whether they be solvated carbonium tosylate or oxonium tosylate ion pairs. Thus, the Brown model predicts similar k_r/k_i ratios for the p-H and p-NO$_2$ systems. Furthermore, since the Brown model excludes aryl participation in ionization, the only difference in ionization rates the model predicts must be due to the small inductive effect.

The Brown model is incompatible with the results on both stereochemical and kinetic grounds. Instead of k_r/k_i values being similar for the p-H and p-NO$_2$ systems, they differ by factors of 800–1800 in acetic acid and by a factor of 23,000 for the *threo* isomer in formic acid. Instead of the rates of ionization for the p-H and p-NO$_2$ systems differing by factors of 1.5–4.3, they differ by factors of 190–560. In contrast, these results are completely consistent with the original interpretation[2] in which aryl and solvent compete with one another for participating at the back of secondary carbon in ionization. In the p-H system, phenyl assists in ionization, producing a rate enhancement, and channels the reaction through a phenonium ion to produce ester of retained configuration. In the p-NO$_2$ system, the nitro group depresses the ability of neighboring phenyl to assist in ionization, thereby reducing the rate, and this leaves solvent to assist in the ionization from the back, producing inversion. Thus, the remote theoretical difficulties with the phenonium ion imagined by Brown[10] have been swept away with the broom of experimental fact.

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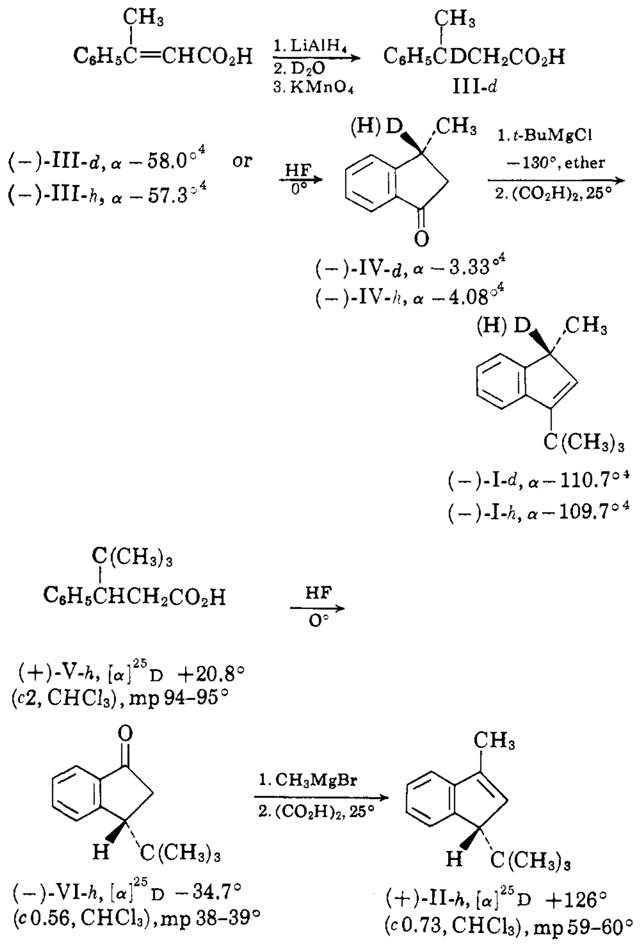
Factors That Control 1,3-Asymmetric Induction and Intramolecularity in Base-Catalyzed 1,3-Proton Transfer in an Indene System[1]

Sir:

As part of our investigation of the mechanism of base-catalyzed proton transfers of carbon acids, we envisioned 1,3-dialkylindenes as systems that would allow study with a variety of weak bases of the stereochemical and isotopic changes that accompany 1,3-proton (allylic proton) transfers.[2] The key intermediate, (+)-I-*h*, had been synthesized when the first 1,3-asymmetric induction result of Bergson, *et al.*, appeared.[3a] After survey, we selected reaction I → II[3b,c] as most ideally suited for investigation.

Preparation of compounds (−)-I-*h* and (−)-I-*d* (0.99 atom of deuterium per molecule, mass spectrometry, ±0.5%) of maximum rotation is formulated.[4] Synthesis of deuterated 3-phenyl-1-butanol paralleled that of its protonated analog.[5] Acid V[6] was resolved to maximum rotation through its brucine salt (methanol–ethanol). Indene (+)-II-*h* was separated from the 10% exocyclic isomer by vpc on a 17% silicone nitrile on 60–80 Firebrick column. The configuration and maximum rotation of (−)-III-*h* were previously determined,[7] and optically pure (−)-III-*h*(*d*) gave optically pure (−)-I-*h*(*d*). Acid (+)-V-*h*, ketone (−)-VI-*h*, and indene (+)-II-*h* did not change melting point or rotation on recrystallization, and the melting point of the corresponding racemates were widely different (*e.g.*, (±)-II-*h*, mp 33–34°). Hence, (+)-II-*h* is at maximum rotation. Optical rotatory dispersion curves (Cary 60 spectropolarimeter) of (−)-I-*h* and (+)-II-*h* in cyclohexane (c 0.03–0.0012) were almost mirror images of one another. Indene (−)-I-*h* exhibited negative Cotton effect with maximum (−) rotations occurring at 298 mμ (Φ 4620°), 287 (Φ 4080°), and 228 (Φ 23,100°), and Φ = 0 at 224 mμ. Indene (+)-II-*h* gave a positive Cotton effect with maximum (+) rotations at 298 mμ (Φ 2850°), 200 (Φ 1470°), and 224 (Φ 32,700°), and Φ = 0 at 215 mμ. Ketones (−)-IV-*h* and (−)-VI-*h* also gave optical rotatory dispersion curves that were roughly mirror images of one another. Thus, (−)-I-*h* and (+)-II-*h* possess opposite configurations.



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[1] This research was supported in part by the U. S. Army Research Office, Durham, N. C., and in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research Grant No. AF-AFOSR-124-65.

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[4] All new compounds gave hydrogen and carbon analyses within 0.2% of theory. All deuterated intermediates contained at least 0.99 atom of deuterium, combustion and falling-drop method. All rotations are neat, l = 1 dm, 25°, λ 589 mμ unless otherwise specified.

[5] R. T. Uyeda and D. J. Cram, *J. Org. Chem.*, 30, 2083 (1965).

[6] C. F. Koelsch, *J. Am. Chem. Soc.*, **65**, 1640 (1943).

[7] (a) D. J. Cram, *ibid.*, **74**, 2137 (1952); (b) *ibid.*, **74**, 2149 (1952).

Table I. Isotopic Exchange, Racemization, and Isomerism of 0.10 *M* Solutions

Run	Starting material	Solvent	Base		*T*, °C	t_m, hr	I, %			II, %		
			Nature	*M*			Obt[a]	Exch	Rac	Obt	Exch	Rac
1	(−)-I-*h*	CH_3OD[b]	CH_3OK	0.10	25	7.7	76.0	64.1	67.3	24.0	86.9	>99.9
2	(−)-I-*d*	CH_3OH	CH_3OK	0.10	25	46.2	75.1	23.2	21.0	24.9	99.7	>99.9
3	(−)-I-*h*	*t*-BuOD[b]	DABCO[c]	0.14	50	16	73.5	0.45	0.2 ± 2	26.5	0.35	1 ± 3
4	(±)-II-*h*	*t*-BuOD[b]	DABCO[c]	0.14	50	16	2.9			97.1	0	
5	(−)-I-*h*	$(CH_3)_2SO$[d]	DABCO[e]	0.10	25	0.83	76.0	2.1	2 ± 1	24.0	1.2	3 ± 1
6	(−)-I-*h*	$(CH_2)_4O$	*n*-$PrND_2$[b]	0.61	25	13.3	74.5	20.3	2 ± 1	25.5	35.8	1 ± 1
7	(−)-I-*h*	$(CH_2)_4O$	*n*-$PrND_2$[b]	0.61	25	1.3	95.3	4.0		4.7	34.7	
8	(±)-II-*h*	$(CH_2)_4O$	*n*-$PrND_2$[b]	0.61	25	13.3	2.5			97.5	0.1	
9	(−)-I-*d*	$(CH_2)_4O$	*n*-$PrNH_2$	0.61	25	44	73.6	20.6	2 ± 1	26.4	94.9	0 ± 1
10	(−)-I-*d*	$(CH_2)_4O$	*n*-$PrNH_2$	0.61	25	13.3	96.0	4.1		4.0	89.7	

[a] Total indene = 100%. Recovery of indene from equilibration experiments was 97–100%. [b] Deuterated 99% in positions indicated [c] Solution 0.0012 *M* in $N(CH_2CH_2)_3ND^+I^-$. [d] 1.0 *M* in *t*-BuOD. Control showed no exchange between two solvents. [e] Solution 0.002 *M* in $N(CH_2CH_2)_3ND^+I^-$.

Use of vpc columns of 3-methyl-3-nitropimelonitrile (4–20%), 2,4,5,7-tetranitrofluorenone (1–3%), Atpet-90 (0.5–0%) on 100–120 acid-washed dimethylsilanized Chromosorb G or 60–80 Firebrick at 80–110° with either nitrogen or helium as carrier gas provided both analytical (±0.5%) and preparative separation of I and II. Deuterium content (±0.5%) of I and II was measured by relative intensities of p and p + 1 peaks in the mass spectra (A.E.I. Model MS-9). Validity of the procedure was confirmed with synthetic mixtures of I-*h* and I-*d*.

Equilibrium constants (*K*) were measured for I ⇄ II under pure nitrogen. Solutions (0.02 *M*) of I-*h* and II-*h* at 102° in *t*-butyl alcohol (0.20 *M* in triethylenediamine or DABCO) gave $K = 6.04$ and 5.99, after 11 and 18 days, respectively. Solutions (0.085 *M*) of I-*h* and II-*h* at 48° in 10 mole % methanol–90 mole % dimethyl sulfoxide (0.39 *M* in DABCO) gave $K = 6.64$ and 6.69 after 20 and 20 days, respectively. Solutions (0.10 *M*) of I-*h* and II-*h* at 25° in tetrahydrofuran (2.0 *M* in *n*-propylamine) gave $K = 7.60$ and 7.50 after 18 and 18 days, respectively. Use of tetradecane as vpc internal standard demonstrated 97–100% recovery of I and II. A plot of log *K* against $1/T$ was linear just within probable error, which suggests that temperature and not solvent effects were largely responsible for the small changes in *K*.

Table I records the conditions for and results of isomerization, isotopic exchange, and racemization reactions. In runs 1–3, 5, 6, and 9, either (−)-I-*h* or (−)-I-*d* was 24–26% isomerized, I and II were separated by vpc, and each was analyzed for deuterium by mass spectrometry and for racemization by polarimetry. In runs 1–5, the isotopic reservoir of the medium at the end of the experiment was diluted by less than 1% by exchanged medium. At the end of runs 6–10, the isotopic reservoir had been diluted not more than 3%. Comparison of the results of runs 3 and 4 and those of 7 and 8 demonstrate that II, once formed, undergoes little isomerization or exchange.

The data indicate the following conclusions. (1) In *t*-BuOD–$N(CH_2CH_2)_3N$–$N(CH_2CH_2)_3ND^+I^-$ (run 3), and in $(CH_3)_2SO$–1 *M* *t*-BuOD–$N(CH_2CH_2)_3N$–$N(CH_2CH_2)_3ND^+I^-$ (run 5), (−)-I-*h* → (+)-II-*h* with 96–100% stereospecificity and with 97–100% intramolecularity. These experiments were carried out in the presence of isotopic reservoirs of essentially the same pK_a as the conjugate acid of the basic catalyst. Very high 1,3-asymmetric induction is visible, and the *t*-ammonium carbanide ion-pair collapse to product must have exceeded ion-pair isotopic exchange with *t*-ammonium iodide or ion-pair reaction with *t*-butyl alcohol by a large factor. (2) In $(CH_2)_4O$ and *n*-$PrNH_2$ or *n*-$PrND_2$ (−)-I-*h* → (+)-II-*d*(*h*) (run 6) and (−)-I-*d* → (+)-II-*h*(*d*) (run 9) with 98–100% stereospecificity and with proton transfer being 65% (run 7) and deuterium transfer being 10% (run 10) intramolecular. (3) In all three media, product of inverted configuration was produced, a fact that indicates that only one face of the intermediate indenyl anion was involved in the proton transfer. These transformations provide further generality of the conducted-tour mechanism for proton conduction along negatively charged π systems.[2] In this system, however, no functional group allows transfer of proton from the front to the back face of the anion. (4) Isotopic exchanges of (−)-I-*h* in $(CH_2)_4O$–*n*-$PrND_2$ and (−)-I-*d* in $(CH_2)_4O$–*n*-$PrNH_2$ (rate constants, k_e) exceed those of racemization (rate constants, k_α) by factors of >7.5 (one-point rate constants for runs 6 and 9). Thus, isotopic exchange of starting material occurs with high retention of configuration by a mechanism already discussed.[2g] This reaction competes with rearrangement. (5) Rearrangements of (−)-I-*h* in CH_3OD–CH_3OK and of (−)-I-*d* in CH_3OH–CH_3OK occurred with <0.1% stereospecificity and with only 13% intramolecularity when H was transferred and <1% when D was transferred (runs 1 and 2). This dissociating and relatively acidic solvent provides no asymmetric induction and only low intramolecularity. (6) The value of k_e/k_α (one-point rate constants) for (−)-I-*h* in CH_3OD is 0.92, while that for (−)-I-*d* in CH_3OH is 1.13 (runs 1 and 2). Thus, isotopic exchange of I in methanol occurs with little stereospecificity, and in this sense resembles other systems in the same medium.[2j] (7) Large combined solvent and kinetic isotope effects of 23 and 29, respectively, are visible from one-point rate constants, k_e and k_α, for (−)-I-*h* in CH_3OD and for (−)-I-d in CH_3OH (runs 1 and 2), but their interpretation requires good kinetic data. Discussion of collapse ratios for the indenyl anion also requires detailed kinetic data, which are being collected.[8]

[8] The methods of Bergson[3] and our methods differ, although some of our conclusions correspond. Our conclusions concerning 1,3-asymmetric induction and intramolecularity in isomerization rest on isolation and analysis of products whose configuration and maximum rotations were independently determined. In three out of our four media, isotopic reservoirs of the same pK_a as the conjugate acid of the basic catalyst were present. In two of our media, both directions of isotopic exchange between substrate and media were examined. The conclusions of Bergson, *et al.*, were drawn solely from kinetic data which involved isolation of neither starting material nor product. Their elegant observation of high 1,3-asymmetric induction and its steric direction[3e] and all of their observations of intramolecularity[3] were made in the absence of isotopic reservoirs of the same pK_a as the conjugate acid of the basic catalyst. Their earlier conclusion of *high* 1,3-asymmetric induction[3d] rested on unsupported assumptions. Their results and conclusions conflict with ours only in one detail. We demonstrated that I gives II reversibly with an equilibrium constant of about 7 at 25°, whereas they state "tautomer (a) [our I] was completely rearranged to (b) [our II] as far as could be determined within the limits of experimental error."

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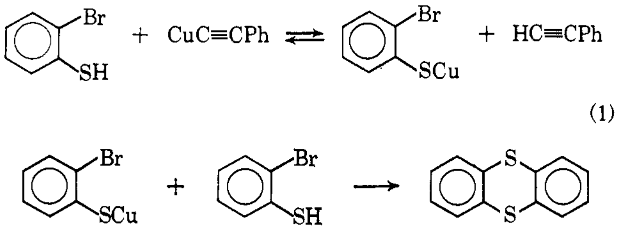
Copper(I) Substitutions. Benzo[*b*]thiophenes

Sir:

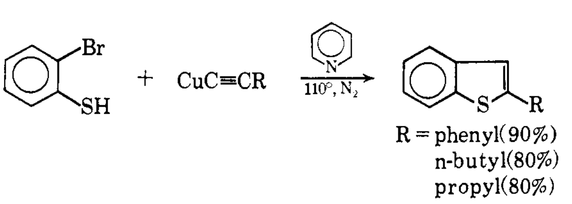
Selected benzo[*b*]thiophenes have been obtained by the pyrolysis of 2-alkylthiophenols over cupric oxide–chromic anhydride,[1] by the acid-catalyzed cyclization of aryl α-keto thioethers,[2] and *via* the reduction of 2-alkylidene-3-ketodihydrobenzothiophenes with sodium borohydride[3] and lithium aluminum hydride.[4]

We wish to report a direct one-step synthesis of 2-substituted benzo[*b*]thiophenes from *o*-bromothiophenol and cuprous acetylides. The reaction is all the more interesting because of our previous inability to obtain this heterocyclic system from these reagents.[5] Thus, reaction of a 1:1 solution of *o*-bromothiophenol and cuprous phenylacetylide in pyridine[6] yields thianthrene and phenylacetylene (1).

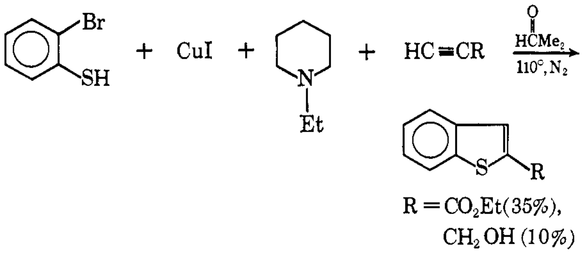


(1)

We now find that this exchange and subsequent substitutions can be circumvented by operating at high dilution of the halothiophenol. Thus, very slow (24 hr) addition of a pyridine solution of *o*-bromothiophenol to a mixture of the acetylide in pyridine affords the benzo[*b*]thiophenes in good yield. The following transformations are illustrative.[7] Less stable acetylides can be generated *in situ* (3).



(2)



(3)

These results suggest the thiophenyl moiety to be easily constructed upon a variety of aromatic systems.

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[4] O. P. Shkurko, *Chem. Abstr.*, **63**, 11474*h* (1965).

[5] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, **31**, 4071 (1966).

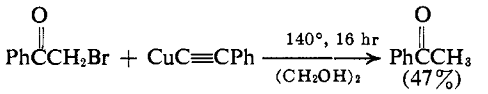
[6] The corresponding *o*-halophenols are readily converted to benzofurans under these conditions.[5]

[7] All compounds have the correct infrared, nmr, elemental analysis, and melting point where it is known. Yields represent purified substances.

Copper(I) Substitutions. Furans from α-Halo Ketones

Sir:

Unlike the lithio salt of dimethylcopper(I),[1] cuprous acetylides are not prone to react with aliphatic halides. Thus, both alkyl and benzyl bromides are inert toward cuprous acetylide under conditions that allow for an easy substitution of aryl halides.[2] Phenacyl bromide affords intractable tars upon long reflex with cuprous acetylides in dimethylformamide and is reduced to acetophenone[2] by either cuprous bromide or cuprous phenylacetylide in ethylene glycol[2] (1). At higher temperatures, these halides can be cleanly substituted.[3] All reactions were conducted in sealed tubes under nitrogen.



$$\mathrm{Ph\overset{\overset{O}{\|}}{C}CH_2Br} + \mathrm{CuC{\equiv}CPh} \xrightarrow[(\mathrm{CH_2OH})_2]{140°,\ 16\ \mathrm{hr}} \underset{(47\%)}{\mathrm{Ph\overset{\overset{O}{\|}}{C}CH_3}} \qquad (1)$$

$$\mathrm{PhCH_2Br} + \mathrm{CuC{\equiv}CPh} \xrightarrow[\text{N-methyl-pyrrolidone}]{245°,\ 5\ \mathrm{min}} \underset{(90\%)}{\mathrm{PhCH_2C{\equiv}CPh}} \qquad (2)$$

$$\mathrm{CH_2{=}CHCH_2Br} + \mathrm{CuC{\equiv}CPh} \xrightarrow[\mathrm{PhNO_2}]{240°} \underset{(83\%)}{\mathrm{CH_2{=}CHCH_2C{\equiv}CPh}} \qquad (3)$$

Most significantly, α-halo ketones can be converted in one step to the corresponding furans. The examples in eq 4–7 are illustrative.

In no case was the uncyclized acetylenic ketone isolated. Cyclization through the copper-coordinated enol[4] is consistent with the ready preparation of benzo-

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[3] The yields of all reactions reported herein do not vary appreciably with the diluents nitrobenzene, N-methylpyrrolidone, or α-methylnaphthalene. Yields are somewhat less when the reaction is conducted without solvent. The yields are given for purified substances.

[4] That is, Cu(I) (like Cu(II)) salts must catalyze the enolization; *cf.* C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, **30**, 587 (1965).