Dynamic Stereochemistry of Imines and Derivatives. 14. Restricted sp^2–sp^2 Carbon–Carbon Bond Rotation in Ortho-Substituted *N*-(1-Arylethylidene)alkylamines

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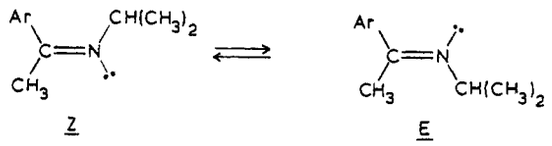
A series of imines, Ar(Me)C=NCHMe$_2$, where Ar = *o*-X-C$_6$H$_4$ (X = Me, Ph, NO$_2$, OCH$_3$) or 1-naphthyl, is shown by ^{1}H NMR spectroscopy to exist in solution as an equilibrating *E*/*Z* isomeric mixture at ambient temperature. The observation of anisochronous *gem*-methyl signals in the *Z* isomer indicates a chiral ground-state conformation where the aryl ring is twisted out of the imino plane. Barriers to rotation around the aryl–imino bond were found by dynamic NMR studies to be $\Delta G^{\ddagger}$ = 14.4–20.4 kcal mol^{-1}, increasing with the steric bulk of the ortho substituent. The ortho-disubstituted chiral imine 2,4,6-Me$_3$C$_6$H$_2$(Me)C=NCH(Ph)Me shows nonequivalent *o*-methyl groups and meta protons up to the maximum temperature investigated (~200 °C) in hydrocarbon solvents, indicating a very high barrier (≥27 kcal mol^{-1}) to ring rotation. However, in chlorinated hydrocarbon solvents, signal collapse is observed below 200 °C. It is suggested that a net ring rotation in the *Z* form is brought about by a mechanism involving imine–enamine tautomerism and stereomutation to the *E* isomer.

Previous papers in this series[1] have dealt with *E*/*Z* equilibria about the C=N bond in imines and the kinetics and mechanisms of the isomerization process. Proton chemical-shift data and a study of molecular models indicated that the *Z* isomer of imines derived from ortho-substituted aryl ketones and aldehydes adopted a nonplanar ground state having the C-aryl ring twisted out of the imino plane.[2,3] We now describe a series of ketimines derived from ortho-substituted acetophenones where the NMR data establish unambiguously that this is the case and enable the rate of rotation around the aryl–imino bond to be investigated.



Z E

1, Ar = 2-CH$_3$C$_6$H$_4$
2, Ar = 2-C$_6$H$_5$C$_6$H$_4$
3, Ar = 2-NO$_2$C$_6$H$_4$
4, Ar = 2-CH$_3$OC$_6$H$_4$
5, Ar = 1-naphthyl

Results and Discussion

The ^{1}H NMR spectra of the ortho-substituted *N*-(1-arylethylidene)isopropylamines **1**–**5** were consistent with the existence of an equilibrating *E*/*Z* isomer mixture in solution, as expected from the results of a previous investigation into the factors controlling imine equilibria in related compounds.[2] In the case of the crystalline compounds **2** and **3**, the *Z* isomer could be isolated by recrystallization and could be observed by NMR to equilibrate slowly on dissolution. The spectra were assigned configurations on the basis that the *N*-alkyl signals (methyl and methine) are shifted to higher field in the *Z* isomer by analogy with related imines.[2,3] Furthermore, the assignments were consistent in that the more shielded CMe$_2$ group exhibited the signal doubling in each case (see below). The equilibrium (Table I) favored the *Z* isomer in **1**, **4**, and **5** but was almost exactly balanced in **2** and **3**. Previous studies of *E*/*Z* equilibria in ketimines derived from aryl alkyl ketones have shown that the *N*-alkyl group can prefer to reside cis to the aryl group if the latter possesses ortho substituents.[2] The *E*/*Z* ratios in **1**, **3**, **4**, and **5** are similar to those found in their *N*-methyl analogues.[2]

An unusual feature in the spectra of compounds **1** and **2** (in CCl$_4$) was that the isopropyl methyl signals from the *Z* isomer were split into two doublets of equal intensity, indicating that the *gem*-methyl groups were diastereotopic. The spectra of **3** and **5** in carbon tetrachloride, on the other hand, showed the normal single doublet for each isomer. However, when the spectra were recorded in benzene-d_6 or toluene-d_8 solution, all five compounds showed doubling of the isopropyl methyl signal in the *Z* form. It is not uncommon for aromatic solvents to resolve accidentally isochronous signals by inducing a differential solvent shift.[4] In the case of imine **4**, geminal anisochronism could not be detected at ambient temperature in either solvent. However, on lowering the sample temperature to −6 °C, the methyl doublet of the *Z* isomer collapsed to a broad resonance and at −12 °C resolved into two components. Therefore, in this case the equivalence of the *gem*-methyl signals at ambient temperature is not accidental, but rather it is due to an environmental averaging process that is fast on the NMR time scale above 6 °C. The isopropyl methyls of the *E* isomer in **1**–**5** remained isochronous down to the lowest temperature investigated (ca. −80 °C).

These results indicate that the *Z* isomer adopts a chiral conformation **6** where the aryl ring is twisted out of the imino plane. Furthermore, rotation through the coplanar states **7** and **8** to obtain the enantiomeric conformation **6′** (i.e., enantiomerization) must be slow on the NMR time scale at ambient temperature (below −6 °C in the case of **4**). This conclu-

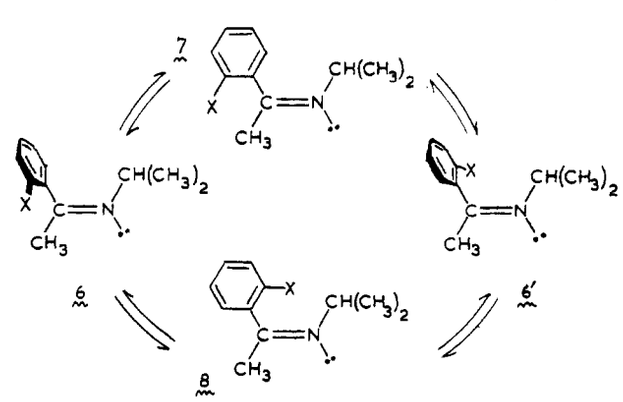


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Table I. NMR Data for Diastereomeric Imines and Barriers to Rotation around the Aryl–Imino Bond in the *Z* Isomer

imine	% $Z^{a,b}$	$\delta_{NCH}{}^b$		$\delta_{C(CH_3)_2}{}^b$		T_c, °C	k (s^{-1})	$\Delta G^{\ddagger}$ (kcal mol^{-1})
		Z	*E*	*Z*	*E*			
1	78	3.19	3.65	1.02, 1.11	1.18	74	23 ± 4[d]	18.3 ± 0.2
	(77)	(3.04)	(3.72)	(0.91, 1.01)	(1.15)			
2	51	3.36	3.54	0.86, 1.03	1.14	63	23 ± 4[d]	17.7 ± 0.2
	(54)	(3.20)	(3.65)	(0.72, 0.93)	(1.14)			
3	47	2.97	3.60	0.98, 1.04	1.13	56	13 ± 3[d]	17.7 ± 0.2
	(48)	(2.93)	(3.86)	(0.95)	(1.13)			
4	76	3.41	3.73	1.13, 1.17	1.20	−6	9 ± 4[e]	14.4 ± 0.4
	(72)	(3.08)	(3.79)	(0.95)	(1.13)			
5	84	3.23	3.80	1.06, 1.08	1.28	82	2 ± 1[e]	20.4 ± 0.4
	(86)	(3.05)	(3.85)	(0.96)	(1.24)			
10	73[g]	2.74, 2.80	3.32	0.87	1.07	61	74 ± 25[f]	16.8 ± 0.3[g]

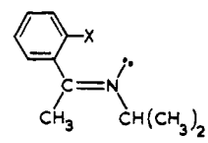
[a] Error limits ±2. [b] Open data were obtained at 100 MHz in toluene-d_8 solution, except for **10** (see footnote *g*); data in parentheses refer to carbon tetrachloride solution. [c] Error limits ± 2 °C in measuring the coalescence temperature (T_c). [d] Rate constant (k) derived by computer-assisted analysis of the exchange broadened isopropyl methyl signals. [e] Estimated from $k = \pi\Delta\nu/2^{1/2}$ applied to the coalesced isopropyl methyl signals (see ref 16). [f] Estimated from $k = \pi(\Delta\nu_{AB}{}^2 + 6J_{AB}{}^2)^{1/2}/2^{1/2}$ applied to the coalesced NCH_2 AB system (see ref 17). [g] Data for this imine were determined in deuteriochloroform solution at 220 MHz (see text).

sion supports our previous suggestions[2,3] (based on chemical-shift data and an inspection of molecular models) that ortho-substituted C-aryl imines adopt a nonplanar conformation of this type.

The anisochronous *gem*-methyl signals of the *Z* isomers were observed to broaden and coalesce on raising the temperature. Rate constants (k) for rotation around the aryl–imino bond in the *Z* isomer at the coalescence temperature (T_c) and derived free energies of activation ($\Delta G^{\ddagger}$) are given in Table I. The magnitude of this rotational barrier is very sensitive to the ortho substituent (X) and decreases along the series X = 1-naphthyl ≫ methyl > phenyl ≈ nitro ≫ methoxyl. Enantiomerization can take place via either of the coplanar states **7** or **8**, which involve X/CH_3 (four-bond) or $X/CH(CH_3)_2$ (five-bond) passing interactions, respectively. An inspection of molecular models suggests that rotation through **7** is the favored pathway. Undoubtedly the barriers are primarily "steric" in origin, though conjugating ortho substituents could also exert an effect on the aryl–imino conjugation in the coplanar states **7** and **8**. However, the effect of conjugation might be reduced by steric inhibition of conjugation between the ortho substituent and the ring in **7** or **8**. The $\Delta G^{\ddagger}$ values for aryl rotation in compounds **1–5** decrease roughly in line with the conformational energy of the ortho substituent (based on cyclohexane axial–equatorial equilibria) with the exception that the phenyl and methyl sequence is reversed. However, the lower barrier in **2** relative to **1** parallels the situation in substituted ethanes where the C–C rotational barrier decreases on replacing methyl by phenyl.[5] The nature of the nonbonded interactions in the transition state for rotation around the sp^2–sp^2 C–C bond in **1–5** will differ somewhat from those obtaining in sp^3–sp^3 ethane systems. Mesomeric effects may also contribute; thus, the methoxyl substituent in **4** could stabilize the coplanar state **7** by increasing the conjugation energy and vice versa for the nitro substituent in **3** (cf. a recent study of central bond rotation in substituted biphenyls[6]).

None of these amines showed any splitting of the isopropyl methyl doublet for the *E* isomer even at low temperature (down to ca. −80 °C). Rotation about the aryl–imino bond in the *E* isomer should be easier than in the *Z* form, since the $X/CH(CH_3)_2$ passing interaction is absent in the coplanar conformation **9**.

Compound **10** which contains a prochiral neopentyl group also exhibits restricted rotation around the 1-naphthyl–imino bond in the *Z* isomer. Thus, at 0 °C in deuteriochloroform solution the NCH_2 signal of the *Z* isomer was broadened, but interpretation was complicated by homoallylic coupling to the



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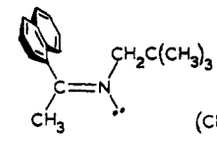

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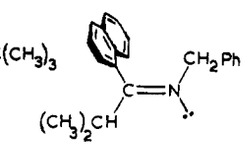
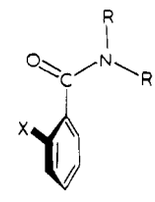


11

$=CCH_3$ protons (^5J = 1.5 Hz). However, the $=CCD_3$ analogue (prepared by exchange with CD_3OD) showed a strongly coupled AB pattern ($\Delta\nu_{AB}$ = 8.0 Hz at 100 MHz; J_{AB} = 12.9 Hz) for the NCH_2 signals of the *Z* isomer at −10 °C. The signal separation, $\Delta\nu_{AB}$, was too small to allow the dynamic coalescence point to be located, particularly since $\Delta\nu$ decreased on raising the temperature. Furthermore, $\Delta\nu_{AB}$ was even smaller (or zero) in other solvents (including toluene-d_8). Variable-temperature spectra were therefore recorded at 220 MHz in deuteriochloroform solution. The lower barrier in **10** relative to **5** (Table I) reflects the somewhat smaller steric requirements of the neopentyl group relative to isopropyl in this system. The barrier in **10** is also much lower than that reported[7] for naphthyl ring rotation in **11** ($\Delta G^{\ddagger}$ 23.6 kcal mol^{-1}), in line with the greater steric bulk of the *C*-alkyl group in the latter compound.

The stereochemical situation in these imines is somewhat similar to that obtaining in ortho-substituted benzamides (**12**)



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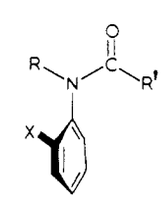

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and anilides (**13**) which also adopt chiral nonplanar conformations and exhibit restricted rotation around the aryl–C(O) or N–aryl bonds.[8,9] The aryl rotational barrier in amide **12** (X = CH_3; R = CH_2CH_3)[8] appears to be ~15 kcal mol^{-1} as compared with $\Delta G^{\ddagger}$ = 18.3 kcal mol^{-1} in imine **1** and 20.0 kcal mol^{-1} in anilide **13** (X = CH_3; R = CH_2Ph; R′ = CH_3).[9] Replacement of the *o*-tolyl moiety in **12** and **13** by 1-naphthyl also raises the barrier to aryl ring rotation (cf. imines **1** and **5**).[8,9]

Restricted aryl ring rotation cannot normally be detected in symmetrically ortho-disubstituted compounds, with the

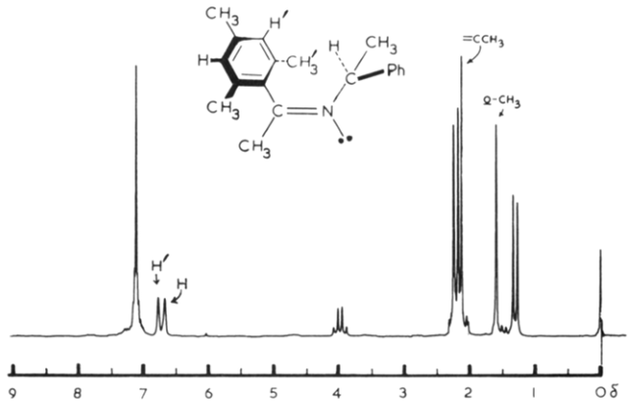
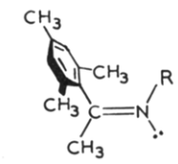


Figure 1. ^{1}H NMR spectrum of **15** at 100 MHz in carbon tetrachloride solution at 32 °C.

aid of prochiral *N*-alkyl probes (e.g., **14**), since such compounds possess a molecular σ plane that passes through the N–R moiety in the bisected conformation depicted in **14;** hence, the paired geminal substituents in the N–R group are enantiotopic and isochronous.[4] However, if R is chiral (e.g., **15**) the *o*-methyl groups (and the *m*-hydrogen atoms) will be



14 R = $CH(CH_3)_2$
15 R = $CH(Ph)CH_3$
16 R = CH_3

diastereotopic and potentially anisochronous, provided that rotation of the ring through the coplanar conformation is slow on the NMR time scale. The stereochemical situation is similar to that in chiral 2,6-dimethoxybenzamide investigated by Siddall and Garner.[10] Accordingly, compound **15** was prepared from 1-(2,4,6-trimethylphenyl)ethanone and (±)-1-phenylethylamine. The ^{1}H NMR spectrum in CCl_4 solution (Figure 1) showed one predominant isomeric form with signals at δ 1.29 (3 H, d, $^3J_{HCH}$ = 6.4 Hz, $CHCH_3$), 1.59 (3 H, s, *o*-CH_3), 2.11 (3 H, s, $=CCH_3$), 2.17 and 2.24 (each 3 H, s, *o*-CH_3' and *p*-CH_3), 3.98 (1 H, q, $^3J_{HCCH}$ = 6.4 Hz, NCH), 6.68 (1 H, s, meta H), 6.78 (1 H, s, meta H'), and 7.11 (5 H, br s, C_6H_5). The $=CCD_3$ analogue of **15** (prepared by deuterium exchange with CD_3OD) showed the same chemical shifts in CCl_4 solution, except that the signal at δ 2.11 had disappeared, thus confirming the assignment of this signal to the $=CCH_3$ group. The highest field singlet was assigned to one of the *o*-methyl groups on account of the site exchange observed at high temperature in other solvents (see below). This imine will exist predominantly in the *Z* configuration (as depicted in **15**) by analogy with compound **1** and the closely related imine **16** (R = CH_3) which has been reported to exist at equilibrium as 95% *Z* isomer.[2] Minor signals in the spectrum of **15** at δ 1.46 (d, $^3J_{HCCH}$ = 6.5 Hz, $CHCH_3$) and 4.68 (q, $^3J_{HCCH}$ = 6.5 Hz, $CHCH_3$) are attributed to a small proportion (ca. 6%) of the *E* isomer.

The chemical-shift difference between the diastereotopic *o*-methyl groups in the predominant *Z* isomer is remarkably large (ca. 0.6 ppm in CCl_4 solution). One of these signals (δ 1.59) is at unusually high field for an aryl methyl group which typically resonates near δ 2.3. This may be rationalized in terms of a preferred ground-state conformation of the *N*-alkyl group which places one of the *o*-methyl groups in the strongly shielding region above the face of the phenyl ring in the 1-phenylethyl group as depicted in Figure 2.

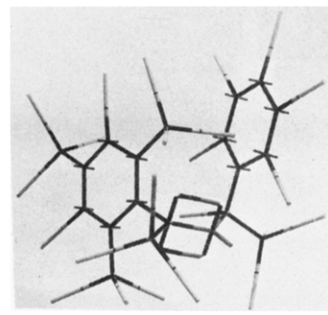


Figure 2. Framework model illustrating the postulated conformation of **15.**

Variable-temperature NMR studies on **15** in diphenyl ether indicate a very high barrier to ring rotation. Thus, the two *o*-methyl signals did not coalesce up to 200 °C, the highest temperature attainable. Accordingly, $\Delta G^{\ddagger}$ can be estimated to be $\geq$27 kcal mol^{-1} based on a maximum observed exchange broadening of 0.7 Hz. Similarly, in decalin solution, the meta protons remained nonequivalent up to the highest temperature investigated (188 °C). However, in diphenyl ether solution at 200 °C the methyl and methine signals of the 1-phenylethyl group in the minor (*E*) isomer had broadened significantly. Clearly *E*–*Z* isomerization about the imino bond was occurring at an appreciable rate on the NMR time scale at 200 °C (the greater exchange broadening of the *E* isomer is expected as $k_{E\rightarrow Z} > k_{Z\rightarrow E}$).

Site-exchange phenomena were more evident in spectra recorded in 1,2,4-trichlorobenzene solution. The spectrum of **15** in this solvent at 50 °C was similar to that observed in carbon tetrachloride at ambient temperature, except for a virtual superimposition of the *p*-methyl, iminomethyl, and low-field *o*-methyl resonances (Figure 3a). However, at 198 °C the two *o*-methyl signals had coalesced to a broad resonance, and, furthermore, the NCH and $NCCH_3$ signals of the minor (*E*) isomer (originally at δ 4.62 and 1.36 from octamethylcyclotetrasiloxane) had coalesced with the corresponding signals of the *Z* isomer at δ 3.93 and 1.17 (Figure 3b). Therefore, mesityl ring rotation in the *Z* isomer and *E*–*Z* isomerization were both becoming fast at the same temperature (ca. 198 °C). Similar effects were observed in pentachloroethane solution, though at lower temperature (Figure 4). The nonequivalent meta-proton signals in the *Z* isomer and the NCH signals of the *E* and *Z* isomers both coalesced at ca. 150 °C, and, furthermore, the *o*-methyl signals had broadened and were approaching coalescence at 150 °C. Spectra recorded in hexachlorobutadiene solution at 150 °C showed similar effects. Accordingly, mesityl ring topomerization in the *Z* isomer and *Z*–*E* imine isomerization appear to be linked stereodynamic processes. Mesityl ring rotation is relatively unhindered in the minor (*E*) isomer; hence, *Z*–*E* imine isomerization could also bring about coalescence of the *o*-methyl signals in the *Z* isomer. Support for this suggestion is derived from the observation that the addition of a trace amount of benzoic acid to the decalin solution at 188 °C also brought about coalescence of the two meta-proton signals in the *Z* isomer and of the (*E*)- and (*Z*)-NCH signals. Previous work has shown that benzoic acid catalyzes *E*–*Z* isomerization;[11] hence, the observation that it also catalyzes rotation around the C–mesityl bond affords further evidence that this process is linked to the former.

Kessler[12] has previously postulated a similar linked mechanism for *N*-aryl rotation in the *E* isomer of amide **17**

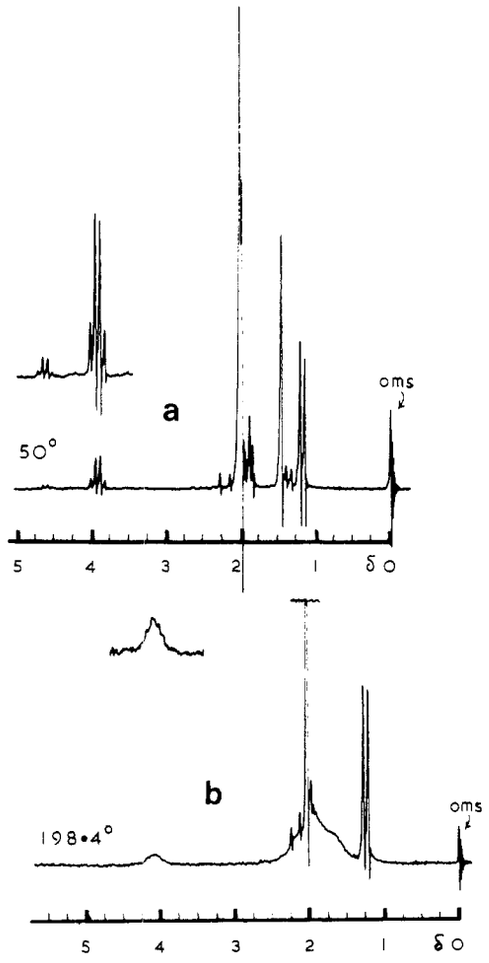
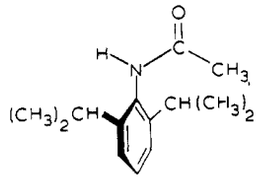


Figure 3. (a) 100-MHz NMR spectrum of **15** in 1,2,4-trichlorobenzene at 50 °C; (b) same solution at 198 °C (oms = octamethylcyclotetrasiloxane).

involving rotation around the amide bond and fast *N*-aryl rotation in the less hindered *Z* form.



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However, the situation in **15** appears to be more complex, since the $=CCH_3$ signal also collapsed to a broad resonance in the same temperature range where the other coalescence phenomena were observed (see Figures 3 and 4). Similar behavior has previously been observed in the high-temperature NMR spectra of other imines containing a $=CCH_3$ group and is due to rapid proton exchange involving transient formation of the enamine tautomer.[13] Therefore, fast imine–enamine tautomerization can bring about both *E*–*Z* isomerization and a net topomerization of the diastereotopic *o*-methyl groups in the *Z* isomer (see Scheme I). The aryl bond-rotation step may take place in the *E* isomer or possibly in the enamine tautomer and is probably not rate determining. Apparently, the rate of imine–enamine tautomerization is greater in the chlorinated solvents as compared with diphenyl ether. This could be due to a solvent effect or to catalysis of the tautomerization by trace amounts of acid material generated in the

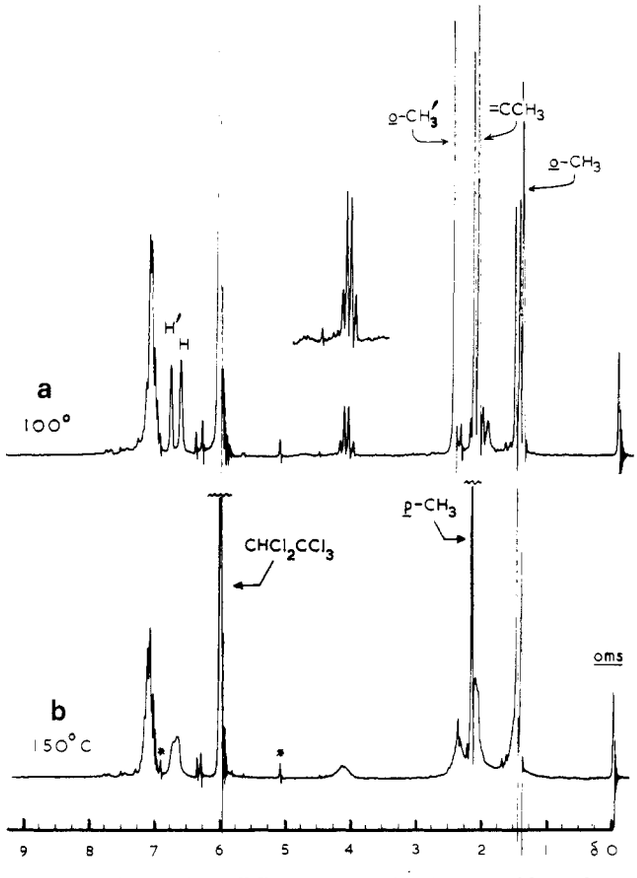


Figure 4. (a) 100-MHz NMR spectrum of **15** in pentachloroethane at 100 °C; (b) same solution at 150 °C (oms = octamethylcyclotetrasiloxane; * denotes ^{13}C satellites of the solvent signal).

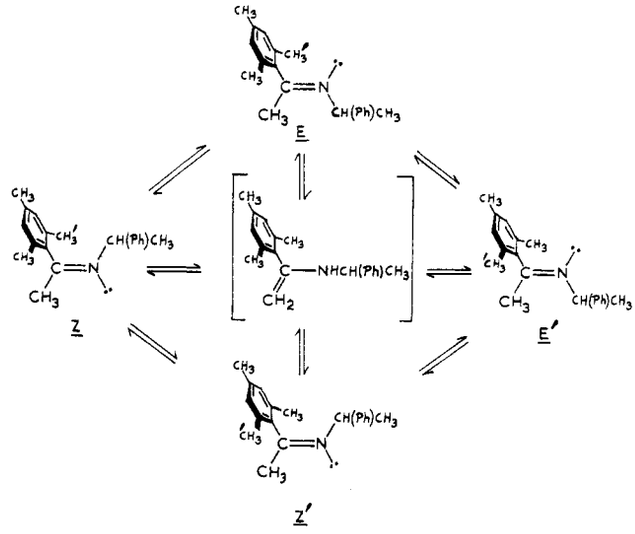
chlorinated solvents at high temperature. It has previously been noted that isomerization around the C=N bond in hydrazones is accelerated in chlorinated solvents.[14]

In conclusion, the mechanism that brings about a net rotation around the aryl–imino bond in the *Z* isomer of imine **13** appears to be facilitated by high temperature, acidity, and imine–enamine tautomerism.

Experimental Section

NMR spectra were recorded at 100 MHz on a Varian XL-100 or a Perkin-Elmer R14 spectrometer (all variable-temperature studies were performed on the XL-100). Solvents for dynamic NMR studies

Scheme I



were washed with sodium carbonate solution and stored over anhydrous potassium carbonate. Probe temperature calibration and band-shape analyses were performed as described previously.[11]

2'-Phenylacetophenone (10 g, 95%) was prepared by reaction of the Grignard reagent from 2-iododiphenyl (12 g) with acetic anhydride (30 cm^3) in ether at −70 °C under nitrogen, bp 80 °C (0.1 Torr) (lit.[15], 104–105 °C (1.0 Torr)). The other ketones were obtained commercially.

***N*-[1-(2'-Methylphenyl)ethylidene]isopropylamine (1)** was obtained in 66% yield by refluxing 1-(2'-methylphenyl)ethanone (2.0 g), isopropylamine (16 cm^3), and titanium(IV) chloride (1.0 cm^3) in benzene for 3 h under nitrogen according to the procedure reported previously,[2] bp 58–60 °C (0.05 Torr).

Anal. Calcd for $C_{12}H_{17}N$: C, 82.2; H, 9.8; N, 8.0. Found: C, 82.2; H, 9.7; N, 7.8.

***N*-[1-(2'-Diphenyl)ethylidene]isopropylamine (2)** was similarly prepared from 2-phenylacetophenone (3.0 g), isopropylamine (20 cm^3), and titanium(IV) chloride (3.0 cm^3). Recrystallization from dry ethanol gave crystals of the *Z* isomer (2.3 g, 64%), mp 121 °C.

Anal. Calcd for $C_{17}H_{19}N$: C, 86.0; H, 8.1; N, 5.9. Found: C, 86.3; H, 8.4; N, 5.6.

***N*-[1-(2'-Nitrophenyl)ethylidene]isopropylamine (3)** was similarly obtained from 1-(2'-nitrophenyl)ethanone (3.0 g), isopropylamine (16 cm^3), and titanium(IV) chloride (1.5 cm^3). Distillation under reduced pressure followed by recrystallization from light petroleum afforded crystals of the *Z* isomer (2.2 g, 59%), mp 74–77 °C.

Anal. Calcd for $C_{11}H_{14}N_2O$: C, 64.0; H, 6.8; N, 13.6. Found: C. 64.25; H, 6.9; N, 13.7.

***N*-[1-(2'-Methoxyphenyl)ethylidene]isopropylamine (4)** was likewise obtained from 1-(2'-methoxyphenyl)ethanone (3 g) in 80% yield, bp 65 °C (0.05 Torr).

Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.95; N, 7.3. Found: C, 75.6; H, 8.6; N, 7.2.

***N*-[1-(1'-Naphthyl)ethylidene]-2,2-dimethylpropylamine (10)** was similarly prepared in 45% yield from 1-(1'-naphthyl)ethanone (2 cm^3), 2,2-dimethylpropylamine (10 cm^3), and titanium(IV) chloride (1 cm^3), bp 110 °C (0.1 Torr).

Anal. Calcd for $C_{17}H_{21}N$: C, 85.35; H, 8.8; N, 5.85. Found: C, 85.6; H, 8.8; N, 5.6.

***N*-[1-(2',4',6'-Trimethylphenyl)ethylidene]-1-phenylethylamine (15)** was obtained in 50% yield from 1-(2',4',6'-trimethylphenyl)ethanone (2.0 g), (±)-1-phenylethylamine (16 cm^3), and titanium(IV) chloride (1.0 cm^3), bp 128–130 °C (0.1 Torr).

Anal. Calcd for $C_{19}H_{23}N$: C, 86.0; H, 8.7; N, 5.3. Found: C, 85.7; H, 9.0; N, 5.6.

Replacement of the $=CCH_3$ protons in **10** and **15** by deuterium was achieved by allowing a solution of the imine in deuteriomethanol (99.8%) to stand for a few hours. The solvent was then removed and the process repeated until NMR analysis showed that this methyl signal had essentially disappeared. Imine **5** has been reported previously.[2]

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Registry No.—(*E*)-**1**, 66674-84-8; (*Z*)-**1**, 66674-85-9; (*E*)-**2**, 66674-86-0; (*Z*)-**2**, 66674-87-1; (*E*)-**3**, 66674-88-2; (*Z*)-**3**, 66674-89-3; (*E*)-**4**, 66674-90-6; (*Z*)-**4**, 66674-91-7; (*E*)-**5**, 38512-09-3; (*Z*)-**5**, 38512-03-7; (*E*)-**10**, 66674-92-8; (*Z*)-**10**, 66674-93-9; **15**, 66674-94-0; 2'-phenylacetophenone, 2142-66-7; 2-iododiphenyl, 2113-51-1; 1-(2'-methylphenyl)ethanone, 577-16-2; isopropylamine, 75-31-0; 1-(2'-nitrophenyl)ethanone, 577-59-3; 1-(2'-methoxyphenyl)ethanone, 579-74-8; 1-(1'-naphthyl)ethanone, 941-98-0; 2,2-dimethylpropylamine, 5813-64-9; 1-(2',4',6'-trimethylphenyl)ethanone, 1667-01-2; (±)-1-phenylethylamine, 618-36-0.

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New Furanoid *ent*-Clerodanes from *Baccharis tricuneata*[1]

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Because of the antitumor and antiviral properties of a crude extract, the constituents of the Colombian medicinal plant *Baccharis tricuneata* (L.f.) Pers. var. *tricuneata* have been investigated. The hexane extract yielded four new *ent*-clerodanes, bacchotricuneatins A–D (**1**, **2**, **3**, and **4a**), whose structures were elucidated, primarily by ^1H and ^{13}C NMR spectrometry. Proof for the structure and stereochemistry of A and B was obtained by X-ray analysis. Isolated from the ether extract were cirsimaritin, cirsiliol, and scopoletin.

Previous reports[2–4] on the pharmacological activity of some South American *Baccharis* species and their constituents made it of interest to examine the Colombian species *Baccharis tricuneata* (L.f.) Pers. var. *tricuneata*, which is widely used in folk medicine. Initial pharmacological screening revealed that an ethanol extract possessed significant antitumor and antiviral activity which corresponds to the medicinal use of the plant in Colombia;[5,6] consequently, we undertook a study of its constituents. We now wish to report the isolation and structure determination of four new closely related *ent*-clerodane diterpenoids, bacchotricuneatin A–D (**1**, **2**, **3**, and **4a**). The flavonoids cirsimaritin (**6a**) and cirsiliol (**6b**) and the coumarin scopoletin (**7**) were also isolated.[7]

The hexane extract of the aerial parts of *B. tricuneata*

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