soc.*, 1294 (1956).

[14] H. Rutner and P. E. Spoerri, *J. Org. Chem.*, **28**, 1898 (1963).

[15] M. Robba, *Ann. Chim (Paris)*, **5**, 351 (1960).

[16] H. Rutner and P. E. Spoerri, *J. Heterocycl. Chem.*, **2**, 492 (1965).

[17] A. Hirshberg and P. E. Spoerri, *J. Org. Chem.*, **26**, 1907 (1961).

An Evaluation of Base–Solvent Systems Using Olefin Isomerization as a Probe

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The base-catalyzed olefin isomerization reaction has been used to probe the efficacy of a wide variety of base–solvent systems. Changes in base type have produced changes in reaction rate that range over eleven powers of ten. The metal alkylamides in hexamethylphosphoramide are the most active. With a given type of anion, both its ligands and the metal cation have pronounced effects. Solvent variation produced a smaller range of reactivity (10^3). Dielectric constant and solvent proticity also play critical roles.

During the past 10 years the use of dipolar aprotic solvents has provided numerous advantages for the organic chemist.[1-3] Perhaps the most significant of these is the discovery of homogeneous base–solvent systems that promote anionic reactions of very weak organic acids under mild conditions. Although the role of the base and solvent are critical to the reaction, a comprehensive study of the relative effectiveness of various combinations is not available. The present work was initiated to provide both practical and theoretical information.

The base-catalyzed olefin isomerization reaction was selected as the probe for this study for several reasons. First, considerable information about the reaction has been obtained and many of the mechanistic details have been elucidated.[4-8] Second, the reaction is experimentally simple since it is homogeneous in both olefin and base. Third, preliminary experiments indicated that the reaction is exceedingly sensitive to variations in the efficacy of the base–solvent system. Fourth, a wide variety of olefin structures are available and, by appropriate selection, olefins of widely varying isomerization capability are obtained easily. Finally, and most important, base-catalyzed olefin isomerization involves the activation of the very weak carbon–hydrogen bond. Accordingly, a broad study of the

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[1] For a comprehensive review see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965.

[2] A. J. Parker, *Chem. Rev.*, **69**, 1 (1969).

[3] H. Normant, *Russ. Chem. Rev.*, **39**, 457 (1970).

[4] S. Bank, C. A. Rowe, Jr., A. Schriesheim, and L. A. Naslund, *J. Org. Chem.*, **33**, 221 (1968).

[5] S. Bank, C. A. Rowe, Jr., A. Schriesheim, and L. A. Naslund, *J. Amer. Chem. Soc.*, **89**, 6897 (1967), and references cited therein.

[6] L. A. Yanovskaya and Kh. Shakhidayatov, *Russ. Chem. Rev.*, **39**, 859 (1970).

[7] H. J. Hubert and H. Reimlinger, *Synthesis*, **1**, 97 (1969).

[8] H. Kloosterziel and J. A. A. van Drunen, *Recl. Trav. Chim. Pays-Bas*, **89**, 37 (1970), and references cited therein.

effect of base and solvent upon the relative rates of isomerization of select olefins was undertaken.

Results and Discussion

Effect of Base.—Attention was focused on several aspects of base variation. Initially, representative classes of bases were selected for study. Table I records the general classes with examples and a suitable solvent for those bases that were screened. Of the three groups, the alkoxides and hydroxides were studied in dimethyl sulfoxide (DMSO). The metals, organomagnesium reagents, metal amides, and borohydrides required the more weakly acidic solvent hexamethylphosphoramide (HMPA). No suitable solvent was obtained for the group including hydrides and metal alkyls.

TABLE I

RELATIVE RATES OF BASE-CATALYZED OLEFIN ISOMERIZATION AS A FUNCTION OF BASE TYPE

Class	Example	Solvent	Olefin[a]	$k_{\text{rel isom}}$
M	K	HMPA	**1**	10^3
MOH	KOH	DMSO	**1**	10^{-2}–10^{-3}
MOR	KO-*tert*-Bu	DMSO	**1**	1.0
MH	NaH			
MMH_x	$NaBH_4$	HMPA	**2**	10^{-7}
MR	LiBu			
	$NaCH_2SOCH_3$	HMPA	**1**	10^1–10^2
	$MgPh_2$	HMPA	**1**	10^{-1}
MNH_2	$NaNH_2$			
MNR_2	$LiNMe_2$	HMPA	**3**	10^5–10^6

[a] **1**, 2-Methyl-1-pentene; **2**, allylbenzene; **3**, 2,4,4-trimethyl-1-pentene.

Direct comparison of the relative reactivities of the bases in the first two groups was precluded by necessary changes in solvent, cation, temperature, and olefin structure. Nevertheless, a sufficient number of direct comparisons were made such that corrections for the variations achieved approximate relative reactivities. The relative rate constants were obtained from the observed rate constants (tabulated in the Experimental Section) with the following corrections. Data obtained in HMPA was correlated with data in DMSO since the same reaction is known to be 5.8 times faster in DMSO (*vide infra*). Data for the several olefins were compared since the order of activity of the olefins with a single base–solvent system has been shown to be[9] 2,4,4-trimethyl-1-pentene:2-methyl-1-pentene:allylbenzene, 9.1×10^{-3}:1:$7.8 \times 10.^5$ Data at various temperatures were correlated by the known activation energies and in all cases normalized to 55°. Finally, corrections for cation variation were applied from studies with a single anion (*vide infra*).

The most dramatic effect revealed by Table I is the enormous range, $\sim 10^{11}$, of relative reactivities. This suggests that by suitable selection of the base type, one could design anionic reaction conditions to be very facile or very selective. Table I reveals both expected and unexpected behavior. Not surprisingly, the metal itself provides a very active system, and the trends found for hydroxides, alkoxides, and borohydrides follow the expected order. However, the enhanced reactivity of nitrogen anions relative to carbon anions, and the metal itself for that matter, is unusual. Equally perplexing is the very low reactivity of the organomagnesium reagent. These data reinforce the view that the state of aggregation of the base in the solvent is of critical importance and may take precedence over the order expected from simple electronegativities.[10–12] Finally, these data demonstrate the need for experimental determination of relative reactivities.

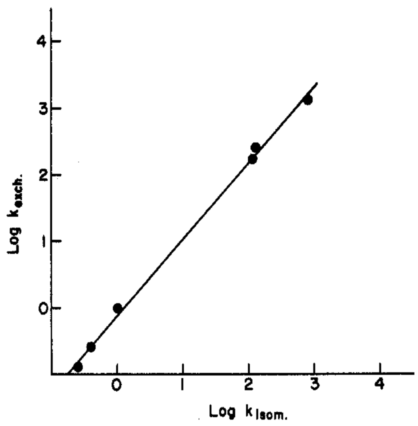

Figure 1.—Relationship between base-catalyzed tritium exchange and base-catalyzed olefin isomerization (data taken from Table II).

Bases having cation and anion variations on a given central atom were studied to allow a more detailed investigation of the important factors in base strength. The metal alkoxides were used with a single olefin and a single solvent.

Table II records data for the isomerization reaction and the related base-catalyzed isotopic exchange of tritiated toluene with solvent.[13] Figure 1 illustrates the close parallel between the two base-catalyzed reactions, and supports the view that data obtained for olefin isomerization can be validly extrapolated to other base-catalyzed reactions.

TABLE II

BASE-CATALYZED REACTIVITIES OF ALKALI METAL ALKOXIDES

Base	Olefin isom, 10^3K, sec^{-1}[a]	k_{rel}	Exchange, k_{rel}[c]
LiO-*tert*-Bu	0.0013[b]	0.0011	0.00077
NaO-*tert*-Bu	0.0106	0.0091	0.006
KO-*tert*-Bu	1.16	1.00	1.0
RbO-*tert*-Bu	2.84	2.5	3.9
CsO-*tert*-Bu	4.47	3.9	7.8
KOMe	0.0092[b]	0.008	0.004
KO-*i*-Pr			0.67

[a] For isomerization of 1-butene at 55° in DMSO solution. [b] Rate constant estimated from measured rate constant for isomerization of 1-pentene and factor derived for difference between 1-butene and 1-pentene at 55° using KO-*tert*-Bu (ref 9). [c] For reaction $PhC^3H_3 + CH_3SOCH_3 \xrightarrow{B} PhCH_3 + CH_3SOC^3H_3$ [J. E. Hofmann, R. J. Muller, and A. Schriesheim, *J. Amer. Chem. Soc.*, **85**, 3000 (1963)].

The reactivity for base-catalyzed reactions was found to be strongly dependent on both the cation and anion. For example, Li^+ and Cs^+ *tert*-butoxides gave the rate

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(9) A. Schreisheim, C. A. Rowe, Jr., and L. A. Naslund, *J. Amer. Chem. Soc.*, **85**, 2112 (1963).

(10) T. E. Hogen-Esch and J. Smid, *ibid.*, **88**, 307 (1966).

(11) S. Bank and B. Bockrath, *ibid.*, **93**, 430 (1971).

(12) J. I. Brauman, N. J. Nelson, and D. C. Kohl, *ibid.*, **90**, 490 (1968).

(13) J. E. Hofmann, unpublished data.

difference of 10^4. The anion variation from methoxide to *tert*-butoxide gave a similar 10^4 increase in rate. In principle, then, a table of bases ranging in reactivity of more than 10^8 could be constructed from the series LiOMe to CsO-*tert*-Bu.

Base catalytic activity was found to increase with increasing cation atomic weight. Interestingly, the largest difference was found between sodium and potassium, which finds analogy in some alkali metal compounds.[14] A reasonable explanation is the decreasing electronegativity of the cation with increasing atomic number. Since the ionic character of the metal–oxygen bond depends in part upon the electronegativity difference between the metal and oxygen, CsO-*tert*-Bu is expected to be the most ionic. One could argue that the greater the ionic character of the metal oxygen bond, the greater the reactivity of oxygen anion for proton activation. While this may be true in part, solvation terms are probably very important as well, and unfortunately these factors are inseparable here.

Anion variations followed the expected order of solution basicity, namely *tert*-BuO$^-$ > *i*-PrO$^-$ > MeO$^-$. This is the reverse order of gas-phase reactivities,[15] and amplifies the view that solvation terms are critical, that is, *tert*-butoxide is a stronger base than methoxide because it is not solvated as well. What is surprising, is that the difference should be so great in a so-called "aprotic" solvent where solvation of anions is not expected to be a large factor, therefore, minimizing differences between anions. Indeed the gas-phase order might have been expected insofar as thermodynamic basicities and kinetic basicities can be related. Of the several interpretations of this anomaly, the one favored is that the solvent is not truly aprotic. Recent work by Brauman has shown that KO-*tert*-Bu in DMSO is in actual fact a mixture of the dimsyl and the *tert*-butoxide anions,[16] and, therefore, alcohol is present and solvates the anion. This point of view leads to two interesting facets. First, a so-called aprotic solvent may be just that for some anions but need not be that for all. Second, if indeed the gas-phase basicities may be related to reactivities, then in a truly aprotic solvent media methoxide would be a stronger base than *tert*-butoxide.

The final aspect of base variation concerned structural changes in the organic moiety. The bases chosen for this series were the highly active lithium organoamides in HMPA using the very unreactive olefin 2,4,4-trimethyl-1-pentene. Solutions of the lithium amides in HMPA are not stable indefinitely, and it was found that the observed rate constant slowly decreased as a function of the period of time the lithium amide HMPA solutions were stored. However, there was no noticeable change in the observed rate constant until a period of 5–15 hr had elapsed. Accordingly, all rate studies were performed with freshly prepared solutions.

The data in Table III can be accounted for on the basis of steric and electronic factors. The suggestion that reactivity difference between lithium dimethylamide and lithium diisopropylamide is largely steric is borne out by the relative rate increase in going to the piperidine amide. Clearly, the electronic factors of the isopropyl compound and the piperidine compound are similar whereas the acyclic isopropyl compound has a significantly greater steric effect. As expected based on thermodynamic basicity, the aromatic amide lithium anilide is considerably less reactive than lithium cyclohexylamide. Finally, note is made of the enormous reactivity difference ($\sim 10^5$) between these bases and what is often thought to be a strong base, potassium *tert*-butoxide. This could have synthetic applications for a variety of anionic reactions.

TABLE III

RATES OF BASE-CATALYZED ISOMERIZATION OF 2,4,4-TRIMETHYL-1-PENTENE AT 20° FOR SELECT LITHIUM METAL AMIDES

Amide	k_{isom},[a] sec^{-1} × 10^4	k_{rel}
$LiNMe_2$	40	7×10^5
LiN-*i*-Pr_2	1.8	3×10^4
Li piperidide	9.8	1.7×10^5
LiNH-*c*-C_6H_{10}	1.4	2.3×10^4
$LiNH$-C_6H_5	0.00013	2.5
KO-*tert*-Bu	0.00006[b]	1.0

[a] Using 0.7 *M* base in HMPA. [b] Estimated from conversion factors for 2,4,4-trimethyl-1-pentene and 2-methyl-1-pentene.

Effect of Solvent.—The base potassium *tert*-butoxide dissolves in diglyme and gives solutions that are stable at 55°. With the introduction of the terminal olefin 2-methyl-1-pentene, there is a very slow conversion to the internal isomer ($t_{1/2}$ ~80 days). In striking contrast, using the same base, olefin, and temperature but substituting DMSO for diglyme brings about a rapid conversion to the internal isomer ($t_{1/2}$ ~2 hr). Clearly, that solvent has a dramatic effect upon the rate of base-catalyzed olefin isomerization requires no additional support. Our detailed investigation sought to probe for the factors which contribute significantly to the effect.

The isomerization of representative olefins with a single base was studied in solvents of varying dielectric constant. Table IV summarizes the results and Figure 2 depicts the relationship between the rates and the dielectric constants. Overall the rate variation was $\sim 10^3$ and the relative rates increased with increasing dielectric constant. Figure 2 reveals, except for diglyme, a linear relationship for the plot of the log k against the recipricals of the dielectric constant. Such a

TABLE IV

EFFECT OF SOLVENT ON THE BASE-CATALYZED OLEFIN ISOMERIZATION REACTION

Solvent	10^4k, sec^{-1}[a]	k_{rel}	Dielectric constant
DMSO, 100%	1.22[b]	1580	48.8
DMSO, 95%–THF, 5%[c]	1.05[b]	1370	45.5[d]
DMSO, 90%–THF, 10%[c]	0.68[b]	525	42.3[d]
DMSO, 75%–THF, 25%[c]	0.48[b]	370	34.0[d]
HMPA	0.60[b]	465	30.2
TMU[e]	0.021[b]	16.4	24.5
NMP[f]	0.405[g]	311	33.1
Diglyme	0.0013[b]	1	7.7

[a] Using 0.7 *M* KO-*tert*-Bu at 55°. [b] For 2-methyl-1-pentene. [c] By volume. [d] Measured by a Sargent oscillometer calibrated from known standards. [e] Tetramethylurea. [f] *N*-Methyl-2-pyrrolidone. [g] Estimated from observed rate using 1-butene and conversion factor from ref 9.

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[14] O. L. Brady and J. Jakobovits, *J. Chem. Soc.*, 767 (1950).

[15] J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **92**, 5896 (1970).

[16] J. I. Brauman, J. A. Bryson, D. C. Kohl, and N. J. Nelson, *ibid.*, **92**, 6679 (1970).

relationship is expected for a reaction in which charge is developed in the transition state. This relationship holds reasonably well for solvents of higher dielectric constant, but the assumptions that necessarily go into the simple treatment are no longer valid for the very low dielectric constant solvent, diglyme. The behavior of diglyme is a function of specific solvation rather than of bulk dielectric properties.[10]

Other important solvent properties include solubility of reactants and lack of reactive hydrogens. Previous work has shown that the addition of the hydroxylic species *tert*-butyl alcohol to the system potassium *tert*-butoxide–dimethyl sulfoxide brings about a marked decrease in rate with increasing concentration of *tert*-butyl alcohol.[17] As expected, the hydrogen-bonded base is weaker. The acidity of the solvent protons affects the rate since they produce hydrogen-bonded bases. The several dipolar solvents studied had varying acidities and the term aprotic is not very revealing. In large measure whether the solvent is protic or aprotic is a function of the reference base. In actual fact all of the solvents had some acidity and an estimation of the relative acidity was obtained from the relative rates of base-catalyzed proton exchange with tritiated toluene.[13] For some solvents, side reactions rendered kinetic interpretation impossible; however, in general, it was possible to correlate relative acidities on the basis of the time elapsed for 10% exchange. Using this technique, the following order of solvent acidities was found: DMSO > NMP > TMU > HMPA.

Experimental Section

Materials.—All the alkali metal *tert*-butoxides as well as potassium methoxide and isopropoxide were purchased from Mine Safety Appliances. They were the alcohol-free, sublimed powders and were used without further purification. Sodium hydride and sodium borohydride were purchased from Ventron, Inc. Butyllithium was obtained from the Lithium Corporation of America. Diphenylmagnesium was prepared by dioxane precipitation of phenylmagnesium bromide obtained from Araphoe Chemical Co. Sodium amide was obtained from Matheson Coleman and Bell. The several lithium alkylamides were prepared by addition of the appropriate amine to butyllithium in the drybox. The resulting solids were washed with *n*-heptane and stored in the drybox.

Dimethyl sulfoxide (Matheson Coleman and Bell) was dried and distilled over Linde 13X molecular sieves. Diglyme (Matheson Coleman and Bell) was distilled under reduced pressures from lithium aluminum hydride. Hexamethylphosphoramide (Eastman) was dried and distilled under reduced pressures over Linde 13X molecular sieves. Tetramethylurea (OTT Chemical Co.) was distilled under vacuum from barium oxide. *N*-Methyl-2-pyrrolidone (Matheson Coleman and Bell) was obtained as the Spectroquality material and used without further purification.

The olefins 2-methyl-1-pentene, 1-butene, 2,4,4-trimethyl-1-pentene, and allylbenzene were API samples. Gas chromatographic analysis indicated a purity greater than 99.6%.

Kinetic Procedures.—A typical experiment was carried out as follows: A 0.60 *M* stock solution was prepared in a nitrogen-blanketed drybox from 6.74 g (0.060 mol) of potassium *tert*-butoxide and sufficient dimethyl sulfoxide to give 100.0 ml of solution. The solution was stirred magnetically for 12 hr before use. A 7.0-ml aliquot of this solution was placed in a 10-ml vial that was then capped with a self-sealing neoprene septum. The vial was removed from the drybox and placed in a thermostated bath at 55.2°.

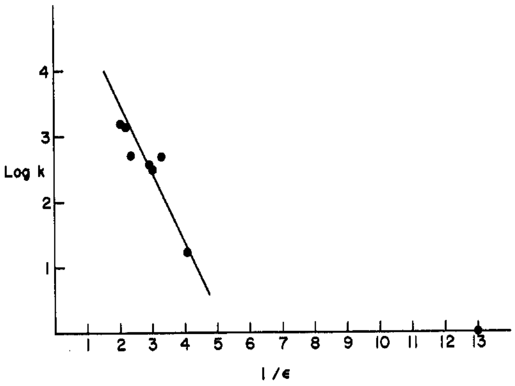

Figure 2.—Relationship between the rate constants for base-catalyzed olefin isomerization and the solvent dielectric constant.

TABLE V

RATE OF BASE-CATALYZED OLEFIN ISOMERIZATION OF VARIOUS BASES

Base	Base concn	Temp, °C	k, sec^{-1}
K	0.43^{a,b}	33	2.33×10^{-2}
KOH	0.43^{a,c}	55	1.23×10^{-6}
KO-*tert*-Bu	0.56^{a,c}	55	1.22×10^{-4}
NaH	0.40^{a,b}	55	*e*
$NaBH_4$	0.40^{b,d}	55	2×10^{-7}
LiBu	0.40^{f}	25	*f*
$Na^+\bar{C}H_2SOCH_3$	0.70^{a,c}	40	1.48×10^{-5}
$MgPh_2$	0.70^{a,b}	55	1.2×10^{-5}
$NaNH_2$	0.70^{a,b}	55	*e*
$LiNMe_2$	0.70^{g,b}	20	4.0×10^{-3}

[a] Using 2-methyl-1-pentene, 0.45 *M*. [b] HMPA. [c] DMSO. [d] Using allylbenzene, 0.40 *M*. [e] After 100 hr at 55° there was no measurable 2-methyl-2-pentene as determined by gc. It should be noted that the amide and hydride are insoluble in HMPA and studies in DMSO are precluded due to reaction. [f] Rate studies were precluded by the fact that in all solvents butyllithium decomposed as measured by conversion to butane. [g] 2,4,4-Trimethyl-1-pentene, 0.40 *M*.

A mixture of 5.86 g (0.069 mol) of 2-methyl-1-pentene and 1.38 g (0.016 mol) of the internal standard 2,3-dimethylbutane was placed in another 10-ml vial sealed with a rubber septum. The vial was placed in the thermostated bath and a sample removed (~2 μl) by hypodermic syringe for gas chromatographic analysis. The analyses were performed on a Model 500 F & M gas chromatograph equipped with a 21-ft column containing 20% DC 200 on Chromosorb P, 60–80 mesh. Complete separation of the internal standard (2,3-dimethylbutane), the starting olefin (2-methyl-1-pentene), and the product olefin (2-methyl-2-pentene) was obtained at 50° with 10 psig of helium pressure.

After thermal equilibration (~0.5 hr) a-0.50-ml (0.34-g) aliquot of the hydrocarbon solution containing 280 mg (3.3 mmol) of 2-methyl-1-pentene and 65 mg (0.77 mmol) of 2,3-dimethylbutane was injected into the vial containing the potassium *tert*-butoxide solution. The reaction mixture was agitated by hand (~5 sec) and returned to the bath. The first sample was taken at 1 min.

Samples (0.50 ml) were taken by inserting a hypodermic syringe through the self-sealing neoprene septum. These samples were quenched in 5.0 ml of ice water containing 0.5 ml of cyclohexane. Nine samples covering more than three half-lives ($t_{1/2}$ ~40 min) of the isomerization reaction were taken at various intervals. The aqueous dimethyl sulfoxide layer was frozen and the supernatant cyclohexane extract was analyzed by gas chromatography.

The analyses revealed a monotonic decrease in the concentration of 2-methyl-1-pentene with time and a corresponding increase in the concentration of 2-methyl-2-pentene. There was no loss of total olefin relative to the internal standard. First-order rate constants were obtained from plots of the logarithm of the concentration remaining *vs.* time (obtained by a least-squares computer program) for conversions up to about 70%. For higher conversions, deviations from linearity in this plot were obtained since the isomerization reaction is an equilibration. For longer reaction times adequately linear lines were obtained from the plot of the logarithm of the concentration remaining minus concentration at equilibrium *vs.* time. The desired rate constant for the forward reaction (k_f) was obtained from the slope of this

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[17] A. Schriesheim and C. A. Rowe, Jr., *J. Amer. Chem. Soc.*, **84**, 3160 (1962).

line (obtained by a least-squares computer program) which is $k_f + k_r$ and the equilibrium constant, k_f/k_r.[18] The rate constants obtained by the two methods agreed within ±5%.

Analogous procedures were used for the isomerization of the other olefins (Table V). The gas chromatographic analyses for 2,4,4-trimethyl-1-pentene were performed on 21 ft of 20% DC 200 on Chromosorb P 60–80 mesh. The 1-butene analyses were performed on a 10-ft sqalene on acid-treated Chromosorb 40–60 mesh. The allylbenzene isomerizations were analyzed on 21 ft of Carbowax 20 M.

Registry No. **1**, 763-29-1; **2**, 300-57-2; **3**, 107-39-1; K, 7440-09-7; KOH, 1310-58-3; KO-*tert*-Bu, 865-47-4; NaH, 7646-69-7; NaBH$_4$, 16940-66-2; LiBu, 109-72-8; NaCH$_2$SOCH$_3$, 32249-19-7; MgPh$_2$, 555-54-4; NaNH$_2$, 7782-92-5; LiNMe$_2$, 26480-00-2;; LiO-*tert*-Bu, 1907-33-1; NaO-*tert*-Bu, 865-48-5; RbO-*tert*-Bu, 3934-10-9; CsO-*tert*-Bu, 3934-09-6; KOMe, 865-33-8; KO-*i*-Pr, 6831-82-9; LiN-*i*-Pr$_2$, 26396-97-4; Li piperidino, 24316-38-9; Li cyclohexylamine, 26372-63-4; Li aniline, 32249-32-4.

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[18] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 186.

A Novel Intramolecular Free-Radical Cyclization in the Vapor-Phase Arylation of Methyl Benzoate

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Nitrobenzene reacts with methyl benzoate at 500–600° to give phthalide, methyl biphenylcarboxylate, dimethyl biphenyldicarboxylate, and benzene as major products. Methyl *p*-nitrobenzoate with methyl benzoate at 600° gives the same products. Experiments with labeled reagents show that the products arise by hydrogen abstraction, cyclization, and decomposition of the carbomethoxy group of methyl benzoate. Arylation in the liquid phase gives no phthalide; the free-radical cyclization occurs only in the gas phase. Meta substitution predominates in the gas phase, whereas ortho substitution is favored in the liquid phase; apparently thermodynamic factors operating in the intermediate σ complex control the isomer distribution in the gas phase.

Earlier work from this laboratory on high-temperature arylations dealt with the arylation of benzene, aromatic fluorine derivatives, toluene, pyridine, and thiophene.[1] Those reactions involved the thermal decomposition of nitrobenzene above 500° to a phenyl radical and NO$_2$ in the presence of an excess of the aromatic substrate, and yielded biphenyl and substituted biphenyls as the major products. We have extended the scope of these arylations to include the reactions of methyl benzoate with nitrobenzene and methyl *p*-nitrobenzoate, compared the liquid- and vapor-phase arylations of methyl benzoate, and discovered a novel intramolecular free-radical cyclization.

Experimental Section

Reactions were run in a Vycor tube filled with Vycor chips in an electric furnace under pure dry nitrogen with contact times of 10–18 sec. Solutions of reactants were fed by a syringe whose needle fitted through a rubber septum in a glass adaptor connected to the Vycor tube. The syringe was pumped by an infusion pump (Harvard Apparatus Co., Dover, Mass., compact infusion pump, Model 974) at a rate to give the required contact time. During the reaction a sample of the noncondensable gases was taken for mass spectrometric analysis. The vapors from the reaction were condensed at −60°, the condensate was distilled to recover unreacted material, and the distillates and residues were analyzed by gas chromatography and mass spectrometry.

In a typical experiment, a solution of 6.2 g (0.05 mol) of nitrobenzene and 68 g (0.5 mol) of methyl benzoate was passed through a Vycor tube filled with Vycor chips at 600° under a nitrogen flow of 20 cc/min; contact time was 18 sec. The vapors were condensed in a flask at −60°; the condensate was distilled to give 2.9 g of low-boiling products (40–55° at 200 mm), 40.0 g of methyl benzoate, and 9.3 g of residue whose analysis is shown in Table I.

TABLE I

REACTION OF NITROBENZENE AND METHYL *p*-NITROBENZOATE WITH METHYL BENZOATE

Conditions			
Temp, °C	600	600	600
Nitrobenzene, mol	0.05		
Methyl *p*-nitrobenzoate, mol		0.05	0.05
Methyl benzoate, mol	0.50	0.25	0.50
Contact time, sec	18	13	11
Per cent conversion of nitro aromatic	94	72	72
Products[a]	Yield, mol %[b,c]		
Methyl biphenylcarboxylates	25	15	27
Dimethyl biphenyldicarboxylates	4	12	19
Phthalide	17	17	28
Biphenyl	9	3	6

[a] Other products included carbon monoxide, carbon dioxide, formaldehyde, methanol, methane, and methyl terphenylcarboxylates, as well as benzene and methyl benzoate. [b] Calculated on the basis of 0.05 mol of nitrobenzene and methyl *p*-nitrobenzoate giving a theoretical yield of 0.05 mol of each product. [c] Determined by gas chromatography.

Preparation of Aniline-d_5.—A mixture of 10 g of nitrobenzene-d_5, 150 ml of ethanol, 35 ml of 65% hydrazine, and 0.5–0.8 g of wet Raney nickel was refluxed for 1 hr. The filtered reaction mixture was distilled to obtain 5.4 g of deuterated aniline, bp 42° (0.2 mm); isotopic composition 0.1% d_3, 3.7% d_4, 95.2% d_5, 1.0% d_6.

Reaction of Diazotized Aniline-d_5 with Methyl Benzoate.—A solution of 3 g of aniline-d_5, 41 g of methyl benzoate, and 5 g of amyl nitrite was stirred for 5 hr at 120°. The reaction mixture was distilled at 200 mm to give 2.2 g of low-boiling products, 30 g of methyl benzoate, and 11 g of residue. Mass spectrometric analysis showed that the lower boiling products consisted of 96% benzene-d_5 and 4% benzene-d_4; the residue was methyl biphenylcarboxylates-d_5 with small amounts of methyl terphenylcarboxylates-d_9 and -d_{10}.

Analyses.—Mass spectra were measured on a modified Consolidated Model 21-103 instrument with the inlet system at 140°. Isotopic compositions were derived from low-ionizing voltage measurements in which possible isotope effects on sensitivity were ignored. Gas chromatographic separations were run on a column of 10% OV17 on Chromosorb W.

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[1] (a) E. K. Fields and S. Meyerson, *Intra-Science Chem. Rept.*, **3**, 219 (1969); (b) *J. Amer. Chem. Soc.*, **88**, 21 (1966); (c) *J. Org. Chem.*, **35**, 62, 67 (1970); (d) A. I. Feinstein, E. K. Fields, and S. Meyerson, *ibid.*, **35**, 303 (1970).