Anomalous Shielding and Hidden Partner Chemical Exchange in the ^{1}H NMR Spectra of the Bisurethane Diazetidines, the 1,2-Diaryl-3,5-dialkyl-6,7-dialkoxycarbonyl-4-oxo-6,7-diazabicyclo[3.2.0]hept-2-enes

Donald Mackay,* Deane D. McIntyre, and Ian D. Wigle
Guelph-Waterloo Centre for Graduate Work in Chemistry, Waterloo Campus, Department of Chemistry, University of Waterloo, Waterloo, Ontario N2L 3GI, Canada

The bicyclic diazetidines (**3**), (**11**), and (**17**), have *trans*-pyramidal nitrogens, the ester group on N(7) being sterically protected and very unreactive. Its alkyl group is close to the face of the aryl ring attached to C(1) and shows remarkable shielding effects in its ^{1}H NMR spectrum, while the alkyl group of the N(6) ester shows a more normal resonance. In the methyl esters the OMe group of the N(7) ester is *ca.* 1 ppm upfield of the other ester OMe group and in each of the oxymethylene compounds one of the protons of the N(7) ester group is upfield of its (unshielded) diastereotopic partner by *ca.* 2 ppm.

These shielded resonances are extremely broadened at room temperature, especially at high field. DNMR studies show that on cooling, the shielded absorption in each case broadens further and then sharpens into two peaks, an effect due to the interconversion of two major conformations with one or more of very low population, an example of 'hidden partner exchange.' The exchange processes responsible, which occur between protons in the N(7) ester group in very shielded (major conformations) and normal (minor)environments, must involve either N(7) inversion or N(7)–CO rotation.

The di-methyl and -trichloroethyl compounds (**3a**) and (**3c**), were investigated in detail in CD_2Cl_2 and C_7D_8. In (**3a**) the N(7) ester OMe resonance of the minor partner was found at δ 3.65 (*ca.* 3%, 200 K, CD_2Cl_2), its identity being confirmed by low-temperature examination of the deuteriated isomers (**20**) and (**21**). In (**3c**) there are two minor conformations, *ca.* 2% each.

Two major and at least one minor conformation were observed for the dibenzyl and dimethyl esters (**3d**) and (**11**); the latter also showed a very shielded Me in the ring C(5) ethyl group. The presence of a minor conformation was not conclusively detected in the diethyl ester (**3b**), but was inferred from the broadening of the upfield signals of its two major conformations. The acecylcone derived compound (**17**) showed three major conformations (46:36:18%), the second and third together (unresolved) being the most shielded in the N(7) group, though less so than in the other diazetidines.

Rotation of the C(1) Ph ring has also been identified as a conformational process in all the diazetidines [except (**17**)] but is quite independent of the processes leading to anomalous shielding of the ester groups.

The reaction of azo esters with 2,5-dimethyl-3,4-diphenylcyclopentadienones gives the Diels–Alder adducts (**1**) which are labile and isomerize reversibly to the 1,3,4-oxadiazines (**2**) and irreversibly to the 1,2-diazetidines (**3**).[1] Compound (**3**) is thus the thermodynamically most stable of the three isomers, though photolytic reversion of (**3**) [as well as of (**2**)] to (**1**) is possible. When the ester group R is large [e.g. in (**1c**) or (**1d**)] decarbonylation of (**1**) to (**4**) is a competing reaction. When R = Me a fourth isomer, the oxazolidinyl hydrazone (**5**) can be obtained by treating (**2a**) with NaOMe in MeOH, but this reaction is not an intramolecular isomerization since we have shown that the ester OMe group is lost at the expense of OMe from the solvent.[2]

A number of properties of the diazetidines are in fact unusual, and have been described earlier. Chemically the two ester groups differ greatly in reactivity, that on N(6) showing normal behaviour, but that on N(7) being very unreactive. Hydrolysis by base of (**3a**) readily removes the ester group on N(6), but not the other ester group, to give (**6a**); forcing conditions on (**3a**) or (**6a**) cause complete degradation.[3] Treatment of (**3a**) with acid leads to ring expansion and demethylation to (**7**),[4] also formed from the isomers (**1a**), (**2a**),[4] and (**5**)[2] under the same conditions. The basic diazetidine (**6a**) with acid undergoes a profound reorganization to the pyridone (**8**).[3] Hydrogenolysis of (**3d**) readily gives (**6d**), and only much more slowly the free diazetidine (**9**), itself a surprisingly stable substance, once isolated.[5]

Not only is the N(7) substituent difficult to remove, it is also difficult to replace. Thus acylation of (**9**) occurs rapidly at N(6) [*e.g.* MeOCOCl gives the regioisomer of (**6a**)], but not at all at N(7); this site also resists alkylation.[5]

The most remarkable property of the diazetidines concerns the chemical shift of the alkoxy protons of the N(7) ester group. In the first diazetidine studied,[1] [the diester (**3a**)], the N(7) OMe group is extraordinarily shielded at 2.82 δ($CDCl_3$) at 297 K. Initially we rejected the structure (**3a**) out of hand, strictly on the basis of this chemical shift alone. An *X*-ray analysis of the *p,p'*-dibromophenyl derivative of (**3a**) [N(7) OMe, δ 3.10], which confirmed the structure, showed that the N(7) ester group in the crystal lies in a pocket between the N(6) ester and the phenyl groups (Figure 1).† It is close to (methyl carbon *ca.* 3.5 Å) and

† Figure 1 has been redrawn using the original crystallographic data,[6] to illustrate better these stereochemical features. We are grateful to Dr. N. J. Taylor of this department for obtaining the revised diagram.

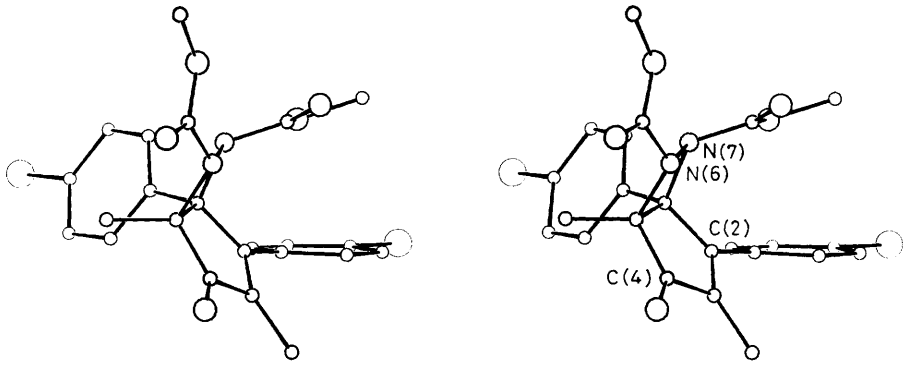
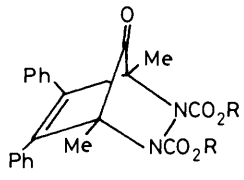
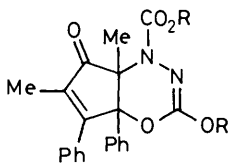


Figure 1. Stereo ORTEP diagram of the *p,p'*-dibromo derivative of (**3a**).



(**1**)



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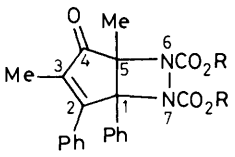
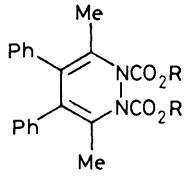
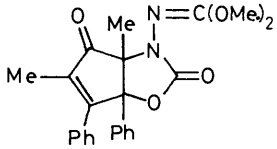


(**3**)

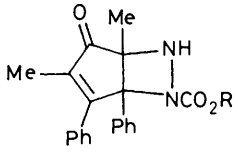


(**4**)



(**5**)

a; R = Me
b; R = Et
c; R = CH_2CCl_3
d; R = CH_2Ph



(**6**)

above the face of the vinylic phenyl ring. The methyl protons (*ca.* 2.5 Å at their closest) are thus in a highly shielded location. If we assume that the conformational minimum in the crystal is also a favoured one in solution, a qualitative explanation of the shielding is provided.

The shielding effect is quite general. In this paper, we wish to discuss briefly the following aspects of it. (*i*) The effect in an N(7) CO_2CH_2R group in which only one of the protons is shielded, (*ii*) the results of DNMR experiments which include the fact that the shielded peak broadens, *and then sharpens*, as the temperature is lowered, and that these line widths are field dependent at high temperatures, and (*iii*) the conformational possibilities in solution that can explain the observed dynamic NMR and shielding effects, with detailed emphasis on the dimethyl and bis-trichloroethyl esters (**3a**) and (**3c**).

Results and Discussion

Preparation of Diazetidines.—The diazetidines (**3**) used in this work have been described earlier.[1,5] The bridged adduct (**10**) and its isomeric diazetidine (**11**) were made in the usual way from the red monomeric cyclone 2,5-diethyl-3,4-diphenylcyclopentadienone;[7] the isomeric oxadiazine was not isolated, but the dihydropyridazine (**12**) was identified as a by-product in the isomerization.

The acecyclone (**13**),[8] which is a minor component in solution in complex equilibrium with dimers,[9] reacted at room temperature* with dimethyl azodicarboxylate to give a good yield of the oxadiazine (**15**), with no detectable amounts of the expected isomeric bridged adduct (**14**). Small amounts of the latter must, however, be in equilibrium with (**15**), since on heating, (**15**) gave the pyridazine (**16**) (68%) as well as a low yield (10%) of the desired diazetidine (**17**). They were separated by fractional crystallization.

Shielding Effects.—The ambient temperature ^1H NMR data for the diazetidines are listed in Table 1, with the absorptions of interest, those of the N(6) and N(7) ester groups, aligned together for comparison. For the dimethyl esters (**3a**), (**11**), and (**17**), in which only one absorption can be observed for each group, the shielding can be gauged only by the difference in the N(6) and N(7) absorptions. In the compounds with an N(7) CO_2CH_2R group (**3b–d**) one of the CH_2 protons is in an expected position, and the other is highly shielded. In these cases, the difference is another measure of the shielding. These internal diastereotopic shifts are uniformly large to impressive (0.7–2.0 ppm at ambient temperature; larger, as will be seen, at low temperatures). Shift differences this large can have few parallels in molecules in which the methylene group is not part of a rigid ring.

Shielding effects can be discerned (Table 1) beyond the CH_2 in the N(7) ester group of (**3b**) and in the methyl group of the tertiary (*i.e.* C_5) ethyl substituent in (**11**).

Variable-temperature and -field Behaviour.—Not only is a highly shielded absorption noticeable in one ester group of the diazetidines, but that absorption is also broadened at ambient temperature. In (**3a**) the broadening is just detectable at 60 MHz but it increases rapidly with field strength, H_0.

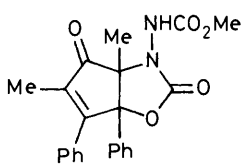
As the temperature was lowered the most significant changes

* We are grateful to Dr. David Jones of Leeds University, for pointing out to us the need to carry out the reaction at room temperature to trap successfully the monomer.

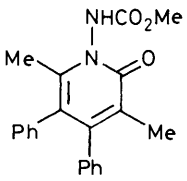
Table 1. Aliphatic ^{1}H NMR shifts (δ) of the diazetidines in $CDCl_3$ at 297 K and 250 MHz.

	N(6) ester		N(7) ester		Cyclopentenone alkyl group	
Diazetidine	α-H	β-Me	α-H	β-Me	3-R	5-R
(**3a**)	3.80		2.82		2.09	1.13
(**3b**)	4.23, 4.31	1.31	2.85, 3.87	0.73	2.07	1.18
(**3c**)	4.79, 4.88		2.78, 4.76		2.10	1.27
(**3d**)	5.14, 5.24		3.71, 4.95		2.05	1.10
(**11**)	3.80		3.04		2.48 (CH_2)[a]	1.67, 2.29 (CH_2)
					1.12 (Me)	0.38 (Me)
(**17**)	3.87		3.31		2.20	1.69

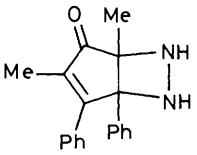
[a] Centre of multiplet.



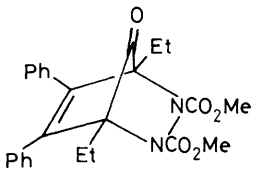
(**7**)



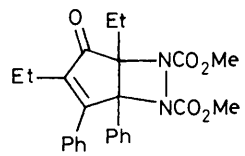
(**8**)



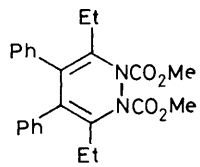
(**9**)



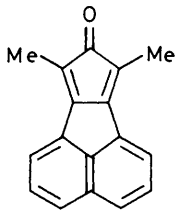
(**10**)



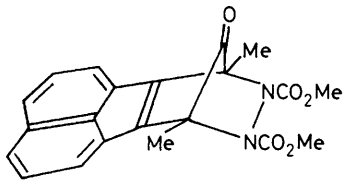
(**11**)



(**12**)



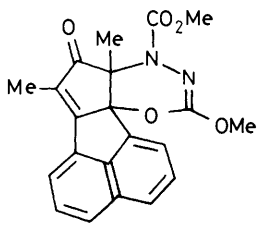
(**13**)



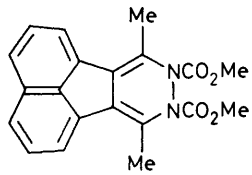
(**14**)

a; R = Me

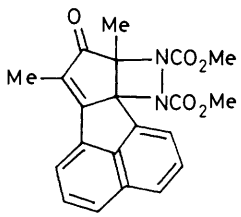
b; R = Pr^i



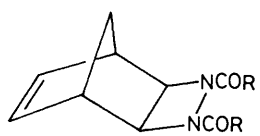
(**15**)



(**16**)



(**17**)



(**18**)

a; R = Ph

b; R = *p*-C_6H_4OMe

c; R = *p*-$C_6H_4CF_3$

d; R = OEt

in the spectrum of (**3a**) occurred in the N(7) OMe group.* At 80 MHz the line broadened to a maximum of 6.8 Hz at 248 K *and thereafter sharpened.* The variable temperature experiment at higher field strengths gave the same result, except that the temperature of maximum broadening increased [as should be expected[10] the line widths were proportional to $(H_0)^2$ at temperatures well above maximum broadening, and to H_0 at the temperature of maximum broadening]. The effect is general, the shielded protons in the N(7) group of all other diazetidines showing broadening followed by sharpening as the temperature was lowered.

Only one possible line-broadening mechanism, chemical exchange,[10] can explain these temperature dependent effects on line shapes.

For chemical exchange between two equally populated conformations ($p_A = p_B = 0.5$) the familiar pattern, observed on cooling, changes predictably when the populations become unequal ($p_B > p_A$). As p_A diminishes the low-temperature sharp line (slow exchange conditions) of the major conformation approaches the high-temperature time-averaged position (rapid exchange conditions). An extreme case is possible in which the population of the minor conformation is so small that its absorption at slow exchange is almost unobservable or is obscured by other peaks. If the low-temperature, slow exchange, resonances are sufficiently far apart (Δν large) the observed (major) line may still show detectable broadening at intermediate rates of exchange. At still faster rates of exchange

* 'N(7) OMe group' means the OMe group of the ester group bonded to N(7). We have employed this abbreviated form throughout to avoid the awkwardness of the longer but more precise usage.

this would be followed by line sharpening, with only a slight change in the position of the line.* This behaviour, which has come to be known as 'hidden partner exchange' is clearly operational here. Quantitative relationships between $\Delta\nu$ and p_A are in general complex,[11] but simplify considerably when $p_A < 0.1$.[12,13]

Examples of hidden partner exchange have been observed for a number of nuclei which, as well as protons, include ^{17}O in dilute aqueous solutions of paramagnetic ions,[14] ^{19}F and ^{31}P in diphosphinoamines,[15] ^{195}Pt in a tris(pentasulphane-1,5-diyl)-platinate(IV) anion,[16] and ^{13}C in a variety of compounds.[17] The proton examples were first recognized in exchange reactions of bulk MeOH with MeOH co-ordinated to dilute solutions of paramagnetic cations,[18] and have been observed in organo-uranium[19] and -thorium compounds.[20]

In organic molecules not subject to the influence of a paramagnetic atom, factors creating a large enough proton shift to allow a very minor component to confer detectable broadening on the peak of its major exchange partner are in general going to be absent. One example, other than in the present work, is found in an acetoxymethyl group located over an aromatic ring in a naphthalenophane; a shift of 0.5 ppm was estimated.[21]

Conformational Processes in 1,2-*Dialkyoxycarbonyldiazetidines.*—For the interpretation of our diazetidine results an understanding of the conformational processes expected in such compounds is necessary. In simple unsubstituted or in *N,N'*-dialkyldiazetidines two conformational processes are possible, *N*-inversion and ring reversal, though only one barrier has been observed by dynamic NMR spectroscopy. It has been attributed to *N*-inversion in a series of dialkyldiazetidines,[22] and in perfluorinated dimethyldiazetidine.[23] In 1,2-diethoxycarbonyl-diazetidine the barrier has been attributed to *N*-inversion,[24] and ring reversal[25] by different authors. In fused diazetidines, such as those of Table 1, ring reversal is not possible, but rotation around the N to acyl or acyloxy bond is expected to be important, as is *N*-inversion. In conformational studies on the norbornadiene fused diazetidines (**18a–d**) Landis[26] has found that inversion of the acyl groups in (**18a–c**) was the only process involved. Inversion was also observed in the diethoxycarbonyl derivative (**18d**), as well as rotation, which was judged to be at the N–C bond since the high temperature ^{13}CO peak separated on cooling into eight peaks, in four pairs of different intensities; the inversion and the rotation barriers were clearly of comparable magnitude. Alkoxycarbonyl-group rotation at pyramidal N is thus established for diazetidines.[26] Pyramidal N is in fact likely the norm for all diacyl or dialkoxycarbonyl mono- or bi-cyclic hydrazines in small or medium-sized rings.†

In strainless amides, urethanes, bishydrazides, or bis-urethanes, the rotational minima have the atoms in the C–N bond and their four substituents all in a common plane. In cyclic variants with pyramidal N, N to CO overlap must decrease with the deviation from planarity at N, but it should still dictate that the N lone pair and the carbonyl Cp–π atomic orbitals remain nearly coplanar (though no longer parallel). Thus the geometry round the two C–N bonds in a diazetidine diester is still stereochemically definable (*e.g.* as *E* or *Z*). Together with the configurational (*trans*) variations at N this leads to a maximum of eight distinct ester NMR absorptions (*e.g.* ^{13}CO), just as observed by Landis[26] for (**18d**).

The stereochemical orientation around the NCO group described above can be clearly seen in Figure 1. It is also evident in the crystallographic structures of a number of acylated heterocycles with pyramidal nitrogen found in the literature.[28]

In an environment as congested as that of the diazetidine rings in the present work the eight conformational possibilities are not all expected to be important. *The remarkable shielding effects in the ester groups allow us, in fact, to detect routinely two major and either one or two minor conformations, and to make reasonable assumptions about their structures.* The analysis has been carried out in detail on two of the diazetidines, (**3a**) and (**3c**), by variable-temperature NMR spectroscopy in CD_2Cl_2 and $C_6D_5CD_3$.

Diazetidine (**3a**).—At 250 MHz a solution of (**3a**) has to be heated to about 370 K in C_7D_8 for the methoxy peaks to become equally sharp (fast exchange), but the N(7) peak is still 0.6 ppm upfield of the other.

As the solution in CD_2Cl_2 is cooled the N(7) OMe peak is at its broadest (intermediate exchange) at 258 ± 1 K [Figure 2(*a*) shows the complete spectrum] and begins to sharpen on being further cooled and move upfield. At 230 K it absorbs at δ 2.73. Below this temperature (227 ± 3 K) the peak becomes skewed, an upfield shoulder emerging the peak maximum of which is detectable at 200 K, 3.5 Hz from the main peak at δ 2.73 (slow exchange). There are no further changes down to 183 K.

The N(6) OMe peak (δ 3.76 at 297 K) begins to show slight broadening below 250 K, but remains symmetric until 233 ± 3 K when separation of an upfield peak becomes evident. At 200 K the absorptions are well resolved [Figure 2(*b*)], at δ 3.77 and 3.81; the smaller represents about a fifth of the total of both. In addition a very small peak appears near these below 230 K, at δ 3.65.

Like the N(6) OMe group the ring methyl groups also broaden slightly on cooling with partial separation of a downfield peak in each case, which remains unresolved to 183 K.

Though the low temperature resolution of the ring methyl groups, like that of the N(7) ester methyl, is incomplete, it is obvious that in all three the proportions were qualitatively in the same *ca.* 4:1 ratio observed for the N(6) ester group, and that they represent the two dominant conformations in solution.

The aromatic region also shows variable-temperature effects. At 258 K [Figure 2(*a*)] the tertiary phenyl (*i.e.* C_1) group is the broadened singlet at δ 7.49, while the vinylic phenyl group shows two complex absorptions at δ 6.96 and 7.29 (relative area 3:2), the *upfield* being those of the *ortho* protons (established by selective proton-decoupled ^{13}C NMR spectroscopy). This phenyl group shows little change with temperature, suggesting an anchored arrangement of the ring, probably close to that observed in Figure 1. The tertiary phenyl group, however, broadens and is then resolved, at slow exchange, into a complex set of peaks at low temperature in the ratio of 1:1:2:1 at δ 7.10, 7.53, 7.60, and δ 7.91 [Figure 2(*b*)], which are likely the *ortho*-, *para*-, *meta*-, and *ortho*-protons, respectively. The low-field *o*-proton also has a satellite absorption at δ 7.88 of a quarter of the intensity, representing the second conformation.

The extreme broadening observed at higher temperatures in the anomalously shielded N(7) group cannot of course be due to exchange broadening between the very narrowly separated peaks at δ 2.72 and 2.73. Because they move *upfield* on cooling the 'hidden partner' responsible for the broadening is expected to be at much lower field. The obvious candidates are the peak at δ 3.65 or one hidden under either of the peaks at δ 3.77 or 3.81. Since it was not possible to determine from the spectrum of (**3a**)

* In the unlikely absence of temperature dependence of shifts the high temperature line is exactly $p_B\,\Delta\nu$ from the A resonance towards the B resonance.

† In fact the literature on the conformational analysis of such compounds has tacitly linked rotational barriers with planar N. Recognition of the destabilizing effect of non-bonded interactions[25] and of the imposition of severe angle strain at the nitrogens,[27] in the diplanar arrangement, are minority views.

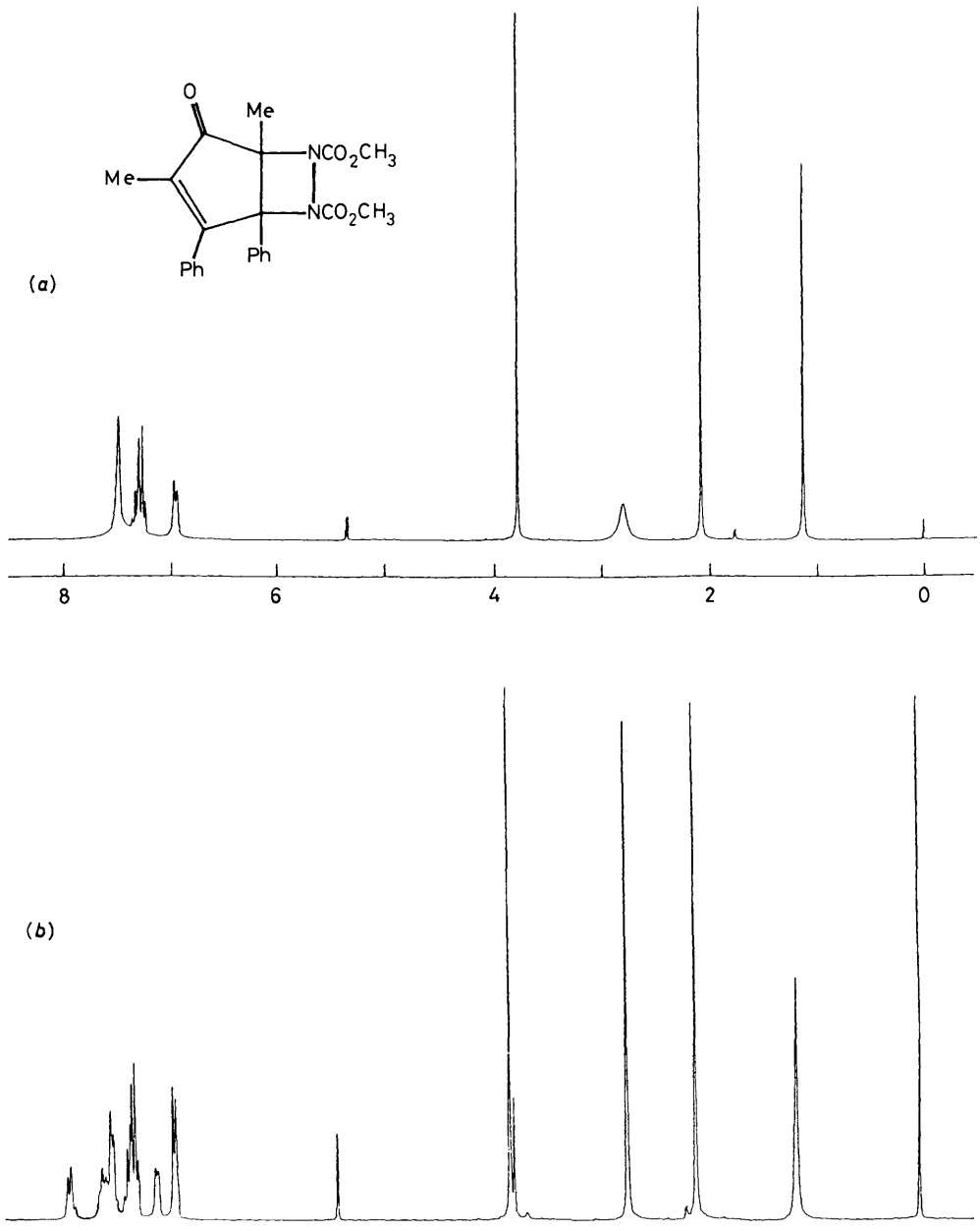


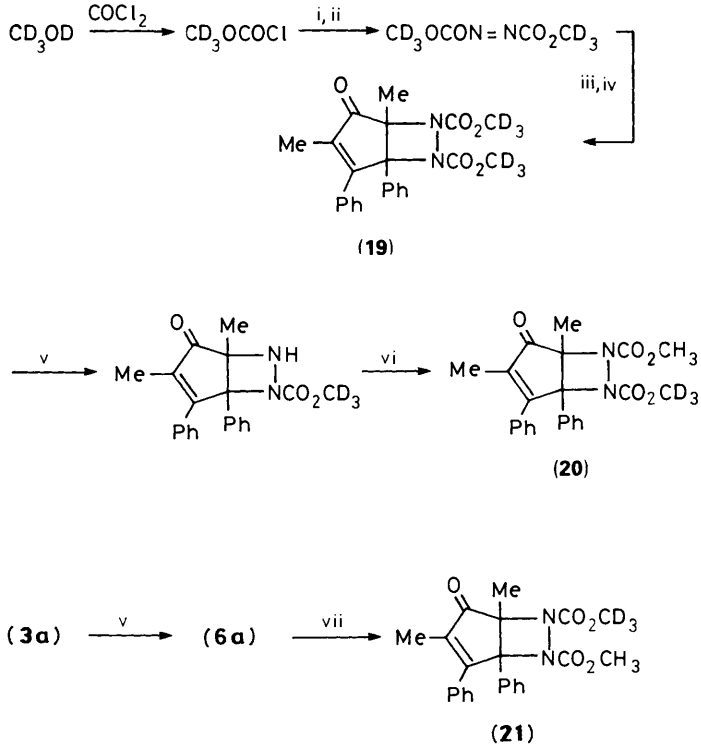
Figure 2. The 250 MHz spectra of (**3a**) in CD_2Cl_2: (*a*) at the temperature (258 K) of maximum broadening (intermediate exchange), showing the extreme shielding of the N(7) OMe group and (*b*) at 200 K showing the resolution of the individual conformations at slow exchange, in particular the N(7) peaks of the very minor conformation at δ 3.65 and the major ones at δ 2.72 and 2.73. The small signals at δ 5.3 and 1.8 in (*a*) and δ 5.4 and 2.1 in (*b*) are due to residual $CHDCl_2$ and dissolved H_2O in the solvent.

which of these was responsible for the broadening,* we decided to synthesize the deuteriated variants of (**3a**), compounds (**20**) and (**21**). They gave unambiguous answers.

Starting with CD_3OD (99.6 atom % D) the [$^2H_6$]methoxy-deuteriated diazetidine (**19**) was obtained. From (**19**) and (**6a**) conversion into the trideuteriated N(7) and N(6) regioisomers (**20**) and (**21**) followed proven methods (Scheme).[3,4] The OMe regions of (**3a**), (**20**), and (**21**) at 200 and 297 K are aligned in Figure 3. They show that the δ 3.77 peak is the exchange partner of the N(6) peak at δ 3.81, and the δ 3.65 peak is the partner of the N(7) peaks at δ 2.72 and 2.73. The N(7) partnership is also established by the low-temperature ^2H NMR spectrum of (**20**) in CH_2Cl_2 in which the very minor and the major peaks are again observed at δ 3.65 and 2.73. Resolution of the two peaks at δ 2.72 and 2.73 was not of course observed in the deuterium spectrum. The proportion of the very minor (hidden partner) peak is 3.0 ± 0.3%, based on the ^1H NMR spectra of (**3a**) and (**21**) in CD_2Cl_2 and the ^2H spectrum of (**20**) in CH_2Cl_2. From the N(6) OMe peaks in the ^1H NMR spectrum of (**3a**) in CD_2Cl_2 the dominant peaks are judged to be in the ratio of 20 ± 2 to 80 ± 2%, from one of which a 3% contribution must be subtracted since the N(6) OMe peak due to the very minor conformation is hidden under it.

The eight conformational possibilities of the diazetidines (**3**)

* The rate of conversion of a very minor peak into a major is much greater than the reverse rate, and so the minor peak disappears before the broadening of the major peak is noticeable. Thus in a spectrum with more than one conformationally mobile ester group the partnering of major and very minor peaks may be ambiguous or obscured.



Scheme. *Reagents:* i, N_2H_4; ii, NBS–py; iii, 2,5-dimethyl-3,4-diphenylcyclopentadienone; iv, heat; v, OH^-; vi, CH_3OCOCl; vii, CD_3OCOCl.

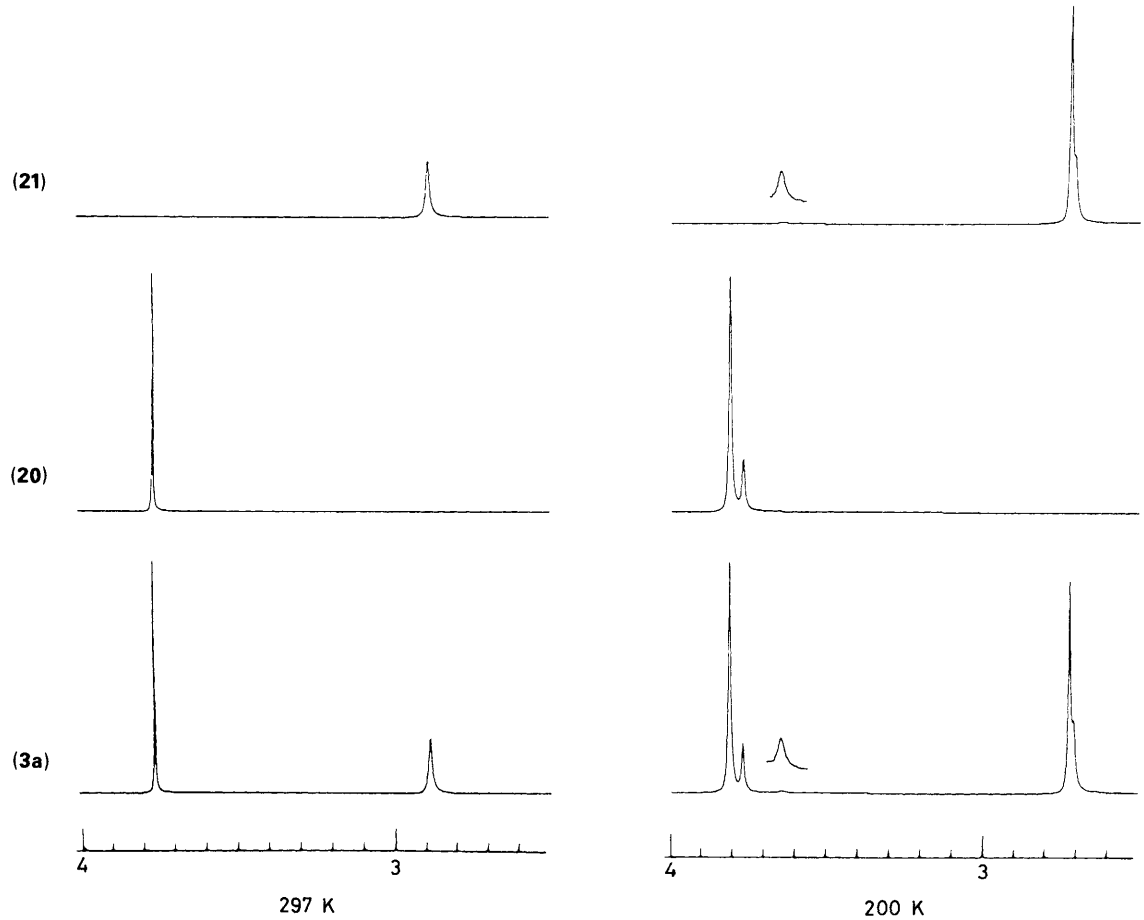
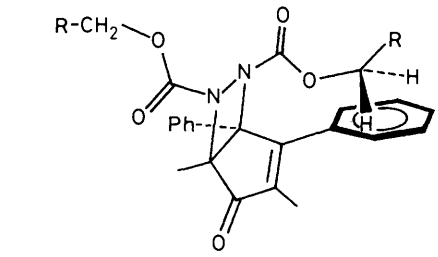
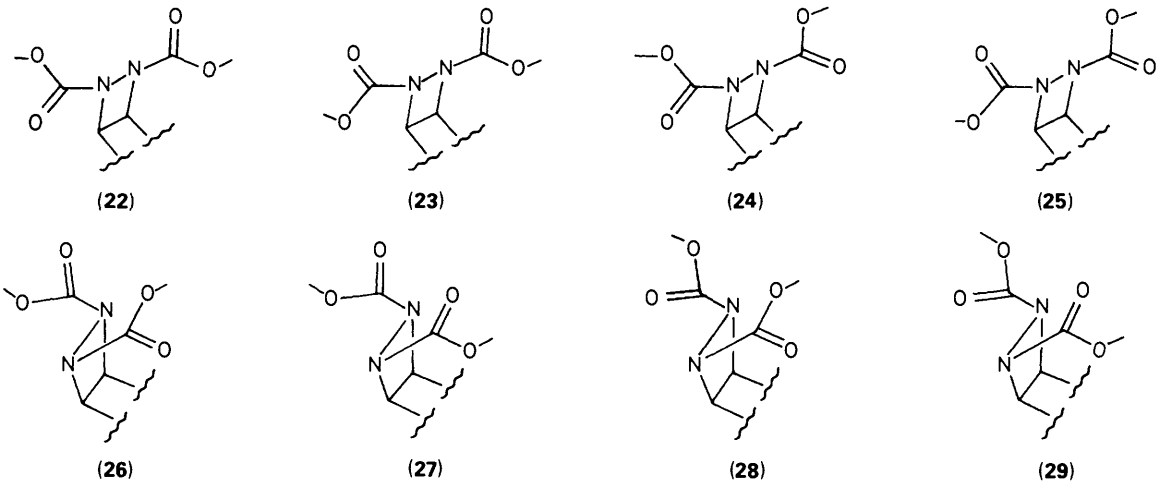


Figure 3. The 250 MHz ^1H NMR spectra at 200 and 297 K in CD_2Cl_2 of the ester region of the isotopic isomers (**3a**), (**20**), and (**21**) showing that the small signal at δ 3.65 is due to the N(7) methoxy peak of the very minor conformation. Insets are × 10.



(22) **a**; R = H
b; R = Me
c; R = CCl_3
d; R = Ph



(22) (23) (24) (25)

(26) (27) (28) (29)

Figure 4. (**22**) is a representation of the likely major conformation (*cf.* Figure 1) of compounds (**3**), showing the proximity of the ester α hydrogens to the face of the vinylic phenyl ring. (**22**) is also shown in schematic form as one of the eight rotameric possibilities in the two *trans* invertomer sets, as discussed in the text.

are shown schematically in Figure 4. In only two of these, (**22**) and (**23**), are the N(7) protons in the anomalously shielded environment. Thus the two major conformations of (**3a**) observed by NMR spectroscopy are (**22a**) and (**23a**) with the N(7) OMe close to the face of the vinylic Ph ring. They differ as rotamers at the N(6) CO group. The more abundant isomer is arbitrarily taken as (**22a**), which corresponds with that found in the crystal of the *p,p'*-dibromo derivative (Figure 1). The hidden partner, the N(7) absorption of which is in a normal position,* must be the N(7) rotamer of either (**22a**) or (**23a**), *i.e.* (**24a**) or (**25a**), respectively, or any one of the four rotamers in the other invertomer set, *i.e.* (**26a**)–(**29a**). We have, again arbitrarily, drawn it as (**24a**), the N(7) rotamer of (**22a**). Using these assignments the NMR absorptions are shown, as far as possible, for (**3a**) in Table 2.

The variable-temperature spectra of (**3a**) in C_7D_8 complement and confirm the results in CD_2Cl_2. The low temperature, slow exchange, methyl absorptions are shown, again as far as possible, in Table 2. The major peaks are in the ratio *ca.* 5:2. The identity of the hidden partner peak at δ 3.18 was confirmed by the low-temperature spectrum of (**21**). The aromatic region behaves as it does in CD_2Cl_2, the tertiary phenyl group being resolved into absorptions in which the *ortho* protons are widely separated (nearly 2 ppm). Each of these appears as two doublets very close together, also in the ratio *ca.* 5:2.

From the N(7) OMe peak in the 200 K spectrum of (**21**) in C_7D_8 the hidden partner was judged to be 2.4 ± 0.2% of the total. Together with the *ca.* 5:2 ratio observed for the two major peaks this suggests a solvent effect in the conformational population between CD_2Cl_2 and C_7D_8. Dilution studies wherein CD_2Cl_2 was added to a solution of (**3a**) in C_7D_8 confirmed that the dominant conformation in both solvents is in fact the same.

The large changes in the aromatic region, arising from rotation of the tertiary phenyl group, are independent of the inversion–rotation processes of the ester group. The two rotational minima are identical, the ring location probably being similar to that in Figure 1, with one *ortho* hydrogen over the C_5 ring and the other over the N(7) ester group. The *ortho* proton pair undergoes a larger change in environment [Δδ 0.81 ppm in conformation (**22a**) in CD_2Cl_2; 1.93, 1.91 ppm in conformations (**22a**), (**23a**) in C_7D_8] than the more remote *meta* protons. Whether rotation is fast or slow has, predictably, no significant effect on the shifts of the methyl groups. Confirmation of this comes from the variable-temperature spectrum of (**17**) (see below) where the ester region shows similar shielding effects to those observed in (**3a**), while the rigidly fused aromatic system at 200 K shows additional peaks due to the freezing out of ester conformations, but none of the profound changes observed in the low temperature spectrum of (**3a**).

The ^{13}C NMR spectrum of (**3a**) in CD_2Cl_2 shows single sharp resonances (fast exchange) for every carbon atom at 297 K. No ester resonances show any unusual shielding. At 200 K two lines are observed for almost all carbon atoms, and are in a ratio similar to that observed in the ^1H spectrum in the same solvent.

The natural-abundance ^{15}N resonances at fast exchange (298 K) observed at 135.0 and 138.5 ppm (referenced to nitromethane at 376.9 ppm), are, to our knowledge, the first example of diazetidine shifts on record.

* We can now rule out the presence of any conformation, other than the three discussed, in an amount greater than 1% since all other conformations must have the N(7) OMe peak in the normal region of the spectrum. The 200 K spectra of the trideuteriated compound (**21**) would reveal them.

Table 2. Slow-exchange aliphatic ^{1}H NMR assignments (δ) of the diazetidines[a] at 200 K and 250 MHz[b]

Diazetidine	R	Solvent	Conformation	Relative intensities[c] (%)	N(7)OR	N(6)OR	Cyclopentenone alkyl group 3-R	Cyclopentenone alkyl group 5-R
(**3a**)	Me	CD_2Cl_2	(**22a**)	77[d]	2.73	3.81	2.08	1.15
			(**23a**)	20	2.72	3.77		1.13
			(**24a**)	3	3.65			
(**3a**)	Me	C_7D_8	(**22a**)	71	2.35	3.12	1.68	1.09
			(**23a**)	27	2.39	3.24	1.62	1.35
			(**24a**)	2	3.18		1.78	
(**3b**)	Et	CD_2Cl_2	(**22b**)[e]		4.26[f] (CH_2)	2.57, 3.81 (CH_2)	2.07	1.21
					1.32 (Me)	0.62 (Me)		
(**3b**)	Et	C_7D_8	(**22b**)	80	3.74, 3.87 (CH_2)	2.42, 3.62 (CH_2)	1.69	1.20
					0.30 (Me)	0.79 (Me)		
			(**23b**)	20	0.30 (Me)	0.95 (Me)	1.63	1.42
(**3d**)	CH_2Ph	CD_2Cl_2	(**22d**)	77	3.27, 4.87	5.20, 5.25	2.07	1.14
			(**23d**)	23	3.12, 4.87	5.16, 5.31	2.09	1.21
(**11**)		CD_2Cl_2	(**22**)	90	2.81	3.82	2.4–2.5 (CH_2)	1.47, 2.4 (CH_2)
							1.15 (Me)	0.35 (Me)
			(**23**)	10	3.77			
		C_7D_8	(**22**)	76	2.45	3.16	2.22[f] (CH_2)	1.40, 2.68 (CH_2)
							1.20 (Me)	0.47 (Me)
			(**23**)	22	2.49	3.30	1.12 (Me)	
			(**24**)	2		3.42		0.16 (Me)
(**17**)		CD_2Cl_2	(**22**)[g]	46	3.62	3.98	2.23	1.78
			(**23**)	36	3.30	3.96		1.74
			(**24**)	18		3.87		1.71

[a] Except for (**3c**) which are listed in Table 3. [b] Where no entry appears, signals corresponding to that conformation did not emerge clearly. [c] Measurement error is estimated at ±3% for the major conformations. [d] This assumes that the N(6) peak of the 3% conformation is under the N(6) peak of the major conformation at δ 3.81, rather than under the N(6) peak of the conformation at δ 3.77. [e] The spectrum becomes more complex at 200 K, but the signals due to the other conformations did not become sufficiently well resolved to be readily assigned. [f] Centre of multiplet. [g] Clearly, due to the differences in structure between this fused system, and compounds (**3**) the assignment of a conformation is, at best, a guess.

Diazetidine (**3c**).—As the temperature is lowered in CD_2Cl_2 at 250 MHz, the shielded and broadened absorption at δ 2.78 due to one of the N(7) methylene protons sharpens to a normal doublet (*J* 11.6 Hz) and moves upfield. Further cooling causes changes in all peaks in the spectrum analogous to those observed for (**3a**), due to the slowing of exchange between two major conformations, in this case in a ratio of about 1.8:1. With a single exception (Table 3) separation is observed, in both CD_2Cl_2 and C_7D_8, in each Me group and all four ester protons, *i.e.* two pairs of doublets in a 1.8:1 ratio, one doublet in each conformation being highly shielded. These high-field signals again must be due to the N(7) proton close to the face of the phenyl ring in each of the two N(6) CO rotamers, (**22c**) and (**23c**). Figure 5(*a*) shows the complete spectrum of (**3c**) in C_7D_8 at 297 K and Figure 5(*b*) the non-aromatic portion of the spectrum at 200 K, with the major conformations taken, again arbitrarily, to correspond with (**22c**) and (**23c**).

Not one, but two hidden partners, shown arbitrarily as (**24c**) and (**25c**) in Table 3, are responsible for the high-temperature broadening observed in the spectrum of (**3c**). They are of comparable intensities, about 3% in CD_2Cl_2 and 2% in C_7D_8. The evidence for them is sparse in the aromatic and methyl regions, but all eight ester protons (two doublets from each conformation) are observed at slow exchange in the high amplitude spectrum in C_7D_8 and all but two in CD_2Cl_2. The assignments, which are established as far as possible by decoupling experiments, are listed in Table 3.

The chemical shifts of the N(7) ester protons both at 297 K and in the two major conformations at 200 K are very similar in CD_2Cl_2 and C_7D_8. As indicated before, this ester group is largely buried within the molecule and thus insulated from the solvent. The N(6) ester protons, which in either rotameric conformation are exposed to the solvent, show a strong shielding effect in C_7D_8. Relative to the values in CD_2Cl_2 they are shielded at 200 K at 0.59 and 1.14 ppm for conformation (**22**), and 0.48 and 1.09 ppm for conformation (**23**). The net effect of this considerable shielding in C_7D_8 of the N(6) ester protons over the N(7), and the inherent extreme shielding of the one N(7) proton, make for a remarkable dispersion of ester shifts [Figure 5(*b*)] of nearly three ppm.

The upfield *ortho*-proton of the tertiary group in the low-temperature spectrum of (**3a**), described earlier, is also much more shielded in C_7D_8 than in CD_2Cl_2. This effect is observed in all the diazetidines (**3**) examined, and also in (**11**).

Other Diazetidines.—The variable-temperature spectra of the remaining diazetidines examined reveal the presence of two dominant conformations in (**3b**), (**3d**), and (**11**) and three in (**17**). The non-aromatic resonances at 200 K (slow exchange) for these are listed as far as possible in CD_2Cl_2 or C_7D_8 in Table 2. For spectral details in $CDCl_3$ at ambient temperature see Table 1.

Compound (**3b**) shows similar variable-temperature behaviour to (**3c**), although the presence of the two major conformations at 200 K is clearer in C_7D_8 than in CD_2Cl_2. All aliphatic peaks, except for the N(7) ester Me, showed two conformations in the ratio of *ca.* 4:1 in C_7D_8.

The peak doubling is evident in both ring and one of the ester Me groups, and in two of the four ester methylene protons. Each conformation has a very shielded methylene proton in its N(7) group; the other three are in a normal position. The N(7) ester Me group is also remarkably shielded. At δ 0.30 it is upfield of its N(6) counterpart by 0.49 ppm in the major and 0.65 ppm in the minor conformation. Changes in the aromatic region are exactly like those noted for (**3a**) and (**3c**).

Ambient-temperature (intermediate) exchange broadening is observed in the shielded N(7) methylene proton (a broad hump at δ 2.85, fully resolved at low temperature) and its attached Me

Table 3. Slow-exchange aliphatic ^{1}H NMR assignments (δ) of the different conformations of (**3c**) in CD_2Cl_2 and C_7D_8 at 200 K and 250 MHz.

Solvent	Conformation	C(5)-Me	C(2)-Me	N(7) O-CH_2[a] A	N(7) O-CH_2[a] B	N(6) O-CH_2[a] A	N(6) O-CH_2[a] B
C_7D_8	(**22c**)	1.39	1.64	2.21	4.96	3.53	4.63
	(**23c**)	1.30	1.59	2.13	5.00	3.77	4.46
	(**24c**)	*b*	*b*	3.71[c]	4.77	3.37	4.83
	(**25c**)	*b*	*b*	4.13[c]	4.26	4.07	5.13
Relative[d] intensities		64:36	68:32	*e*		65:31:2:2	
CD_2Cl_2	(**22c**)	1.40	2.12	2.26	4.81[f]	4.67	5.22
	(**23c**)	1.28	2.15	2.20	4.81[f]	4.86	4.94
	(**24c**)	1.13	*b*	4.87[g]	*b*	4.61[g]	5.09[g]
	(**25c**)	*b*	*b*	5.13[g]	*b*	4.70[g]	5.36[g]
Relative[d] intensities		60:36:4	66:34	*e*		62:32:3:3	

[a] Except as noted,[c] resonances listed as A and B resonances for a given conformation of the N(6) or N(7) methylene groups have been shown to be spin-coupling partners by decoupling experiments. The higher-field resonance is chosen as the A resonance in each case. [b] Not detected. [c] These appear as broadened humps at 200 K which are presumably the still exchanging exchange partners of the high field N(7) resonances at 2.13 and 2.21 ppm; exchange partners with a smaller chemical shift separation are, of course, already sharp at this temperature. These must therefore be the spin-coupling partners of the resonances at 4.26 and 4.77 ppm, which are not demonstrably coupled to any other low-field doublets. [d] Proportions are calculated on the basis of the intensity of signals actually assigned. Since undetected signals are likely to be contributing to the intensities of assigned signals, these proportions may well be in error to that extent. [e] Measurement of N(7) methylene signals arising from the two major conformations was not possible, as they obscure one another and, in the [$^2H_8$]toluene spectrum, are in turn obscured by the quintet due to residual $C_6D_5CD_2H$ in the solvent. [f] Coincident at 200 K. [g] The assignment of these resonances to N(6) or N(7) is based on analogy with the spectrum taken in toluene (*cf.* footenote *c*). It is assumed that the remaining N(7) resonances were not detected because they are still exchange broadened or are 'lost' in the more crowded methylene region of this spectrum.

group, but the hidden partner responsible remains just that, at least in the ester CH_2 region, at 200 K. Small peaks in the C–Me region of the spectrum, not detected at higher temperatures, suggest the presence of a conformation at about the 3% level.

The variable-temperature spectra of (**3d**), characterized as they are in the methylene region by pairs of doublets, are almost duplicates of those of (**3c**), except that the aromatic region is more complex and the low-temperature ratio of the major conformations is more biased, again about 4:1. Evidence for the slow tertiary phenyl rotation can be found among the absorptions of the four phenyl groups. The highly shielded N(7) ester proton is again extremely broad at room temperature. The only indication, however, of a very minor exchange partner was a peak (*ca.* 2% of total population) at δ 0.95, upfield of the tertiary Me peaks and missing at higher temperature.

In the ring ethyl compound (**11**) the ester and aromatic regions are unremarkable at 297 and 200 K in so far as they behave just like those of (**3a**). Again, C_7D_8 is the preferred solvent for resolving different conformations. The N(6) OMe group in particular shows good resolution of two signals at δ 3.16 and 3.30 of relative intensities 76 and 22%, respectively, at slow exchange. In addition, a small signal (relative intensity 2%) emerges at δ 3.42 which must correspond to either N(6) or N(7) in the minor conformation, and which has been arbitrarily assigned to N(6) in Table 2. The most novel feature of the spectra is the degree of anisotropy experienced by the tertiary ring ethyl group at all temperatures. The methyl group is in a shielded environment (δ 0.35, CD_2Cl_2; δ 0.45, C_7D_8) whereas the methylene hydrogens are, respectively, in normal (δ 1.62, CD_2Cl_2; δ 1.71, C_7D_8) and deshielded (δ 2.31, CD_2Cl_2; δ 2.47, C_7D_8) environments (all values at 297 K). From these values if we consider a methyl group in the same location, as is the case in all of compounds (**3**), we would predict, as we find, its shift to be neither particularly shielded nor deshielded.

The 297 K spectrum of the acecyclone derived diazetidine (**17**) in CD_2Cl_2 shows a broadened and shielded N(7) OMe group, but the degree of both broadening and shielding (δ 3.31) are less than in the other diazetidines. At 200 K this absorption separates into two, a sharp (δ 3.62) and a broad one (δ 3.30), in relative areas of about 2:3, the latter containing two unresolved peaks. There are three major conformations, observed as triple signals for the N(6) and tertiary Me peaks, in relative intensities of 46, 36, and 18%. No very minor peak could be unambiguously detected.

It is evident that the rigid aromatic tricyclic system is less effective in shielding the N(7) ester protons than is the freely rotating tertiary phenyl group in the the other compounds studied. Not only is the N(7) OMe group much less shielded than in the other diazetidines, but so too is the tertiary Me group (δ 1.69). Inspection of Figure 1 shows that in diazetidines such as (**3**) this Me group is considerably shielded by the tilted tertiary Ph group, an effect that is not possible in (**17**).

Experimental

^{1}H NMR spectra were routinely obtained at 250 MHz on a Bruker AM-250 spectrometer. Typically, spectra were of sweep width 3 000 Hz with 16K data points. In addition, for field-strength studies, the following spectrometers were used: Perkin-Elmer R-12B (60 MHz); Varian HA 100 (100 MHz) and HR 220 (220 MHz); Bruker WP 80 (80 MHz), and WH 400 (400 MHz). Chemical shifts are reported in ppm downfield of internal tetramethylsilane.

^{13}C NMR spectra were obtained at 62.9 MHz on a Bruker AM-250 spectrometer. The carbon resonance of $CDCl_3$ at 77.0 ppm served as an internal chemical-shift reference.

The natural-abundance ^{15}N NMR spectrum of (**3a**) was obtained on a Bruker WH-400 spectrometer at 40.5 MHz. The sample was a saturated solution in $CDCl_3$ with $Cr(acac)_3$ added to reduce relaxation times.

Compounds were generally recrystallized twice and, after being powdered, were dried *in vacuo* several hours before use. [$^2H_2$]Dichloromethane (99.8 atom% ^{2}H) and [$^2H_8$]toluene (99.6 atom% ^{2}H), both from Merck, Sharpe and Dohme Isotopes, were used throughout. Sample concentrations were generally *ca.* 5–10 mg cm^{-3} in CD_2Cl_2 and saturated (*ca.* 0.5–5 mg cm^{-3}) in C_7D_8. All samples were filtered before use.

Melting points are uncorrected. Elemental analyses were obtained from Guelph Chemical Laboratories Ltd., Guelph, Ontario, Canada.

Diazetidines (**3**).—The syntheses of (**3a–c**)[1] and (**3d**)[5] have been described previously.

2,3-*Dimethoxycarbonyl*-1,4-*diethyl*-5,6-*diphenyl*-7-*oxo*-2,3-*diazabicyclo*[2.2.1]*hept*-5-*ene* (**10**).—Dimethyl azodicarboxylate (4.8 g, 27 mmol) and 2,5-diethyl-3,4-diphenylcyclopentadienone[7] (6.8 g, 27 mmol) were refluxed for 2 h in benzene (10 cm^{-3}). The solvent was removed to give an oil which crystallized on being triturated with hexane–ether. Recrystallization from 2,2,4-trimethylpentane gave (**10**), m.p. 125.5–126.5 °C; $\nu_{max.}$(CCl_4) 1 796 (keto CO), 1 750 and 1 719 cm^{-1} (ester CO); δ($CDCl_3$) 7.3–6.8 (10 H, m, 2 Ph), 3.58 (6 H, s, 2 MeO), 2.35 (4 H, q, *J* 7 Hz, 2 CH_2), and 0.95 (6 H, t, 2 Me)

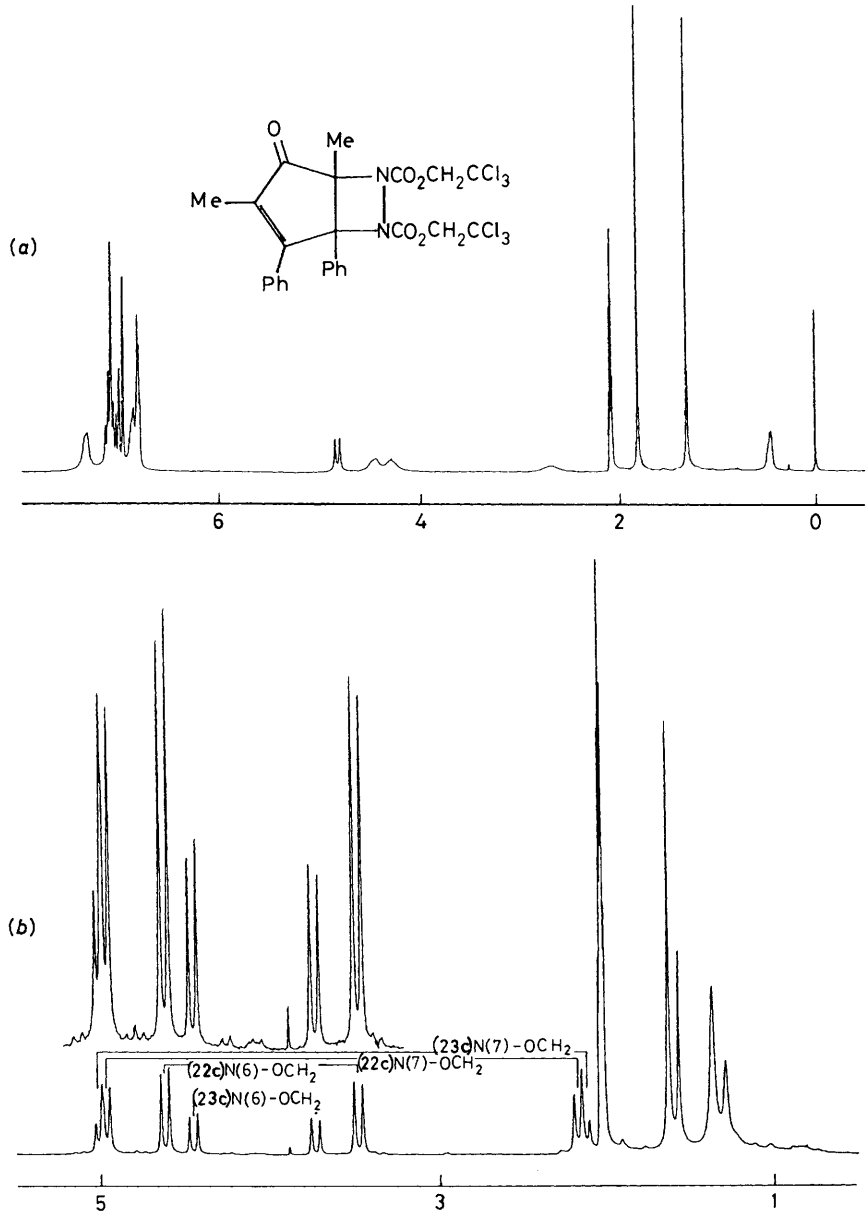


Figure 5. The 250 MHz ^{1}H NMR spectra of (**3c**) (*a*) at 297 K and (*b*) its non-aromatic region at 200 K in C_7D_8. The very broad signal in the 297 K spectrum at δ 2.71 and the doublet at δ 4.82 are those of the N(7) OCH_2, and the two humps at δ 4.29 and 4.45 are those of N(6) OCH_2. In the 200 K spectrum connecting lines indicate all the diastereotopic CH_2 pairings in the two major conformations. The inset (×4) shows the doublets due to the *two* low population conformations. Small signals at δ 3.9 and 2.9 in the 200 K spectrum appear at δ 4.3 and 3.0 in the 297 K spectrum and are trace impurities. The peak at δ 0.45 in the 297 K spectrum is from dissolved H_2O. The quintet from residual $C_6D_5CD_2H$ at δ 2.1 (both spectra), its ^{13}C satellites and those of the ring methyl peaks are also visible and complicate the search for the low intensity signals of the low-population conformations.

(Found: C, 69.2; H, 5.9; N, 6.7. Calc. for $C_{25}H_{26}N_2O_5$: C, 69.1; H, 6.0; N, 6.4%).

3,5-*Diethyl*-6,7-*dimethoxycarbonyl*-4-*oxo*-1,2-*diphenyl*-6,7-*diazabicyclo*-[3.2.0]*hept*-2-*ene* (**11**) *and* 3,5-*Diethyl*-1,2-*dimethoxycarbonyl*-4,5-*diphenyl*-1,2-*dihydro*-1,2-*pyridazine* (**12**).—Dimethyl azodicarboxylate (0.70 g, 4.8 mmol) was refluxed with the cyclone (1.3 g, 4.8 mmol) in bromobenzene (10 cm^3) for 1 h. The solvent was removed, 2,2,4-trimethylpentane (10 cm^3) was added, and the diazetidine crystallized out (1.4 g, 70%). After recrystallization from methanol it had m.p. 159–159.5 °C; $\nu_{max.}$(Nujol) 1 755 and 1 730 (ester CO), and 1 706 cm^{-1} (keto CO); δ($CDCl_3$) 7.5–6.8 (10 H, m, 2 Ph), 3.79 (3 H, s, OMe), 3.04 (3 H, s, OMe), 2.50 (2 H, q, *J* 7 Hz, 3-CH_2Me), 1.78 (2 H, q, *J* 7 Hz, 5-CH_2Me), 1.12 (3 H, t, 3-CH_2*Me*), and 0.38 (3 H, t, 5-CH_2*Me*) (Found: C, 69.0; H, 6.0; N, 6.6. Calc. for $C_{25}H_{26}N_2O_5$: C, 69.1; H, 6.0; N, 6.4%).

The 2,2,4-trimethylpentane filtrate was evaporated to yield the pyridiazine (**12**) (0.5 g, 26%) as a solid which was recrystallized from 2,2,4-trimethylpentane, m.p. 135–135.5 °C; $\nu_{max.}$(CCl_4) 1 730 cm^{-1} (CO); δ($CDCl_3$) 7.2–6.8 (10 H, m, 2 Ph), 3.88 (6 H, s, 2 MeO), 2.9–2.1 (4 H, m, AB of ABX_3, 2 CH_2), and 0.96 (6 H, t, *J* 7 Hz, 2 Me) (Found: C, 70.4; H, 6.3; N, 6.9. Calc. for $C_{24}H_{26}N_2O_4$: C, 70.9; H, 6.4; N, 6.9%).

When (**10**) was refluxed in bromobenzene for 1 h the same products (**11**) and (**12**) were obtained.

Oxadiazine (**15**).—The acecyclone (**13**)[8] (0.67 g, 2.9 mmol) and dimethyl azodicarboxylate (0.46 g, 3.1 mmol) were kept for 3 days at room temperature in methylene chloride (10 cm^3).

Evaporation gave a residue which on titration with cold ether yielded the oxadiazine (0.97 g, 89%). Recrystallization from chloroform–hexane gave the yellow (**15**), m.p. 146–147 °C; $\nu_{max.}$(Nujol) 1 745 (ester CO), 1 720 (keto CO), and 1 662 cm^{-1} (C=N); δ($CDCl_3$) 8.1–7.3 (6 H, m, Ar), 3.93 (3 H, s, OMe), 3.80 (3 H, s, OMe), 2.23 (3 H, s, vinylic Me), and 1.60 (3 H, s, tertiary Me) (Found: C, 67.0; H, 5.0; N, 7.5. Calc. for $C_{21}H_{18}N_2O_5$: C, 66.7; H, 4.8; N, 7.4%).

A reaction in $CDCl_3$ monitored at room temperature showed no trace of the bridged compound (**14**) at any stage.

The Pyridazine (**16**) *and Diazetidine* (**17**).—Solutions of (**15**) in both $CDCl_3$ and C_6H_6 were heated at reflux and the changes in the aliphatic region were monitored by ^1H NMR spectroscopy. The formation of (**16**) and (**17**) was complete within *ca.* 3 days in $CDCl_3$ and 9 h in C_6H_6; at no stage were peaks for the intermediate (**14**) detected. In both cases the final ratio of (**16**):(**17**) was *ca.* 4:1.

The crude product obtained by heating (**15**) (0.64 g, 1.7 mmol) in benzene (10 cm^3) was triturated with warm methanol and the resulting mixture was chilled and filtered to give a fraction (0.45 g) consisting of *ca.* 90% pyridazine. Crystallization from methanol–dichloromethane gave deep yellow (**16**), m.p. 178–179 °C; $\nu_{max.}$(Nujol) 1 757 and 1 729 cm^{-1} (C=O); δ($CDCl_3$) 8.1–7.5 (6 H, m, Ar), 3.81 (6 H, s, OMe), and 2.62 (6 H, s, vinylic Me) (Found: C, 68.9; H, 5.0; N, 7.8. Calc. for $C_{20}H_{18}N_2O_4$: C, 68.6; H, 5.2; N, 8.0%).

The filtrate from the methanol separation was evaporated to a residue (0.12 g) the ^1H NMR spectrum of which showed it to be mainly a mixture of (**17**) (*ca.* 60%) and (**16**). Two crystallizations from carbon tetrachloride gave the diazetidine, which decomposed and melted between 203 and 213 °C. δ($CDCl_3$) 7.98–7.85 (3 H, m, Ar), 7.78–7.26 (3 H, m, Ar), 3.91 (3 H, s, OMe), 3.35 (3 H, s, OMe), 2.22 (3 H, s, vinylic Me), and 1.74 (3 H, s, tertiary Me); *m/z* 350 (*M*–CO^+).

[$^2H_6$]*Dimethyl Hydrazine*-1,2-*dicarboxylate*. [$^2H_3$]Methyl chloroformate was prepared from [$^2H_4$]methanol (99.6% ^2H, Merck, Sharpe and Dohme) by the general procedure of Tarbell and Longosz.[29] Half of the chloroformate (total of 7.42 g, 76 mmol) was added dropwise to an ice-cooled stirred solution of hydrazine hydrate (1.75 g, 35 mol) in water (100 cm^3). The remainder was added, along with solid $NaHCO_3$ (8.0 g, 95 mmol) in portions. Some solid separated. After being stirred for 3 h, the whole was evaporated to dryness, and thoroughly extracted with hot acetone. Removal of the acetone gave the solid colourless product (5.09 g, 94%) of high purity. Recrystallization from MeOH–C_6H_6 (very soluble in MeOH, very insoluble in C_6H_6) gave 4.07 g of the pure deuteriated hydrazine ester, m.p. 131–133 °C, with a further 0.60 g of product being obtained by stirring the mother liquor residue with C_6H_6; the latter fraction could be recrystallized as before: $\nu_{max.}$(Nujol) 3 286 (NH), 2 282, 2 263, 2 200, 2 130, and 2 083 (C–D), 1 740 and 1 708 cm^{-1} (C=O); δ 6.65 (br s, 2 NH), 3.74 (5 lines, isotopic impurity, $OCHD_2$; added normal hydrazine ester absorbs at δ 3.77); *m/z* 154 (*M*$^+$).

[$^2H_6$]-2,3-*Dimethoxycarbonyl*-1,4-*dimethyl*-7-*oxo*-5,6-*diphenyl*-2,3-*diazabicyclo*[2.2.1]*hept*-5-*ene* (**1**; R = CD_3).—To a solution in a separatory funnel of the deuteriated hydrazine ester (3.08 g, 20 mmol) in water and ice (50 cm^3) was added pyridine (1.58 g, 20 mmol), dichloromethane (60 cm^3), and *N*-bromosuccinimide (3.56 g, 20 mmol). The mixture was shaken for 10 min, and the dichloromethane layer was separated and shaken out with 4 × 50 cm^3 of water. The dried solution was evaporated to give the orange azo ester as an oil (2.84 g, 18.7 mmol, 93%).

The azo ester was refluxed in benzene (60 cm^3) with 2,5-dimethyl-3,4-diphenylcyclopentadienone (4.85 g, 18.7 mmol). A portion of the solution was monitored by ^1H NMR spectroscopy which showed the reaction to be complete within 2.5 h. Evaporation and trituration with ether–pentane gave the colourless solid adduct (6.29 g, 82%), which was sufficiently pure for conversion into (**19**); $\nu_{max.}$(Nujol) 1 808 (keto CO), 1 749, and 1 725 cm^{-1} (ester CO); δ($CDCl_3$) 7.4–6.9 (10 H, m, Ph), and 1.82 (6 H, s, CH_3); *m/z* 412 (*M*$^+$).

[OMe-$^2H_6$]-6,7-*Dimethoxycarbonyl*-3,5-*dimethyl*-1,2-*diphenyl*-6,7-*diazabicyclo*[3.2.0]*hept*-2-*ene* (**19**).—A solution of the adduct (**1**) (R = CD_3) was heated at the reflux temperature in bromobenzene in an NMR tube; reaction was complete within 3 h. On a larger scale, the adduct (6.0 g, 14.5 mmol) was refluxed for 3 h in bromobenzene (60 cm^3), the solvent was then evaporated and the residue triturated with ether–hexane to give (**19**) as an off-white solid (4.51 g, 75%) the NMR spectrum of which showed it to be of high purity; there was no incorporation of methoxy after crystallization from methanol (or even after standing in methanol solution for 3 days), m.p. 199–200.5 °C; $\nu_{max.}$(Nujol) 1 758 and 1 734 (ester CO), and 1 716 cm^{-1} (keto CO); δ($CDCl_3$) 7.45 (5 H, s, 1-Ph), 7.3–6.9 (5 H, m, 2-Ph), 2.09 (3 H, s, 3-Me), 1.15 (3 H, s, 5-Me); *m/z* 412 (*M*$^+$).

6-*Methoxycarbonyl*-3,5-*dimethyl*-4-*oxo*-1,2-*diphenyl*-7-*trideuteriomethoxycarbonyl*-6,7-*diazabicyclo*[3.2.0]*hept*-2-*ene* (**20**).—A solution of (**19**) (0.50 g, 1.21 mmol) in NaOH in aqueous ethanol (1:1, 30 cm^3; 1 mol dm^{-3}) was kept at room temperature for 12 h, neutralized with acetic acid and evaporated to dryness.[3] The residue was digested with water and filtered to give the basic ester (**6**; R = CD_3) (0.38 g, 89%) as a pale yellow solid which was pure enough for further reactions, but could be recrystallized from acetone; ($CDCl_3$) 7.6–6.9 (10 H, m, Ph), 5.08 (s, NH), 2.12 (3 H, s, 3-Me), and 1.09 (3 H, s, 5-Me).

The base (0.33 g, 0.93 mmol) was dissolved in dichloromethane (5 cm^3), and pyridine (0.096 g, 1.2 mmol), and methyl chloroformate (0.117 g, 1.2 mmol) were added in turn. After 0.5 h, the solution was extracted with saturated aqueous $NaHCO_3$, dried, and evaporated to give (**20**) (0.37 g, 97%) which was recrystallized from methanol–methylene chloride, m.p. 199–200 °C; $\nu_{max.}$ (Nujol) 1 757, 1 729 (ester CO), and 1 712 cm^{-1} (keto CO); δ($CDCl_3$) 7.45 (5 H, s, 1-Ph), 7.5–6.9 (5 H, m, 2-Ph), 3.80 (3 H, s, OMe), 2.09 (3 H, s, 3-Me), and 1.15 (3 H, s, 5-Me); *m/z* 409 (*M*$^+$).

7-*Methoxycarbonyl*-3,5-*dimethyl*-4-*oxo*-1,2-*diphenyl*-6-*trideuteriomethoxycarbonyl*-6,7-*diazabicyclo*[3.2.0]*hept*-2-*ene* (**21**).—To the base (**6a**)[3] (1.15 g, 33 mmol) in methylene chloride (30 cm^3) was added pyridine (0.39 g, 49 mmol), followed by a solution of [$^2H_3$]methyl chloroformate (0.38 g, 39 mmol) in dichloromethane (10 cm^3). After 20 min the solution was washed out with water (3 × 50 cm^3), and dried and evaporated to give a quantitative yield of the product. Recrystallization from methanol gave (**21**) (1.18 g, 88%), m.p. 199–200 °C; $\nu_{max.}$(Nujol) 1 761, 1 733 (ester CO), and 1 715 cm^{-1} (keto CO); δ($CDCl_3$) 7.45 (5 H, s, 2-Ph), 7.3–6.9 (5 H, m, 2-Ph), 2.92 (3 H, s, OMe), 2.09 (3 H, s, 3-Me), and 1.15 (3 H, s, 5-Me); *m/z* 409 (*M*$^+$).

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