B. The appropriate **35** (24 mmol) and thiophosgene (36 mmol) were heated at 100 °C in a sealed tube for the indicated time and then fractionally distilled. **62a**: 24 h; bp 55 °C (0.1 mm); ρ = 1.57. **62b**: 96 h; bp 53–56 °C (0.1 mm); ρ = 1.49, both colorless liquids.

Stereochemistry of Sequence for Dithiocarbonyl Group Synthesis (Scheme IV). A solution of (*R*)-2-octanol (4.9 g, 37.7 mmol) in toluene (20 mL) was refluxed with sodium (0.69 g, 30 mmol) until all of the sodium had dissolved. After cooling to 25 °C, CS_2 (2.3 g, 30 mmol) was added with stirring. After 10 min, a solution of MeI (4.3 g, 30 mmol) in ether (25 mL) was added and reacted for a further hour. The reaction mixture was washed with water (50 mL), dried ($MgSO_4$), evaporated, and distilled to give pure (*R*)-*O*-2-octyl *S*-methyl dithiocarbonate (**73**): yield, 3.98 g (60%); bp 70–74 °C (0.2 mm) [lit.[34] bp 102 °C (0.4 mm)]; $[\alpha]^{25}_D$ + 6.44 (lit.[34] for *S* isomer, –6.75); NMR δ 5.70 (m, J = 6.1 Hz, 1 H), 2.54 (s, 3 H), 1.0–1.9 (m, 13 H), 0.88 (skewed t, 3 H). The starting (*R*)-2-octanol used had $[\alpha]^{25}_D$ –8.5° (lit.[45] –9.9°).

The optically active xanthate **73** (3 g, 13.6 mmol) was reacted with **35a** (1.73 g, 13.6 mmol) which was slowly added at 0 °C. After additional standing at 25 °C for 2 h, the 2-chlorooctane was separated by distillation: yield, 0.80 g (40%); bp 50 °C (10 mm); $[\alpha]^{25}_D$ +12.09°; NMR δ 4.03 (m, J = 6.4 Hz, 1 H), 1.50 (d, J = 6.5 Hz, 3 H), overlapping 1.0–1.8 (m, 10 H), 0.88 (skewed t, 3 H).

Acknowledgment. We thank Steven J. Eastep and Pamela M. Fier for expert technical assistance, and John K. Lofdahl, Steve J. Rudd, Lori J. Enloe, and Jeff K. Rowe for their enthusiastic contributions. Financial support from the National Institutes of Health (GM 28934 and Research Career Development Award to G.B., AM 01099), Research Corporation (Leo H. Baekeland Grant), and Chicago Community Trust (Searle Scholars Program) is gratefully noted.

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Registry No. **1**, 51615-88-4; **2**, 51615-91-9; **3**, 87462-93-9; **4**, 87462-94-0; **5**, 87462-97-3; **6**, 87462-98-4; **7**, 15110-08-4; **8a**, 2812-72-8; **8b**, 2812-73-9; **9**, 2757-23-5; **10a**, 87462-91-7; **10b**, 87462-92-8; **11a**, 18369-83-0; **11b**, 2941-64-2; **12a**, 13063-89-3; **12b**, 13221-50-6; **14a**, 1468-37-7; **14b**, 502-55-6; **15a**, 19708-81-7; **15b**, 023-54-1; **16a**, 26404-95-5; **16b**, 623-79-0; **17a**, 868-84-8; **17b**, 623-80-3; **18**, 10596-55-1; **19a**, 1115-13-5; **19b**, 762-03-8; **20**, 82810-48-8; **21a**, 79-22-1; **21b**, 541-41-3; **22a**, 87463-06-7; **22b**, 87463-07-8; **23a**, 26698-15-7; **23b**, 3278-35-1; **24a**, 18804-17-6; **24b**, 2905-52-4; **25a**, 25170-09-6; **25b**, 1851-77-0; **26a**, 74568-23-3; **26b**, 1851-71-4; **27a**, 616-38-6; **27b**, 105-58-8; **28a**, 38103-95-6; **28b**, 38103-96-7; **29a**, 14919-12-1; **29b**, 3554-12-9; **30a**, 2314-48-9; **30b**, 2314-49-0; **31a**, 16696-91-6; **31b**, 35447-70-2; **32**, 594-42-3; **33a**, 87463-08-9; **33b**, 87463-09-0; **34a**, 20524-84-9; **34b**, 20524-84-9; **35a**, 26555-40-8; **35b**, 26555-35-1; **36a**, 55048-60-7; **36b**, 30654-33-2; **37a**, 64231-91-0; **37b**, 30453-25-9; **38a**, 5813-48-9; **38b**, 1496-75-9; **39a**, 30411-03-1; **39b**, 30411-04-2; **40a**, 624-92-0; **40b**, 110-81-6; **41a**, 3658-80-8; **41b**, 3600-24-6; **42a**, 5756-24-1; **42b**, 13730-34-2; **43a**, 26555-39-5; **43b**, 6365-90-8; **44a**, 34520-64-4; **44b**, 35832-93-0; **45**, 71133-44-3; **46**, 51480-12-7; **47**, 87463-10-3; **48**, 2786-62-1; **49**, 87462-99-5; **50**, 16188-45-7; **51a**, 87463-11-4; **51b**, 87463-00-1; **52**, 19009-45-1; **53a**, 3012-99-5; **53b**, 40088-76-4; **54a**, 87462-95-1; **54b**, 87462-96-2; **55**, 87463-12-5; **56**, 87463-04-5; **57a**, 87463-05-6; **57b**, 87463-01-2; **58a**, 87463-14-7; **59a**, 87463-15-8; **60a**, 87463-16-9; **61**, 87463-13-6; **62a**, 87463-02-3; **62b**, 87463-03-4; **63a**, 87463-17-0; **63b**, 87463-18-1; **64**, 20333-39-5; **65a**, 1190-35-8; **65b**, 36955-31-4; **66a**, 65605-22-3; **67a**, 28685-60-1; **68a**, 62603-94-5; **69**, 2254-94-6; **70**, 4285-42-1; **71**, 611-92-7; (*R*)-**73**, 77714-50-2; **74i**, 16844-08-9; **74ii**, 18651-57-5; $EtOCS_2K$, 140-89-6; EtSNa, 811-51-8; $MeOCS_2K$, 2667-20-1; MeSNa, 5188-07-8; EtSH, 75-08-1; *i*-Pr_2NH, 108-18-9; PhNH(Me), 100-61-8; $CSCl_2$, 463-71-8; MeCl, 74-87-3; EtCl, 75-00-3; MeSSSSSMe, 7330-31-6; (*R*)-2-octanol, 5978-70-1.

Supplementary Material Available: Additional experimental details, including all compounds not explicitly described in text, and tabulations of all spectral, analytical, and chromatographic data (28 pages). Ordering information is given on any current masthead page.

Notes

Structural Effects on the Electron-Donor Ability of Carbonyl Bases. A Quantitative Analysis

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Recent studies[1,2] on the charge-transfer (CT) equilibria between carbonyl bases and iodine in "inert"[3] solvents (reaction 1) have shown the nonadditivity of substituent effects on the free energies of complexation, $\Delta G°_1$, corresponding to the process shown.

$$R_1CO\ R_2 + I_2 \rightleftharpoons R_1CO\ R_2 \cdots I_2 \qquad (1)$$

The results given in Table I for ketones, disubstituted amides (R_1 = Me, R_2 = NMe_2, NEt_2), and tetrasubstituted ureas (R_1, R_2 = NMe_2, NEt_2) clearly illustrate this phenomenon.

It is also known that hydrogen-bonding complexes between carbonyl bases and proton donors are also subject to nonadditive substituent effects.[4] The attempts to rationalize these facts have considered *either* the steric hindrance to the planarity of the N–CO–N moiety[5] *or* the saturation of the electron-accepting power of the carbonyl group.[4] We feel that these two mechanisms are by no means mutually exclusive, and in this work, we have determined several free energies of association between iodine and carbonyl bases in order to achieve their quantitative dissection.

Discussion

The quantitative separation of steric and electronic saturation effects is based upon the following assumptions.

(i) The sum of the inductive and resonance contributions is the same for the methyl and *tert*-butyl groups. This contention is substantiated as follows: the experimental values for $(\Delta G°_1)_{MeCOMe}$ and $(\Delta G°_1)_{MeCO\text{-}t\text{-}Bu}$ are the same within experimental errors, as seen in Table I. We also

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(2) Laurence, C.; Guiheneuf, G.; Wojtkowiak, B. *J. Am. Chem. Soc.* **1979**, *101*, 4793.
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0022-3263/83/1948-4761$01.50/0

Table I. K_c and ΔG°_1 for R_1COR_2[a]

R_1	R_2	K_c, L mol^{-1}	ΔG°_1, kcal mol^{-1}	R_1	R_2	K_c, L mol^{-1}	ΔG°_1, kcal mol^{-1}
Me	Me[b]	1.12 ± 0.06	−0.07 ± 0.03	NMe_2	Cl[c]	0.70 ± 0.08	0.20 ± 0.06
	Me_3C[b]	1.14 ± 0.08	−0.08 ± 0.03		CN[c,d]	0.45 ± 0.13	0.48 ± 0.12
	Me[b]	15.0 ± 0.4	−1.6 ± 0.1		OMe[c]	3.80 ± 0.55	−0.80 ± 0.09
	NMe_2[b]	14.3 ± 0.9	−1.58 ± 0.08		OPh[c]	2.2 ± 0.5	−0.46 ± 0.12
NMe_2	NEt_2[c]	14.3 ± 0.8	−1.58 ± 0.06	NEt_2	Me[b]	18.8 ± 0.5	−1.74 ± 0.08
	Me_3C[c]	6.7 ± 0.4	−1.13 ± 0.03		Me_3C[c]	6.65 ± 0.90	−1.12 ± 0.08
	H[b]	6.45 ± 0.6	−1.10 ± 0.05		NMe_2[c]	14.3 ± 0.8	−1.58 ± 0.06
	Ph[b]	8.1 ± 0.7	−1.24 ± 0.05		NEt_2[b]	11.0 ± 1.0	−1.42 ± 0.07

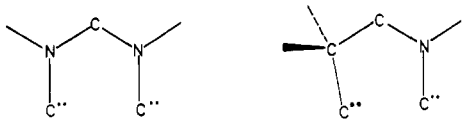
[a] The experimental techniques have been described elsewhere;[1,2] K_c values and ΔG°_1 values are given at the 95% confidence level. [b] Taken from ref 1. [c] This work. [d] Given the low solubility of Me_2NCOCN in *n*-heptane, this value has been calculated from the experimental datum in CCl_4 through the following equation:[2] $\log (K_c)_{C_7H_{16}} = 0.38 + 1.24 \log (K_c)_{CCl_4}$.

have found[2] that for the compounds R–CO–R′, ΔG°_1 can be satisfactorily expressed as a linear combination of the inductive (σ_I) and resonance (σ_R^+) parameters of R and R′ (tetrasubstituted ureas are excluded) (eq 2). Interestingly,

$$(\Delta G^\circ_1)_{RCOR'} = 0.51 + 2.63\sigma_I + 0.94\sigma_R^+ \quad (2)$$
$$n = 28 \text{ and } r = 0.959$$

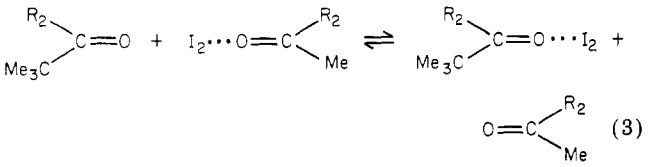
this equation does not include any steric contribution and, as it should, leads to almost identical values for acetone and pinacolone.

(ii) In terms of their mutual steric interactions, Me_3C and NMe_2 are equivalent. We consider this to be so on account of the fact that both substituents carry methyl groups (denoted as C** in the structures shown below)



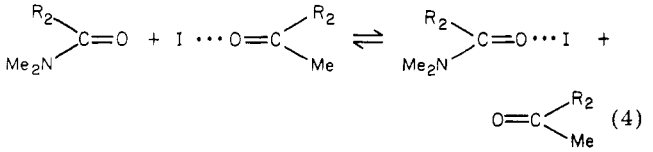
which prevent the planarity of the N–CO–N and C–CO–N systems in molecules such as tetramethylurea and *N,N*-dimethylpivalamide. It is tempting to consider the isopropyl group as a better steric model for NMe_2. Careful inspection of molecular models shows, however, that Me_2CH allows the existence of planar conformations.

We assume, therefore, that the change in free energy, ΔG°_2, corresponding to reaction 3 (R_2 = NMe_2 or NEt_2)



(3)

is a good measure of the steric contributions to the change in free energy, ΔG°[3], involved in process 4.



(4)

(1) Experimental Determination of ΔG°_2. If we apply this criterion to tetramethylurea (A; R_1 = R_2 = NMe_2) and to *N,N*-dimethyl-, *N′,N′*-diethylurea (B; R_1 = NEt_2, R_2 = NMe_2), we obtain eq 5 and 6.

$$(\Delta G^\circ_2)_A = (\Delta G^\circ_1)_{Me_3CCONMe_2} - (\Delta G^\circ_1)_{MeCONMe_2} = 0.47 \text{ kcal mol}^{-1} \quad (5)$$

$$(\Delta G^\circ_2)_B = (\Delta G^\circ_1)_{Me_3CCONEt_2} - (\Delta G^\circ_1)_{MeCONEt_2} = 0.62 \text{ kcal mol}^{-1} \quad (6)$$

It appears that, while the difference between these effects is small, it tends to indicate a larger steric hindrance for B, as can be reasonably expected.

(2) Quantitative Evaluation of Electronic Saturation Effects (ESE). With the assumption of strict additivity of electronic effects, we calculate $(\Delta G^\circ_1)_A$ and $(\Delta G^\circ_1)_B$ as shown in eq 7 and 8.

$$(\Delta G^\circ_1)_A = 2((\Delta G^\circ_1)_{MeCONMe_2} - (\Delta G^\circ_1)_{MeCOMe}) + (\Delta G^\circ_1)_{MeCOMe} = -3.13 \text{ kcal mol}^{-1} \quad (7)$$

$$(\Delta G^\circ_1)_B = ((\Delta G^\circ_1)_{MeCONMe_2} - (\Delta G^\circ_1)_{MeCOMe}) + ((\Delta G^\circ_1)_{MeCONEt_2} - (\Delta G^\circ_1)_{MeCOMe}) + (\Delta G^\circ_1)_{MeCOMe} = -3.27 \text{ kcal mol}^{-1} \quad (8)$$

Table I shows that the experimental values are both equal to −1.58 kcal mol^{-1}. Upon correction for steric contributions (0.47 and 0.62 kcal mol^{-1}) we obtain −2.07 and −2.20 kcal mol^{-1}. We take the difference, $\delta\Delta G^\circ$, between the corrected experimental values and those calculated as a quantitative measure of the ESE. We then find that $(\delta\Delta G^\circ)_A$ = 1.08 kcal mol^{-1} and $(\delta\Delta G^\circ)_B$ = 1.07 kcal mol^{-1}, that is, essentially the same value. This is not unexpected, given the closeness of the electronic properties of NMe_2 and NEt_2. Furthermore, it is reasonable to assume that this is also the ESE value for tetraethylurea (C), and, on this basis, we calculate the steric contribiton to the nonadditivity of substituent effects in C as 0.92 kcal mol^{-1}.

To summarize, the steric contributions to the nonadditivity respectively amount to 30%, 37%, and 46% for A, B, and C. These figures do not seem to support the vistas of others workers[4] who consider these effects to be extremely small.

(3) Regarding the Origin of ESE. From the data given in Table I and after appropriate correction for steric effects, we obtain expression 9. It is useful to compare

$$(\Delta G^\circ_1)_{Me_2NCOR_2} = -1.27 + 3.28\sigma_I + 0.51\sigma_R^+ \quad (9)$$
$$n = 8 \text{ and } r = 0.988$$

this correlation equation to the relationships of the form (eq 10) satisfied by the families MeCOR and PhCOR[1,2]

$$\Delta G^\circ_1 = (\Delta G^\circ_1)_0 + \rho_I\sigma_I + \rho_R\sigma_R^+ \quad (10)$$

involved in the same reaction eq 11 and 12).

$$(\Delta G^\circ_1)_{MeCOR} = 0.15 + 3.22\sigma_I + 1.05\sigma_R^+ \quad (11)$$
$$n = 6 \text{ and } r = 0.986$$

$$(\Delta G^\circ_1)_{PhCOR} = 0.23 + 3.00\sigma_I + 0.88\sigma_R^+ \quad (12)$$
$$n = 8 \text{ and } r = 0.985$$

We observe that, in all cases, the coefficient ρ_I is practically the same, while the coefficient ρ_R^+ increases in the

order $(\rho_R^+)_{Me} > (\rho_R^+)_{Ph} > (\rho_R^+)_{NMe_2}$. This implies that, since the three families display the same sensitivity to inductive effects, the large electronic saturation brought about by the introduction of the first NMe_2 group essentially originates in the saturation of the conjugative ability of the carbonyl group.

Experimental Section

UV Measurements. These experiments have employed a Cary 219 spectrophotometer with matched 1-cm silica window cells. The temperature was kept constant within 0.1 °C by means of water circulation provided by a Lauda LS-15 ultrathermostat.

Materials. The solvents were Merck Uvasol products, stored over molecular sieves (4 Å) and distilled immediately prior to use. The compounds ***N,N*-dimethylpivalamide** (I), **methyl *N,N*-dimethylcarbamate** (II), **phenyl *N,N*-dimethylcarbamate** (III), ***N,N*-diethylpivalamide** (IV), and ***N,N*-dimethyl-*N'*,*N'*-diethylurea** (V) have been obtained by addition of an excess of diethylamine or dimethylamine to an etheral solution of the corresponding chloride. After filtration and removal of the solvent and the excess amine, these materials were purified by low-pressure fractional distillation or by crystallization ($PhOCONMe_2$). ***N,N*-Dimethylcarbamoyl cyanide (VI)** was obtained by treating *N,N*-dimethylcarbamoyl chloride (32 g, 0.3 mol) with potassium cyanide (32.5 g, 0.5 mol) in dry methylene chloride (150 mL) containing a catalytic amount (0.1 g) of 18-crown-6 ether.[6] The mixture was vigorously stirred for 24 h at room temperature and then filtered. Following the evaporation of solvent, the title compound was purified by low-pressure fractional distillation [bp 110 °C (25 torr)]. The yield of pure material was 50%. All these compounds are known and, in every case, their physical and spectroscopic properties were in good agreement with the data reported in the literature.[7]

Registry No. I, 24331-71-3; II, 7541-16-4; III, 6969-90-0; IV, 24331-72-4; V, 14216-18-3; VI, 16703-51-8; *N,N*-dimethylcarbamoyl chloride, 79-44-7; iodine, 7553-56-2.

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Short Regioselective Synthesis of (±)-α-Cuparenone via Three-Carbon Annelation

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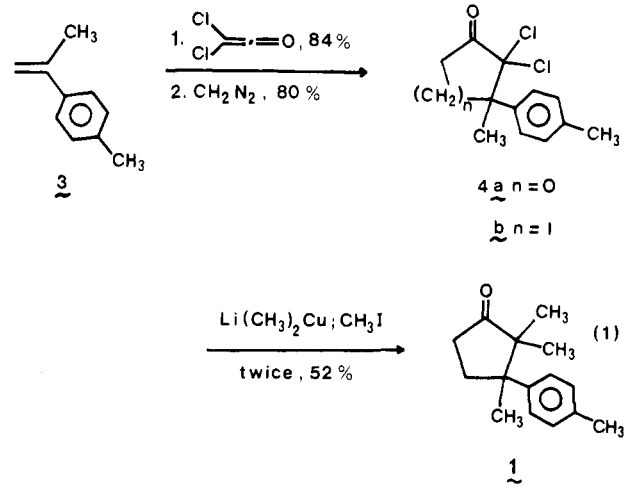
A great many of the syntheses of α- and β-cuparenones (**1** and **2**, from "mayur pankhi"[1]) and related compounds have been carried out primarily to demonstrate new methods of cyclopentanone formation and/or procedures for creating (vicinal) quaternary centers.[2] Nevertheless, there are to date relatively few efficient approaches to these deceptively simple molecules. In this paper we report a brief high-yield synthesis of (±)-α-cuparenone,[3] which is based on a novel reductive geminal dimethylation of α,α-dichlorocyclopentanone **4b**, itself readily produced by three-carbon annelation[4] of tolylpropene **3** (eq 1).



2-(*p*-Tolyl)propene[5] was converted to the α,α-dichlorocyclobutanone **4a** (mp 51–52 °C) in 84% yield through treatment with trichloroacetyl chloride and phosphorus oxychloride in ether in the presence of a zinc–copper couple.[6] None of the isomeric cyclobutanone could be detected. As expected from previous work,[4] ring enlargement of the cyclobutanone **4a** with diazomethane in ether–methanol also proved to be highly regioselective and yielded the α,α-dichlorocyclopentanone **4b** (mp 88–89 °C) in 80% isolated yield.

To complete the synthesis of **1**, replacement of the chloro substituents at the highly crowded α-position in **4b** with methyl groups was required. Previously, we had shown that α,α-dichlorocyclopentanones undergo clean reductive cleavage–methylation on treatment with lithium dimethylcopper followed by methyl iodide.[7] Dichloride **4b**, when subjected twice to these conditions, suffered the desired geminal substitutions[8] to produce in 52% overall

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(2) See: Halazy, S.; Zutterman, F.; Krief, A. *Tetrahedron Lett.* **1982**, *23*, 4385 and references therein. Gadwood, R. C. *J. Org. Chem.* **1983**, *48*, 2098. See also: Chandrasekaran, S.; Turner, J. V. *Tetrahedron Lett.* **1982**, *23*, 3799. Leriverend, M. L.; Vazeux, M. *J. Chem. Soc., Chem. Commun.* **1982**, 866.

(3) A synthesis of β-cuparenone (**2**) using a different approach has also been carried out and will be described separately (Greene, A. E.; Lansard J. P.; Luche, J. L.; Petrier, C., submitted for publication).

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(6) Krepski, L. R.; Hassner, A. *J. Org. Chem.* **1978**, *43*, 2879. See also: Bak, D. A.; Brady, W. T. *Ibid.* **1979**, *44*, 107 and references therein. Chloromethylketene ($CH_3CHClCOCl$, $(C_2H_5)_3N$, cyclohexane, Δ) also underwent cycloaddition; however, the yield of the adduct was unsatisfactory.

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(8) Although reductive cleavage followed by enolate alkylation is a very well-known process, it apparently has not previously been applied iteratively in order to effect geminal dialkylation. See: House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: New York, 1972; p 565. See also footnote 6 in ref 7a. See, however: Coates, R. M.; Pigott, H. D.; Ollinger, J. *Tetrahedron Lett.* **1974**, 3955. Coates, R. M.; Shah, S. K.; Mason, R. W. *J. Am. Chem. Soc.* **1982**, *104*, 2198. Posner, G. H.; Mallamo, J. P.; Hulce, M.; Frye, L. L. *Ibid.* **1982**, *104*, 4180.

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