8.8 (6 H). These n.m.r. data rigorously exclude III from further consideration as a structure for the major isolable product.

Reduction of the product $C_{20}H_{20}N_2O$ with lithium aluminium hydride[4] gave a colorless oil, $C_{20}H_{22}N_2$, which was purified by v.p.c. (*Anal.* Found: C, 82.10; H 7.71) and had no carbonyl band in the infrared. Thus cycloadducts such as IV and V are also eliminated as structures for the product.
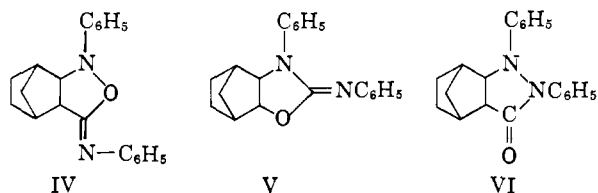

While the 3-pyrazolidone VI is the structure most consistent with the spectral[5] and chemical evidence that can be formally derived from II and phenyl isocyanate by a cycloaddition, it may not be assigned to the product at present.

The reaction of the cyclopentene-phenyl azide adduct, 2-phenyl-2,3,4-triazabicyclo[3.3.0]oct-3-ene (VII), with phenyl isothiocyanate has also been represented as a "1,3-dipolar cycloaddition."[3]
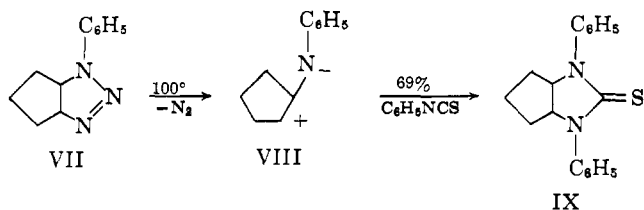
When it became clear that the reaction of the nor-bornene-phenyl azide adduct with phenyl isocyanate does not follow an analogous pathway, the thermal decomposition of VII in the presence of phenyl isothiocyanate was reinvestigated. The major product from the reaction is neither the thiourea IX nor the 3-thio-pyrazolidone X, but rather the thioanilide XI.[6]
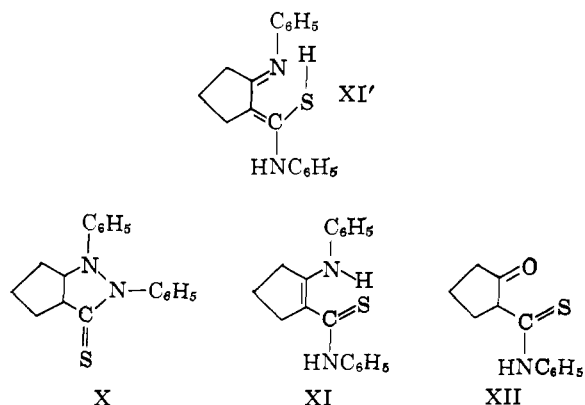
The triazoline VII with an excess of phenyl isothiocyanate in chlorobenzene at 110° gave the product $C_{18}H_{18}N_2S$ [*Anal.* Found: C, 73.36; H, 6.12; N, 9.39; mol. wt., 296 (osmometric in benzene)] as bright yellow needles, m.p. 128.5-130.5° (78% yield, from cyclohexane); $\nu_{max}^{CHCl_3}$ 3390, 1612, 1595, 1580, 1500,

(4) Compare R. L. Hinman, *J. Am. Chem. Soc.*, **78**, 1645 (1956).

(5) B. J. R. Nicolaus, *et al.*, *Helv. Chim. Acta*, **44**, 2055 (1961).

(6) Possible tautomerization between XI and XI' is here neglected.

1390, and 1250 cm.⁻¹ strong; $\lambda_{max}^{CHCl_3}$ 386 (ϵ 24,000) and 314 mµ (ϵ 9000). The n.m.r. spectrum of a solution of the product in deuteriochloroform had absorption at τ −3.0 (1 H), 2.0-3.4 (11 H), a multiplet centered at 7.25 (4 H), and a multiplet centered at 8.15 (2 H).

The infrared, ultraviolet, and n.m.r. spectral data are all incompatible with structure IX.[7] The spectral data may, however, be rationally correlated with an alternate structural proposal, the thioanilide XI. In particular, the 3390 cm.⁻¹ band in the infrared and the τ −3.0 proton in the n.m.r. spectra may be assigned to the NH proton of XI, hydrogen bonded to sulfur.[6]

Conclusive evidence in favor of structure XI was obtained by hydrolysis of the product $C_{18}H_{18}N_2S$ with 70% sulfuric acid to aniline and β-ketothioanilide XII. The hydrolysis product proved identical with an independently synthesized[8] authentic sample of XII as judged by melting point, mixture melting point, and infrared and n.m.r. spectral criteria.

This reaction of triazoline VII may involve 1-anilino-cyclopentene as an intermediate,[8,9] or some more complex mechanism may obtain. It is clear that, at least in our hands, the reaction is no cycloaddition, and that seemingly modest variations in structure, as between the cyclopentene- and norbornene-phenyl azide adducts and between phenyl isothiocyanate and phenyl isocyanate, can divert one high-yield process to alternative modes of behavior. That the reaction of I with phenyl isocyanate involves the dipole II as an intermediate appears extremely doubtful. Preliminary work indicates that the rate of nitrogen evolution from I depends on the phenyl isocyanate concentration.

Whether or not our products VI, m.p. 162°, and XI, m.p. 128.5-130.5°, and those isolated by earlier workers[2,3] and assigned structures III and IX are identical remains to be seen.[10] Kinetic studies of these and similar reactions are in progress.

The present results strongly suggest that "1,3-dipolar cycloadditions" may be less mechanistically homogeneous than has been previously supposed.

(7) For N,N'-diphenylthiourea, λ_{max}^{EtOH} 272 mµ (log ϵ 4.32); M. G. Ettlinger and J. E. Hodgkins, *J. Am. Chem. Soc.*, **77**, 1831 (1955).

(8) W. Reid and W. Käppeler, *Ann.*, **673**, 132 (1964).

(9) G. A. Berchtold, *J. Org. Chem.*, **26**, 3034 (1961); S. Hünig, K. Hübner, and E. Benzing, *Chem. Ber.*, **95**, 926 (1962); R. Fusco, G. Bianchetti, and S. Rossi, *Gazz. chim. ital.*, **91**, 825 (1961).

(10) In ref. 2 and 3, credit for these cycloaddition products is given to unpublished research of R. Huisgen and R. Grashey, Munich, 1959-1960; unfortunately, no melting points or spectral data for the adducts "III" and "IX" are given.

(11) National Science Foundation Undergraduate Research Participant.

NOYES CHEMICAL LABORATORY   JOHN E. BALDWIN
UNIVERSITY OF ILLINOIS   GARY V. KAISER[11]
URBANA, ILLINOIS   JUDITH A. ROMERSBERGER[11]

The Influence of Unsaturation and of Fluorine Substitution on Ketone–Alcohol Equilibrium Constants.
A Measure of α,β-Unsaturated Ketone Resonance Energy and of Halogen Destabilization[1]

Sir:

The destabilization of a carbonyl group by a halogen atom located α to a saturated ketone or α, β, or γ to

TABLE I

Alcohol	Ketone	$K_{eq} \times 10^{-8}$ (eq. 1)[a,c]	ΔF_3°, kcal. (eq. 3)	$\nu_{max}^{CHCl_3}$ cm.$^{-1}$ ketone
A.		0.01	+8.5	1734
B.		1	+5.8	1704
C.		1.8	+5.5	1688; 1697[b]
D.		4	+5.0	1685
E.		22	+4.0	1680
F.		90	+3.2	1675
G.		900	+1.7	1660

[a] Equilibrium constants were reproducible to about ±20% on repeated runs. [b] Doublet. Infrared spectra were determined by Mr. George Scrimshaw on a Beckman IR-7 with Bausch and Lomb replica grating. [c] Equilibrium constants were determined spectrophotometrically in 0.03 M phosphate buffer by following the appearance or disappearance of DPNH at 340 mμ essentially according to the procedure of Talalay and Marcus (ref. 4). In the case of entry G equilibrium was approached from both sides while the others were determined by reduction of the ketone.

an α,β-unsaturated ketone is well-recognized,[2,3] although the magnitude of this effect has not been directly open to experimental determination. Recently we have found that the 3α-hydroxysteroid dehydrogenase of *Pseudomonas testosteroni*[4] catalyzes the reversible, DPNH dependent conversion of Δ^4-3-ketosteroids to the corresponding Δ^4-3α-hydroxy compound (eq. 1) and that a halogen substituent on or adjacent to the unsaturated ketone system facilitates the reduction.[5]

We have now measured the equilibrium constants[6] for the conversion of testosterone and a number of its fluorinated derivatives to the Δ^4-3α-alcohols. This has enabled determination of the magnitude of the halogen effect and, further, comparison of the respective equilibrium constants for the saturated and unsaturated ketone–alcohol systems provides an estimate of the extra resonance energy of an α,β-unsaturated 3-ketosteroid.

$$\text{alcohol} + \text{DPN}^+ \rightleftharpoons \text{ketone} + \text{DPNH} + \text{H}^+ \quad \Delta F_1^{\circ} \quad (1)$$

$$\text{DPN}^+ + 2\text{H} \rightleftharpoons \text{DPNH} + \text{H}^+ \quad \Delta F_2^{\circ} \quad (2)$$

$$\text{alcohol} \rightleftharpoons \text{ketone} + 2\text{H} \quad \Delta F_3^{\circ} = \Delta F_1^{\circ} - \Delta F_2^{\circ} \quad (3)$$
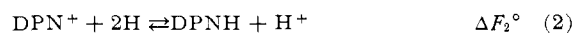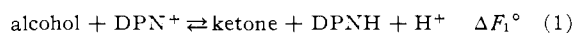
Table I lists the equilibrium constants at 27° corresponding to eq. 1 $[K = ([\text{ketone}][\text{DPNH}][\text{H}^+])/$

(2) *Cf.* E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2301 (1953); J. Allinger and N. L. Allinger, *Tetrahedron*, **2**, 64 (1958); N. L. Allinger, M. A. DaRooge, M. A. Miller, and B. Waegell, *J. Org. Chem.*, **28**, 780 (1963).

(3) H. J. Ringold and A. Bowers, *Experientia*, **17**, 65 (1961).

(4) P. Talalay and P. I. Marcus, *J. Biol. Chem.*, **218**, 675 (1956).

(5) H. J. Ringold, J. Graves, M. Hayano, and H. Lawrence, Jr., *Biochem. Biophys. Res. Commun.*, **13**, 162 (1963).

(6) See ref. 4 for the enzymatic determination of the equilibrium constants of saturated alcohol–ketone systems.

([alcohol][DPN$^+$])] and the standard free energy change, ΔF_3°, corresponding to eq. 3 (alcohol $\rightleftharpoons$ ketone + 2H). The latter value is readily obtained[4] from ΔF_1° by subtracting ΔF_2° (+5.2 kcal.), the standard free energy change for the conversion of DPN$^+$ to DPNH (eq. 2) which has been determined by Burton and Wilson.[7] Testosterone (Table I, G) exhibited $K_{eq} = 900 \times 10^{-8}$. Introduction of a fluorine atom at the 6α- (equatorial), 6β- (axial), 4-, and 2-positions, respectively, led to progressive shifts of the equilibrium constants toward the alcohol. In the case of 2α-fluorotestosterone (C) there was a 500-fold shift relative to testosterone, $K = 1.8 \times 10^{-8}$, which was of the order of magnitude of the saturated 5α-3-ketone B, $K = 1 \times 10^{-8}$ (900-fold shift). Introduction of a 2α-fluoro substituent into the saturated ketone A resulted in a further 100-fold displacement of the equilibrium constant toward the alcohol.

One may derive certain interesting data by making the reasonable assumption that the effects noted are due primarily to electronic stabilization or destabilization of the ketone rather than of the alcohol. Table II lists the effects ($\Delta\Delta F_3^{\circ}$) of the various groups on the equilibrium constants. Subtraction of the free-energy change for the conversion of the 5α-3α-ol to the saturated 5α-3-one from that of the conversion of the Δ^4-3α-ol to the Δ^4-3-one gives a $\Delta\Delta F_3^{\circ}$ of -4.1 kcal., which may be taken as a first approximation of the additional resonance energy of the α,β-unsaturated ketone. An additional 0.3 kcal. should be added to this figure for a net α,β-unsaturated ketone resonance energy of about 4.4 kcal.[8] since the saturated 3α-ol has one additional 1,3-diaxial interaction (3α-OH, 5α-H), which is not present in the Δ^4-3α-ol.

TABLE II

INFLUENCE OF VARIOUS GROUPS ON EQUILIBRIUM: ALCOHOL $\rightleftharpoons$ KETONE + 2H

Group	Entry numbers from Table I	$\Delta\Delta F_3^{\circ}$, kcal.[a]
4(5)-Double bond	G–B	-4.1
2α-Fluoro (saturated ketone)	A–B	$+2.7$
2α-Fluoro (Δ^4-3-ketone)	C–G	$+3.8$
4-Fluoro (Δ^4-3-ketone)	D–G	$+3.3$
6β-Fluoro (Δ^4-3-ketone)	E–G	$+2.3$
6α-Fluoro (Δ^4-3-ketone)	F–G	$+1.5$

[a] Estimated accuracy ±0.15 kcal.

The equatorial α-halo ketone effect, commonly attributed to halogen–oxygen dipole–dipole repulsion, is readily recognized by the bathochromic shift of the carbonyl stretching frequency in the infrared.[9] This effect is seen in the 2α-fluoro-saturated ketone which is destabilized by 2.7 kcal. relative to the unsubstituted saturated ketone, a figure identical with the electrostatic interaction calculated by Corey[2] for an equatorial α-bromocyclohexanone.

The 3.8-kcal. destabilization effect of the 2α-fluoro group and the 3.3-kcal. effect of the 4-fluoro atom in the α,β-unsaturated ketones would appear to be due to a combination of the aforementioned electrostatic interaction and an inhibition of double-bond polariza-

(7) K. Burton and T. H. Wilson, *Biochem. J.*, **54**, 86 (1953).

(8) M. M. Kreevoy and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 4016 (1957), have obtained a value of about 6 kcal. for noncyclic α,β-unsaturated ketones based on the free energy and heat of hydrogenation.

(9) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *ibid.*, **74**, 2828 (1952).

tion. The slightly lower effect of the 4-fluoro atom may be due to the contribution of a stabilizing resonance

$$C-^-$$

form, $O=C-C=F^+$, not possible with a 2-fluoro group. The spectral shifts of the carbonyl group due to the introduction of a γ-fluoro atom into an α,β-unsaturated ketone and the relatively greater effect of an axial substituent have been recognized and explained[3] on the basis of prevention of double-bond polarization. In the present study the 6α-fluoro (equatorial) substituent caused a 10-fold shift in K_{eq} and the 6β-fluoro (axial) group a 40-fold shift or a net destabilization of the unsaturated ketone of 1.5 and 2.3 kcal., respectively. The general parallel between the position of the carbonyl frequency in the infrared and the position of the ketone–alcohol equilibrium (Table I) is worthy of note and supports the contention that the primary effect observed is one of ketone destabilization.

Enzymatic reductions[10] which have demonstrated the facile formation of Δ^4-3-ols from the halogenated unsaturated ketones may now be reinterpreted, in part, to include equilibrium considerations, although the electronic factors leading to high equilibrium concentrations of allyl alcohols appear to be the same as those promoting fast hydride transfer from reduced pyridine nucleotides.

(10) H. J. Ringold, S. Ramachandran, and E. Forchielli, *Biochim. Biophys. Acta*, **82**, 143 (1964).

WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY SHREWSBURY, MASSACHUSETTS
HOWARD J. RINGOLD
HAROLD LAWRENCE, JR.
J. M. H. GRAVES

The Effect of Pressure on the Rate of Hydrolysis of Chloroform. The Nature of the Transition State

Sir:

The dissociation of CCl_3^- to chloride ion and dichlorocarbene is commonly assumed to be the rate-controlling step in the basic hydrolysis of chloroform.[1] The possibility that the chloride ion might be displaced by water has been mentioned by Hine[2]; on the basis of kinetic arguments this path was held to be an unlikely one, although it could not be ruled out. More recently, a study of the base-promoted methanolysis of chloroform[3] showed k_2 to be proportional to h_-. However, the use of acidity functions in assessing the role of solvent molecules is at best highly uncertain, and it remains therefore an open question whether the solvent is to any degree involved in the formation of the intermediate.

Whalley, *et al.*,[4] and the present authors[5] have found knowledge of ΔV^* to be helpful in solving similar problems involving acid catalysis. It therefore appeared to us that a measurement of the pressure coefficient of the rate constant in the hydrolysis of chloroform would reveal to what extent water is involved in the

(1) J. Hine, "Divalent Carbon," The Ronald Press Company, New York, N. Y., 1964, pp. 36–42.
(2) J. Hine, *J. Am. Chem. Soc.*, **72**, 2438 (1950).
(3) R. A. M. O'Ferrall and J. H. Ridd, *J. Chem. Soc.*, 5035 (1963).
(4) For several references, see E. Whalley, "Advances in Physical Organic Chemistry," Vol. 2, V. Gold, Ed., Academic Press, Inc., New York, N. Y., 1964.
(5) W. le Noble and M. Duffy, *J. Phys. Chem.*, **68**, 619 (1964).

rate-determining step in that reaction. As before, any such participation is expected to lead to a negative activation volume, whereas simple dissociation would be characterized by a volume expansion. The data, essentially obtained by techniques described earlier,[6] are shown in Table I.

TABLE I

THE EFFECT OF PRESSURE ON THE RATE OF BASIC HYDROLYSIS OF CHLOROFORM AT 25° IN WATER CONTAINING 3% METHANOL

Pressure, kbar	$k_2 \times 10^5$, 1/mole sec.	Number of observations[a]
0.00	7.39	5
1.07	3.53	4
2.13	2.15	4
3.17	1.62	4
4.21	1.08	4
5.24	0.66	4
6.45	0.70	4

[a] The reaction was followed to about 70% completion; the rate constants were reproducible to about 5%. The base concentration was about 1; the chloroform concentration was below the saturation point by a factor of 10.

A plot of ln k_2 *vs.* p yields a ΔV_0^* of $+16$ cm.^{3}/mole, by far the largest positive activation volume reported to date for a reaction in water.[7] This may be considered conclusive evidence that no water becomes bound in the transition state; the magnitude of the effect strongly suggests, in fact, that water electrostatically bound by the CCl_3^- ion is being released during the reaction and that the transition state goes on to free CCl_2. We are currently investigating other reactions assumed to go through carbene intermediates, and hope to report those results as well as some of the experimental details later.

(6) W. le Noble, *J. Am. Chem. Soc.*, **85**, 1470 (1963).
(7) This value is even more remarkable when it is remembered that ΔV^* tends to be smaller in highly polar solvents: K. R. Brower, *ibid.*, **85**, 1401 (1963).

DEPARTMENT OF CHEMISTRY
STATE UNIVERSITY OF NEW YORK AT STONY BROOK
STONY BROOK, NEW YORK
W. J. LE NOBLE
M. DUFFY

Photoelimination of Ethylene from 2-Pentanone[1]

Sir:

In a recent Communication to the Editor, it was mentioned[2] that Michael and Noyes[3] reaffirmed that the photoelimination of olefins from carbonyl-containing compounds, often called a type II process, occurs *via* a singlet excited state. It was felt worthwhile to report, at this time, some of the additional results obtained in our laboratory which may resolve the controversy concerning the excited state involved in the photoelimination

$$CH_3COC_3H_7^* \longrightarrow C_2H_4 + CH_3COCH_3 \qquad (1)$$
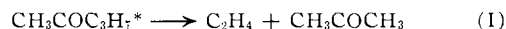
We confirm the findings of Michael and Noyes[3] that at 3130 Å., addition of biacetyl to 2-pentanone quenches

(1) This work was supported by the U. S. Public Health Service, Department of Health, Education, and Welfare.
(2) P. Borrell, *J. Am. Chem. Soc.*, **86**, 3156 (1964).
(3) J. L. Michael and W. A. Noyes, Jr., *ibid.*, **85**, 1027 (1963).