(*E*)-2-(Carbomethoxy)thiacycloundec-4-ene (3). A mixture of 2-vinylthiocane (0.78 g, 5 mmol), methyl diazoacetate (1.0 g, 10 mmol), and dry $CuSO_4$ (0.1 g) in 3 mL of benzene was heated at 40–45 °C under nitrogen. Gas evolution started immediately and continued without further external warming for about 5 min. The mixture was refluxed for 5 min, cooled, and filtered. Solvent evaporation left a residue (1.42 g) whose GLC (column B, 150 °C) showed one major peak (~65%) along with eight additional peaks of shorter retention time. The major product was separated by preparative GLC (150 °C): ^{1}H NMR δ 5.9–5.4 (m, 2 H, olefinic H's), 3.76 (s, 3 H, CH_3), 3.08 (q, J = 11.0 and 3.5 Hz, 1 H, SCH), 2.9–2.2 (m, 4 H), 2.1 (m, 2 H), 1.5 (m, 8 H). By irradiation at δ 2.6, the high-field part of an olefinic AB quartet can be decoupled, J = 15.0 Hz, confirming the E double bond configuration. (For the ^{13}C NMR spectrum, see Table I.) Anal. Calcd for $C_{12}H_{20}SO_2$: C, 63.11; H, 8.82. Found: C, 62.92; H, 9.01.

(*E*)-2-(Carbomethoxy)thiacyclonon-4-ene (1b) was prepared (50%) as described for the eleven-membered analogue, except that separation from the side products was performed via the $HgCl_2$ adduct. The sulfide was regenerated by aqueous KI treatment.[7c] The ^{13}C spectrum at room temperature shows slow exchange between two conformers (Tables I and II). Coalescence is observed on warming, and at 80 °C a sharp ten-signal spectrum is obtained (C_2Cl_4): δ 172.6 (CO), 136.5 (C_5), 125.0 (C_4), 51.9 and 51.6 (C_2 and OCH_3, interchangeable), 37.3 (C_3), 35.9, 25.8, 25.0 (unassigned). The room temperature ^{1}H NMR spectrum is also indicative of two diastereoisomers: the olefinic H absorption occurs as 2 multiplets at δ 6.1–5.5 and 5.4–5.0, 1.25 and 0.75 H, respectively. The latter is a neat ddd pattern (J = 15.0, 10.0, and 4.0 Hz), while the former is a ddd pattern (J = 15.0, 9.5, and 4.0 Hz) centered at δ 5.87 superimposed to an unresolved multiplet at δ 5.7. The behavior is consistent with the major isomer (~75%) giving raise to a two ddd pattern, with the minor isomer absorption occurring at δ 5.7 for both olefinic protons. This behavior is consistent with previous observations of the corresponding 2-carbethoxy derivative.[7d] Anal. Calcd for $C_{10}H_{16}O_2S$: C, 60.00; H, 8.06. Found: C, 59.63; H, 8.12.

Registry No. 1a, 74263-06-2; **1b** (isomer 1), 74263-07-3; **1b** (isomer 2), 74310-57-9; **2**, 74263-08-4; **3**, 74263-09-5; *cis*-**4a**, 74263-11-9; *trans*-**4a**, 74263-13-1; *cis*-**4b**, 74263-15-3; *trans*-**4b**, 74263-17-5; *cis*-**4c**, 74263-19-7; *trans*-**4c**, 74263-21-1; **5**, 74263-22-2; (*Z*)-**6**, 74263-23-3; **7**, 74263-24-4; (*E*)-**8**, 74263-25-5; (*Z*)-**8**, 74263-29-9; **9**, 74263-26-6; 2-chlorothiocane, 74263-27-7; vinyl bromide, 593-60-2; 2-vinylthiocane, 74263-28-8; (*E*)-thiacyclooct-4-ene, 64945-41-1; (*Z*)-thiacyclooct-4-ene, 64945-38-6; thiocane, 6572-99-2; 2-vinylthiepane, 66120-30-7.

Atropisomerism in *o*-Arylacetyl-*N*,*N*-dimethylbenzamides[1]

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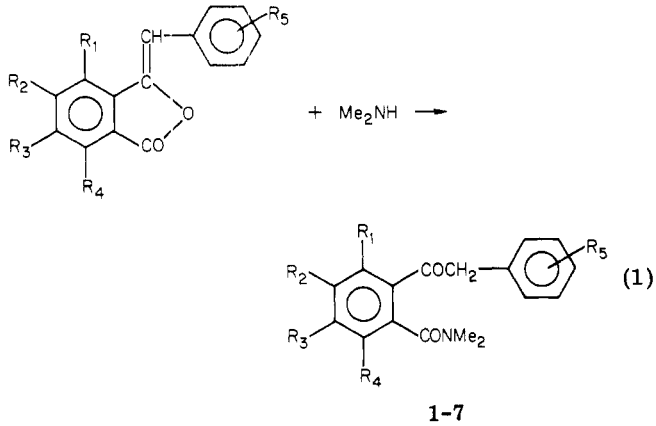
A series of *o*-arylacetyl-*N*,*N*-dimethylbenzamides, **1–7**, being studied as models for chain tautomers, differed markedly in their ^{1}H NMR spectral properties, as a function of the substituents R_1–R_4. In the two cases where substituents were placed ortho to the amide group, the benzylic protons were anisochronous at ambient temperatures. Reported dynamic ^{1}H NMR results are consistent with concomitant C–N and aryl–CO torsional processes. The ^{13}C carbonyl shifts are compared with those of model compounds.

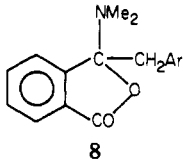
In connection with a dynamic NMR study of ring–chain tautomerism, we have prepared a series of *N*,*N*-dimethylamides, **1–7**, of *o*-arylacetylbenzoic acids from the corresponding enol lactones (eq 1). These, in turn, had each been prepared by condensation of an arylacetic acid under aldol conditions[3] with a phthalic anhydride; the exception was the enol lactone precursor of **3**,[4] which was obtained by aldol condensation of benzaldehyde with 6-nitrophthalide.[5] To our surprise, the benzylic protons in amides **2** and **4** were anisochronous, appearing as well-resolved AB quartets at ambient temperature. All the other amides exhibited the expected singlet for the COCH_2Ar group. Inasmuch as infrared spectra ruled out the nucleophilic[6] ring tautomeric structure **8**, we attribute the nonequivalence of the benzylic protons in **2** and **4** to atropisomerism,[7] the result of restricted rotation about the aryl–carbonyl bond of the amide functional group (vide infra).



(1)

1-7

compd	R_1	R_2	R_3	R_4	R_5
1	H	H	H	H	H
2	H	H	H	Me	H
3	H	H	NO_2	H	H
4	Cl	Cl	Cl	Cl	H
5	H	H	H	H	*o*-Me
6	H	H	H	H	*p*-Cl
7	H	H	H	H	*p*-NO_2



8

Results of dynamic ^{1}H NMR studies of **2**, **4**, and **5** are given in Table I. Data for high-temperature coalescence of both the benzylic and *N*-methyl resonances are shown for **2** and **4**. Low-temperature dynamic behavior of the benzylic resonance of **5** is also reported. Calculation of

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(2) (a) University of New Hampshire Undergraduate Research Participant, Summer 1972; (b) National Science Foundation College Teacher Research Participant, 1971.

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Table I. Dynamic ^{1}H NMR Results for 2, 4, and 5[a]

		benzylic resonance				N-methyl resonance		
compd	solvent	$\Delta\nu_{AB}$, Hz	J_{AB}, Hz	T_c, °C	$\Delta G_c^{\ddagger}$, kcal/mol	$\Delta\nu$, Hz	T_c, °C	$\Delta G_c^{\ddagger}$, kcal/mol
2	$Cl_2CDCDCl_2$	14.5	16.8	135	20.4 ± 0.2	38.3	147	21.1 ± 0.2
4	Me_2SO-d_6	16.8	18.9	149	21.0 ± 0.2	15.4	165	22.9 ± 0.2
5	Me_2CO-d_6	23.1	17.4	−96	8.5 ± 0.3			

[a] Reference 9.

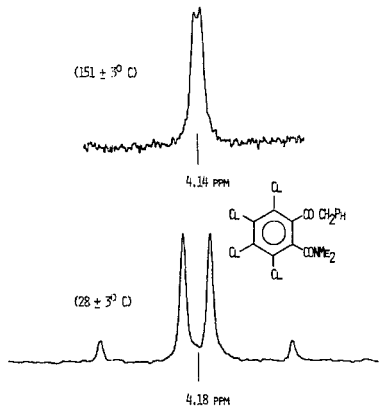
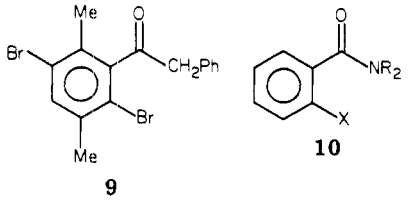


Figure 1. Temperature dependence on the ^{1}H NMR spectrum of 4 (90 MHz, Me_2SO-d_6).

$\Delta G_c^{\ddagger}$ values were based upon eq 2.[8] A transmission coefficient of $\kappa = 1$ was utilized throughout. The AB portion of the spectrum of 4 at ambient temperature and at coalescence is reproduced in Figure 1.[9]

$$\Delta G_c^{\ddagger} = 4.57 T_c[9.97 + \log (T_c/(\Delta\delta^2 + 6J^2)^{1/2})] \quad (2)$$

A priori, geminal anisochronism of the benzylic protons could be the result of rate-limiting restricted rotation about either the ketone or the amide aryl–carbonyl bond. Comparison of the $\Delta\Delta G^{\ddagger}$'s (benzylic between 2 and 5 (12 kcal/mol) and between 2 and 4 (0.6 kcal/mol) strongly indicates that the latter mechanism is operative, at least for the 2,6-disubstitued benzamides. This view is consistent with the low rotational barriers for hindered aryl benzyl ketones measured by Nakamura and Ōki.[10] The highest value reported was $\Delta G_c^{\ddagger}$ = 12.4 kcal/mol (−27 °C, pyridine–CS_2) for 9.



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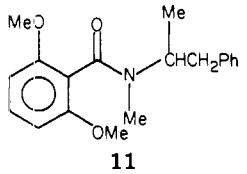
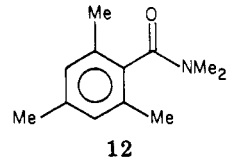


11

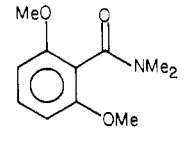
While restricted rotation about the C–N partial double bond of benzamides is a well-documented process,[11] relatively fewer examples of restricted rotation about the aryl–carbonyl bond have been reported.[12-18] Ortho-substituted benzamides, 10, are known to be nonplanar in the solid state, the angle of twist between aryl and amide depending upon substitutent (X) steric size.[15] Reported rotational barriers for 10 vary between 12 and 16 kcal/mol and are dependent not only upon X but also upon the steric size of R. An early indication of restricted rotation in more sterically hindered 2,6-disubstituted benzamides came from the work of Siddall and Garner on 11.[12] From the collapse of the pairs of methoxy resonances of the CN rotamers at high temperature, they estimated an aryl–CO rotational barrier of ≥20 kcal/mol. The only quantitative data available for 2,6-disubstituted benzamides is provided by the recent elegant chiral shift reagent studies of Holik and Mannschreck.[18] Our C(sp^2)–C(aryl) rotational barriers measured for 2 and 4 are in good qualitative agreement with the 23.4 and 22.4 kcal/mol barriers reported for 12 and 13, respectively. The ca. 3-kcal/mol barrier decrease from 12 to 2 is explained by the difference in effective steric size between a flanking methyl group (in 12) and an sp^2 benzoyl (in 2).

Table II. ^{13}C Carbonyl Chemical Shifts of 2, 4, 5 and Model Compounds

	carbonyl shifts, δ_c	
compd	amide	ketone
13	171.4	
14		197.5
5	171.3	198.5
2	170.8	198.7
4	164.5	199.7



12



13

Inspection of molecular models of 2 and 4 convinces us that significant twisting about the dimethylamido C–N bond must take place in the transition state for aryl–CO(amide) rotation in order to avoid steric compression of an N-methyl group and one of the 2,6-substituents. The remarkable 12-kcal/mol $\Delta\Delta G^{\ddagger}$ between 2 and 5 and the large differences between hindered benzamides and the hindered ketones of Nakamura and Ōki[10] are accounted for reasonably by correlated C–N and aryl–CO rotations. Such a coupled-barrier mechanism was alluded to by Siddall and co-workers[19] and has been proposed by

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(9) The use of three different solvents was necessitated by the accidental isochronism of the benzylic protons of 2 in Me_2SO-d_6, the insolubility of 4 in $Cl_2CDCDCl_2$, and the low-temperature requirement for 5. The indicated error limits for $\Delta G_c^{\ddagger}$ were estimated on the basis of a temperature error estimate of ±3 °C. The greater uncertainty in the value for 5 reflects additional uncertainty in $\Delta\nu$ and J_{AB} due to broad lines and a low signal/noise ratio in the slow exchange spectrum.
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Table III. Melting Point, IR, and ^{1}H NMR Results for *o*-Arylacetyl-*N,N*-dimethylbenzamides[a]

amide	mp, °C (solvent)	IR,[b] cm^{-1} ketone	IR,[b] cm^{-1} amide	^{1}H NMR ($CDCl_3$, 34 °C), δ
1	101–104 (PhH/lig)	1684	1635	2.73 (s), 3.12 (s), 4.22 (s), 7.3–8.0 (m)
2	110–112 (lig)	1686	1630	2.28 (s), 2.68 (s), 3.10 (s), 4.2 (AB, J = 16 Hz), 7.2–7.9 (m)
3	148–152 dec ($CHCl_3$-lig)	1694	1640	2.86 (s), 3.17 (s), 4.36 (s), 7.3–8.5 (m)
4	274–277 (Me_2CO-H_2O)	1709	1650	2.83 (s), 3.03 (s), 4.17 (AB, J = 19 Hz), 7.2–7.4 (m)
5	101–103 (lig)	1689	1630	2.27 (s), 2.77 (s), 3.10 (s), 4.28 (s), 7.2–8.1 (m)
6	116.5–119 (EtOH-H_2O)	1686	1630	2.77 (s), 3.11 (s), 4.22 (s), 7.2–8.1 (m)
7	121–123 ($CHCl_3$-lig)	1691	1630	2.81 (s), 3.12 (s), 4.44 (s), 7.4–8.4 (m)

[a] Satisfactory C, H, and N analyses (±0.3%) were obtained for compounds **1–7**. [b] Carbonyl stretching frequency ±2 cm^{-1}.

Sandström and co-workers for thiobenzamides.[20] While our data do not allow a quantitative evaluation of the contribution of amide deconjugation to the process measured by benzylic resonance coalescence, the similarity between those values and the *N*-methyl coalescence values (for **2** and **4**) is strongly suggestive of a concerted torsional process.

The ^{13}C NMR spectra of **2**, **4**, and **5** were examined with respect to model compounds dimethylbenzamide (**13**) and benzyl phenyl ketone (**14**); carbonyl chemical shifts are listed in Table II. The ketone carbonyl is deshielded with increasing ortho substitution due to steric inhibition of resonance (increased twist angle), in agreement with the results of others.[21] The observed insensitivity of the amide carbonyl (except for **4**) is consistent with large twist angles for all members of the series, in agreement with solid-state results for para-substituted dimethylbenzamide.[22] The significant upfield shift of the amide carbonyl of **4** must be the result of a field effect of Cl.

To our knowledge this is the first instance of atropisomerism of benzamides in which an sp^2 functional group is one of the ortho substituents. The high energy barrier to rotation suggests that such compounds should be resolvable, as is the case with the aryl *tert*-butyl ketone described by Pinkus.[23]

Experimental Section

Routine ^{1}H NMR spectra were measured on a Varian Model A-60 or a JEOL JNM-MH-100 instrument. ^{13}C and dynamic ^{1}H NMR experiments were carried out on a JEOL FX-90Q equipped with an NM-VTS temperature controller. An internal ^{2}H lock and 5-mm tubes were employed; $CDCl_3$ was the solvent for the ^{13}C work. Coaxial assemblies containing ethylene glycol or methanol and the appropriate coaxial lock solvent were utilized for measurement of high and low temperatures, respectively. Chemical shifts are reported in parts per million downfield from internal Me_4Si. C, H, and N analyses were determined by Mrs. Linda C. Heavner or Dr. Gail J. Lambert at the University of New Hampshire or by Galbraith Laboratories. Data are reported in Table III.

The phthalic anhydride and phenylacetic acids were commercial samples and were used without further purification.

Preparation of Enol Lactones from Phthalic Anhydrides. The general method of preparation was similar to that described by Weiss.[3] The procedure described below is representative.

3-Benzylidene-4,5,6,7-tetrachlorophthalide. A mixture of 64.5 g (0.225 mol) of tetrachlorophthalic anhydride, 45 g (0.33 mol) of phenylacetic acid, and 0.82 g of freshly fused sodium acetate was heated in an oil bath, with stirring, at 230 °C for 3 h. The yellow residual solid was washed once with boiling ethanol and then recrystallized from benzene to a canary yellow material: 65.9 g (82%); mp 288–290 °C. Anal. Calcd for $C_{15}H_6Cl_4O_2$: C, 50.05; H, 1.68. Found: C, 50.15; H, 1.63.

Other enol lactones were either used without isolation in pure form or were already known, with the exception of 3-(*p*-chlorobenzylidene)phthalide, mp 150–152 °C. Anal. Calcd for $C_{15}H_9ClO_2$: C, 70.18; H, 3.53. Found: C, 70.42; H, 3.40.

Preparation of 2-Arylacetylbenzamides 1–7. To a suspension of 0.01 mol of the appropriate enol lactone in boiling ethanol was added 14 g (0.08 mol) of 25% aqueous dimethylamine, whereupon the mixture turned to a deep red solution. It was heated for 30 min and diluted with an equal volume of water. The precipitated solid was collected, air-dried, and recrystallized.

Registry No. 1, 20871-38-9; 2, 74331-63-8; 3, 74331-64-9; 4, 74331-65-0; 5, 74331-66-1; 6, 74331-67-2; 7, 74331-68-3; 13, 71955-53-8; 14, 451-40-1; phthalic anhydride, 85-44-9; 4-methylphthalic anhydride, 4792-30-7; *o*-methylphenylacetic acid, 644-36-0; *p*-chlorophenylacetic acid, 1878-66-6; *p*-nitrophenylacetic acid, 104-03-0; 3-benzylidene-4,5,6,7-tetrachlorophthalide, 19320-04-8; tetrachlorophthalic anhydride, 117-08-8; phenylacetic acid, 103-82-2; dimethylamine, 124-40-3; 3-benzylidenephthalide, 575-61-1; 3-benzylidene-7-methylphthalide, 13376-03-9; 3-benzylidene-6-nitrophthalide, 15298-16-5; 3-(2-methoxybenzylidene)phthalide, 63400-76-0; 3-(4-chlorobenzylidene)phthalide, 20526-97-0; 3-(4-nitrobenzylidene)phthalide, 27695-16-5; benzaldehyde, 100-52-7; 6-nitrophthalide, 610-93-5.

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