2-Chloromethylenecycloheptan- and -octanones: a Conformational Study by Dipole Moments, Spectroscopy, and Nucleophilic Reactivity

By **Demetrio Pitea,* Pier Luigi Beltrame,** and **Giorgio Favini,** Institute of Physical Chemistry, University of Milan, Milan, Italy

The title compounds were identified as *trans-s-cis* by their spectroscopic properties and experimental and calculated dipole moments. Their reactions with piperidine in ethanol were studied kinetically at 15—45 °C. Measured rate coefficients for 2-chloromethylenecyclo-octanone are larger than those of the parent seven-membered cyclic compound, the rate ratio being 2—3. The decrease in reactivity as ring size decreases is explained in terms of a diminished degree of conjugation in the vinyl-carbonyl skeleton due to deviation from coplanarity. Further support comes from u.v. and n.m.r. spectra as well as dipole moments. A comparison between the nucleophilic reactivity of *s-cis* and *s-trans* derivatives is discussed.

IN the course of our investigations on molecular conformation of β-halogeno- and β-piperidino-vinyl ketones, studies on nucleophilic substitution,[1,2] dipole moment analyses,[3] and theoretical calculations [4] were performed. For 3-chlorocyclohex-2-enone in particular a close agreement was found between experimental dipole moment and electronic spectrum and theoretical values for a structure in which the oxygen and five carbon atoms are coplanar while C(5) is out of plane. The same conformation was found for the parent cyclohex-2-enone.[5] For 3-chloro-5,5-dimethylcyclohex-2-enone, kinetic and

---

[1] P. Beltrame, G. Favini, M. G. Cattania, and F. Guella, *Gazzetta*, 1968, **98**, 381.

[2] D. Pitea and G. Favini, *J.C.S. Perkin II*, 1972, 291.

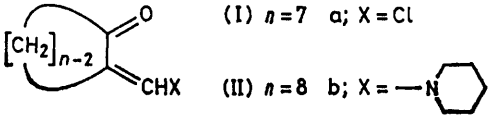
[3] D. Pitea and G. Favini, *J.C.S. Perkin II*, 1972, 142.

[4] G. Favini, D. Pitea, and F. Zuccarello, *Z. Phys. Chem.* (*Frankfurt*), 1973, **84**, 306.

[5] S. A. Manley and J. K. Tyler, *Chem. Comm.*, 1970, 382.

dipole moment results support a structure in which the steric crowding between the 5(*ax*)-methyl and C(1—3) was relieved by twisting of *ca.* 30° around the essentially single bond. Evidence for reduced conjugation in the parent 5,5-dimethylcyclohex-2-enone was also given by other authors [6,7] but this effect was explained in different ways. In ref. 6 an electronic interaction between the axial methyl group and the π cloud of the system was invoked, while a geometry with the oxygen lying slightly below the plane defined by H(2), C(2), C(3), and H(3) and on the same side as C(5) was proposed in ref. 7.

In the present paper we report dipole moments, u.v., i.r., and n.m.r. spectra, and kinetic results of the reaction with piperidine in ethanol for 2-chloromethylenecycloheptanone (Ia) and -octanone (IIa). These compounds



have been selected as models of the *s-cis* conformation. Previously reported data [1-3] concerned labile or fixed *trans-s-trans* compounds.

EXPERIMENTAL AND RESULTS

G.l.c. was performed on a Carlo Erba Fractovap model GV. U.v., i.r., and n.m.r. spectra were taken on a Hitachi–Perkin-Elmer 124, a Perkin-Elmer 21, and a Varian A-60 apparatus, respectively. Dry ethanol was purified by a standard method.[8] Commercial piperidine was stored over KOH pellets and distilled before use; the fraction of b.p. 106—107° was collected.

Compounds (Ia) *and* (IIa).—These compounds were prepared from the corresponding 2-hydroxy-derivatives by reaction with thionyl chloride in diethyl ether.[9-11] Purity was checked by g.l.c. analysis using a column packed with SE 30 (15%) coated on Chromosorb P (45—60 mesh).

Compounds (Ib) *and* (IIb).—The appropriate chloro-derivative and piperidine were separately dissolved in ethanol. The solutions (molar ratio 1 : 2.3) were mixed and the mixture left during 48 h at room temperature. The solvent was evaporated *in vacuo*, anydrous benzene added, and the solution filtered. After evaporation of benzene, an oil was obtained (99.8% yield, based on piperidine hydrochloride). The products were unstable and were analysed as soon as they were obtained. 2-*Piperidinomethylenecycloheptanone* (Ib) (Found: C, 74.95; H, 10.35; N, 6.5. $C_{13}H_{21}NO$ requires C, 75.3; H, 10.2; N, 6.75%) has $\nu_{max.}$ 1 654 (coupled carbonyl stretching mode in the *s-cis* form) [12] and 1 551 (coupled vinyl stretching mode) cm^{-1}; δ ($CDCl_3$) 1.67 (12 H, m), 2.55 (4 H, m), 3.37 (4 H, m), and 7.38 (1 H, t, J 1.5 Hz); $\lambda_{max.}$ (ethanol) 329.5 (ε 17 600). 2-*Piperidinomethylenecyclo-octanone* (IIb) (Found: C, 75.35; H, 10.6; N, 6.0. $C_{14}H_{23}NO$ requires C, 75.95; H, 10.5; N, 6.35%) has $\nu_{max.}$ 1 643 and 1 542 cm^{-1}; δ ($CDCl_3$) 1.60 (14 H, m), 2.60 (4 H, m), 3.43 (4 H, m), 7.47 (1 H, s); $\lambda_{max.}$ (ethanol) 329.5 (ε 20 700).

Kinetics.—Weighted amounts of piperidine and halogeno-derivative were separately dissolved in ethanol and the thermostatted solutions were mixed in a stoppered Pyrex vessel kept at constant temperature ±0.05 °C. Samples for spectrophotometric analysis were removed and quenched by dilution with Spectrograde ethanol at recorded times. The substrate disappearance and the product formation were simultaneously recorded by absorbance measurements at 240 and 245 nm for compounds (Ia) and (IIa) respectively, and at 330 nm for compounds (Ib) and (IIb).

In any case, as the dilution quenching was not perfectly efficient, analyses were performed as soon as possible. Calculated values of absorbance at infinity time were used for rate coefficient calculations owing to the low stability of the products. Some kinetic runs were followed to completion by argentometric analyses. Results by the two methods were in good agreement.

For all reactions, most of which were followed to 60—80% completion, results fitted a second-order rate equation. Table 1 shows the mean values of the rate coefficients (±2—3%). Activation parameters were calculated according to Arrhenius and Eyring equations by a standard computer program (indexes of determination were >0.99; for details of calculations see ref. 2).

TABLE 1

Rate coefficients for substitution of (Ia) and (IIa) (0.001—0.010M) by piperidine (0.002—0.020M) in ethanol [a]

(Ia)

t/°C	15.0	25.0	35.0	45.0
$10^3 \bar{k}$/l mol^{-1} s^{-1}	7.31	12.9	26.7	48.4

E_a 11.6 ± 0.2 kcal mol^{-1}; log A 6.63 ± 0.18; $\Delta H^\ddagger$ 11.0 ± 0.2 kcal mol^{-1}; $\Delta S^\ddagger$ -30.2 ± 0.8 cal mol^{-1} K^{-1}.

(IIa)

t/°C	15.6	25.0	35.0	45.1
$10^3 \bar{k}$/l mol^{-1} s^{-1}	12.8	25.2	56.2	119

E_a 13.9 ± 0.2 kcal mol^{-1}; log A 8.63 ± 0.17; $\Delta H^\ddagger$ 13.3 ± 0.2 kcal mol^{-1}; $\Delta S^\ddagger$ -21.1 ± 0.8 cal mol^{-1} K^{-1}.

[a] The reported values refer to runs at stoicheiometric concentrations; as a check of kinetic order, runs at different initial concentrations were carried out.

Experimental Dipole Moments.—Electric dipole moments of compounds (Ia), (IIa), (Ib), and (IIb) were determined as described previously.[3] The measured properties of the solutions at 25.0 °C, together with the polarization data are given in Supplementary Publication No. SUP 22052 (4 pp).* The μ/D values are: (Ia), 3.12; (IIa), 3.04; (Ib), 4.29; (IIb), 4.46.

Calculated Dipole Moments.—The theoretical dipole moments analysis of chloro-derivatives has been carried out by four different approaches. The compound MeC(1)O·C(2)Me:C(3)HCl was chosen as a model. The bond lengths r_{CO} 1.227, $r_{C(1)C(2)}$ 1.471, $r_{C(2)C(3)}$ 1.337, r_{CCl} 1.718, $r_{C(sp^2)C(sp^3)}$ 1.52, $r_{C(sp^2)H}$ 1.08, and $r_{C(sp^3)H}$ 1.09 Å were selected. All valence angles in the vinyl-carbonyl system were assumed to be 120°.

In the vectorial addition of bond and group moments (procedure A) the total moments were calculated by assum-

---

* Details of Supplementary Publications are in Notice to Authors No. 7 in *J.C.S. Perkin II*, 1976, Index issue. Items less than 10 pp. are supplied as full-size copies.

[6] J. Torri and M. Azzaro, *Bull. Soc. chim. France*, 1974, 1633.

[7] I. H. Elson, T. J. Kemp, D. Greatorex, and H. D. B. Jenkins, *J.C.S. Faraday II*, 1973, 665.

[8] A. I. Vogel, 'Practical Organic Chemistry,' Longman, London, 1959, p. 306.

[9] W. Treibs and H. J. Neupert, *Annalen*, 1955, **595**, 219.

[10] B. Eistert and H. Wurzler, *Annalen*, 1961, **650**, 157.

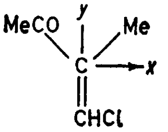
[11] A. E. Pohland and W. R. Benson, *Chem. Rev.*, 1966, **66**, 161.

[12] J. Dabrowski and K. Kamieńska-Trela, *Spectrochim. Acta*, 1966, **22**, 211.

ing that the following link moment values M(A–B) * apply: C–H, 0.00; Me–C, 0.37; C=O, 2.78; C–Cl, 1.59 D. In procedures B and C, the total moment was estimated by dissecting the π component from the σ component. The σ dipole contributions were calculated from the bond moment reported in ref. 3. The π dipole contributions were calculated (a) in procedure B by the HMO method using the following parameters †: $\alpha_O = \alpha_0 + 0.7\beta_0$; $\alpha_{C(1)} = \alpha_0 + 0.1\beta_0$; $\alpha_{C(2)} = \alpha_0$; $\alpha_{C(3)} = \alpha_0 + 0.2\beta_0$; $\alpha_{Cl} = \alpha_0 + 1.7\beta_0$; $\beta_{C(1)O} = 1.04\beta_0$; $\beta_{C(1)C(2)} = 0.476\beta_0$; $\beta_{C(2)C(3)} = 0.995\beta_0$: $\beta_{C(3)Cl} = 0.5\beta_0$; (b) in procedure C by the SCF–MO technique in the Pople approximation.[4] In procedure D, the total dipole moments were calculated by the CNDO/2 method.[13,14]

TABLE 2

Calculated dipole moments (D) for the planar model compound MeCO·CMe:CHCl



Conformation	Procedure	$\mu(x)$	$\mu(y)$	$\mu_{calc.}$
cis-s-cis	A	−4.10	−2.74	4.94
	B	−3.76	−2.16	4.34
	C [a]	−4.53	−3.06	5.46
	D	−3.59	−2.65	4.46
trans-s-cis	A	−1.35	−2.74	3.06
	B	−1.55	−2.16	2.66
	C [b]	−2.06	−3.18	3.79
	D	−1.16	−2.59	2.84

[a] Ref. 4. [b] In Table 2 of ref. 4 the quoted value is erroneous; this is the corrected one.

DISCUSSION

For 2-chloromethylenecyclo-heptanone (Ia) and -octanone (IIa) the $\Delta\nu$ ($\nu_{CO} - \nu_{CC}$) and r_i (ratio of the integrated intensities of the carbonyl and double bond stretching vibrations) values together with the ε values are in line with those expected for an *s-cis* conformation.[15]

TABLE 3

Observed and calculated $\pi^* \longleftarrow \pi$ electronic transitions of (Ia) and (IIa)

		Vapour phase $\lambda_{max.}$/nm	n-Hexane $\lambda_{max.}$/nm (ε)	Cyclohexane $\lambda_{max.}$/nm (ε)	Methanol $\lambda_{max.}$/nm (ε)	Ethanol $\lambda_{max.}$/nm (ε)
(Ia)	Obs.	232.0	238.8 (10 300)	239.3 (9 800)	241.0 (9 200)	241.3 (9 100)
	Calc.[a]	234.0	240.7	241.4	240.2	240.7
(IIa)	Obs.	236.6	242.6 (9 900)	243.2 (9 900)	245.3 (8 700)	245.7 (9 200)
	Calc.[a]	234.0	240.0	240.7	239.6	240.0

[a] From ref. 4.

N.m.r. and dipole moment data support a *trans* configuration. The signals for vinylic proton compare well with δ 7.15 reported for the *trans-s-cis* conformation of 2-chloromethylenecyclohexanone.[15] The theoretical dipole moments are reported in Table 2. The values for the *trans-s-cis* conformation are in the range 2.7—3.8 D in good agreement with experimental values, whilst those for the *cis-s-cis* conformation are significantly higher (4.3—5.5 D).

Compound (IIa) is more reactive than (Ia) by a factor of 2.6 at 50 °C. The difference is rather small but it becomes meaningful when associated with other experimental facts. Table 3 gives the experimental absorption band maxima of (Ia) and (IIa) in the vapour phase and in n-hexane, cyclohexane, methanol, and ethanol solutions. $\pi^* \longleftarrow \pi$ Transition energies calculated within the PPP–SCF–MO approximation[4] are given for comparison. The u.v. data confirm the *trans-s-cis* conformation of (Ia) and (IIa) and show that (IIa) absorbs at higher wavelength than (Ia). The n.m.r. signal is shifted upfield from (Ia) to (IIa). The dipole moment of (IIa) is slightly lower than for (Ia).

The smaller reactivity, the u.v. blue displacement, and the difference in the chemical shift should suggest a reduced coplanarity of the vinyl-carbonyl system in (Ia), with the subsequent lower efficiency in the transmission of the electronic effect. CNDO Calculations performed on the model compound MeCO·CMe:CHCl show an increase in the dipole moment from 2.84 to 2.97 D when the twist angle ω_{12} around the essentially single bond was varied from 0 to 30°. On this basis, the experimental dipole moments are in line with the above suggestions: an interplanar angle lower than 30° may be roughly estimated. This is well consistent with the order of reactivity $k_{(IIa)} > k_{(Ia)}$ when compared with the correlation between order of reactivity and the twist angle reported for 3-chlorocyclohex-2-enone and the corresponding 5,5-dimethyl derivative.[3] The different planarity of the vinyl-carbonyl skeleton in the seven- and eight-membered ring compounds has been also found by a conformational study of the parent 2-methylenecycloalkan-1-ones.[16]

The reactivity of our compounds with piperidine in ethanol can be compared with that of 1-chloro-2-methylpent-1-en-3-one for which the *trans-s-trans* conformation is most probable as shown previously.[1,2,4] Compounds (Ia) and (IIa) are more reactive than 1-chloro-2-methylpent-1-en-3-one by factors of 6 and 16 (at 50 °C) respectively. This comparison, though it involves cyclic and open-chain derivatives, is valid as the vinyl-carbonyl system is in every case equally substituted; to the best of our knowledge, this is the first evaluation of the influence of the *s-cis* and *s-trans*

---

* The convention here used to define link moments is that A is the positive end of the dipole in M(A–B).

† Values of ref. 3 corrected to take into account the perturbating effect of differing substitution.

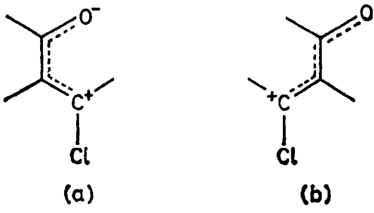
[13] J. A. Pople and G. A. Segal, *J. Chem. Phys.*, 1966, **44**, 3289.

[14] D. P. Santry and G. A. Segal, *J. Chem. Phys.*, 1967, **47**, 158.

[15] H. Martens, G. Hoornaert, and S. Toppet, *Tetrahedron*, 1973, **29**, 4241.

[16] H. J. Köhler, M. Scholz, and M. Mühlstädt, *J. prakt. Chem.*, 1971, **313**, 17.

conformations on nucleophilic reactivity in vinyl systems. It is well known that in the addition–elimination route direct attack at the vinylic carbon by the electron-rich nucleophile suggests that the reaction is facilitated by diminishing the electron density at the double bond.[17] This can be done *e.g.* by a carbonyl group which spreads the negative charge and polarizes the double bond in such a way that a partial positive charge is developed at the β-carbon atom. In the *s-cis* compounds the dipolar structure (a) will be more stabilized than (b) by a direct field effect between the ends of the conjugated systems. The resultant induced dipole (by the carbonyl group) in an *s-cis* arrangement has been estimated as four times that induced in an *s-trans* arrangement.[18] As a consequence, the nucleophilic substitution is more activated in the *s-cis* compounds.* The difference in reactivity due to a conformational effect seems to be greater than that due to a configurational effect. In fact, in the addition–elimination routes for nucleophilic vinylic substitution on chloro-derivatives, $k_{cis} : k_{trans}$ ratios are usually small.[19,20]



From a theoretical point of view this is expected as the *s-cis* ⟶ *s-trans* change involves stronger perturbation in the charge distribution of the conjugated system than does configurational inversion.

Financial support from the Italian C.N.R. is acknowledged.

[6/1922 *Received*, 14*th October*, 1976]

---

* One of the referees suggested that the greater reactivity of the *s-cis*-compounds may be explained by the formation of a six-membered transition state involving a hydrogen bond.

[17] Z. Rappoport, 'Advances in Physical Organic Chemistry,' ed. V. Gold, Academic Press, London, 1969, vol. 7, p. 1.

[18] J. B. Bentley, K. B. Everard, R. J. B. Marsden, and L. E. Sutton, *J. Chem. Soc.*, 1949, 2957.

[19] G. Marchese, F. Naso, and G. Modena, *J. Chem. Soc.* (*B*), 1968, 958.

[20] P. Beltrame, P. L. Beltrame, G. Carboni, and M. L. Cereda, *J. Chem. Soc.* (*B*), 1970, 730.