perature and pressure. After exposure to hydrogen for 24 hr., the reaction mixture was filtered, and the filtrate was dried over potassium carbonate and evaporated. The yellow residue was recrystallized from *n*-heptane to give 0.34 g. (80.9%) of *cis*-**7**, m.p. 95–97°. The product of this reaction was identical (by infrared and mixture melting point) in every respect with that obtained from methods A and B.

1-Methyl-4-phenyl-3-piperidone (8).—A solution of 2.5 g. of 1-methyl-4-phenyl-3,4-epoxypiperidine (**5**) in 25 ml. of ether was placed in a 200-ml. three-neck set-up, and 35 ml. of boron trifluoride etherate was added over a period of 5 min. The mixture was heated under reflux for 8 hr., cooled, and neutralized with 70 ml. of 5 *N* sodium hydroxide. Stirring was continued for 1 hr. The layers were separated, and the water layer was extracted with four 50-ml. portions of ether and four 50-ml. portions of chloroform. The organic layers were combined, dried over potassium carbonate, and evaporated to give 1.62 g. (65%) of crude 1-methyl-4-phenyl-3-piperidone (**8**).[8] The product was characterized as the oxime which was prepared by heating a mixture of 1.5 g. of crude **8**, 1.04 g. of hydroxylamine hydrochloride, and 0.60 g. of sodium hydroxide in a water–methanol solution. Concentration of the reaction mixture by evaporation gave 0.60 g. (37.5%) of **8** oxime, m.p. 166–168°, after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90. Found: C, 70.65; H, 8.11.

The Reduction of 1-Methyl-4-phenyl-3-piperidone (8) with Lithium Aluminum Hydride.—A solution of 5 g. of 1-methyl-4-phenyl-3-piperidone **8** in 15 ml. of 1,2-dimethoxyethane was added dropwise to a slurry of 1.0 g. of lithium aluminum hydride in 40 ml. of 1,2-dimethoxyethane. The reaction mixture was heated under reflux for 1 hr. and the excess lithium aluminum hydride was decomposed with water. The resulting precipitate was separated by filtration and washed with two 10-ml. portions of ether. The combined ether extracts were dried over anhydrous potassium carbonate and evaporated to give 3.8 g. (76%) of a yellow oil. Gas chromatographic analysis of the crude product indicated that it was 53.6% *trans*-**7** and 20.3% *cis*-**7**. A picrate, m.p. 224–230°, isolated from the crude product was identical in every respect with the picrate of *trans*-**7**, m.p. 226–229°.[6]

1-Methyl-4-phenylpiperidine-3,4-diol (9). A.—A solution of 0.5 g. of 1-methyl-4-phenyl-3,4-epoxypiperidine (**5**) in 50 ml. of 1 *N* hydrochloric acid was stirred at room temperature for 10 hr. The mixture was saturated with potassium carbonate, and the precipitate which formed was removed by filtration. Recrystallization of the solid from acetone gave 0.47 g. (86.2%) of **9**, m.p. 157–159°. This compound seemed to be identical with the compound prepared by McElvain and Safranski[2] and was identified as **9**.

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found[9]: C, 69.58; H, 8.32; N, 6.50.

B.—To a solution of 3.5 g. of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (**1**) in 4.8 g. of trifluoroacetic and 30 ml. of acetic acids was added a solution of 5.2 g. of *m*-chloroperoxybenzoic acid in 25 ml. of acetic acid. The reaction was exothermic and the addition required 15 min. After stirring at room temperature for 8 hr., the reaction was cooled in an ice bath; 325 ml. of 20% sodium hydroxide was added while maintaining the temperature below 40°. The mixture was extracted four times with 100-ml. portions of ether, and the ether extracts were dried over potassium carbonate. The solvent was removed from the extracts by distillation to give 3.15 g. of oily residue, which was shown by gas chromatographic analysis to contain about 37% unreacted **1**. The oily residue was dissolved in acetone, and deposited 1.35 g. (35.4%) of 1-methyl-4-phenylpiperidine-3,4-diol (**9**). On recrystallization from acetone the product was shown by infrared spectroscopy, melting point, and mixture melting point to be identical with the **9** prepared by opening the epoxide **5**.

Acknowledgment.—The authors wish to express appreciation to the National Heart Institute of the National Institutes of Health for partial support of this research by Grant HE-01713 and continuation grants. The *m*-chloroperoxybenzoic acid used in this research was generously supplied by FMC Corporation.

(8) This compound has been prepared previously but spectroscopic data were not available: for comparison, see S. M. McElvain and P. M. Laughton, *J. Am. Chem. Soc.*, **73**, 448 (1951).

(9) The analyses of **9** were obtained using an F and M carbon, hydrogen, and nitrogen analyzer, Model 180, and represent an average of three determinations.

Ring Closure of Ylidenemalononitriles. IV.[1,2a] Attempted Cyclizations of Saturated Malononitrile Derivatives

E. CAMPAIGNE AND WENDELL L. ROELOFS[2b]

Chemistry Laboratories of Indiana University, Bloomington, Indiana

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Cyclization attempts employing concentrated sulfuric acid or polyphosphoric acid with saturated malononitrile derivatives obtained from the reduction of various ylidenemalononitriles produced only diamides and sulfonated products in the β-arylpropanonitrile and δ-arylpentanonitrile series, with one exception. A bulky *t*-butyl group in the former promoted cyclization to form an indenamine. The enamine was converted to an indanone, whose structure was proved by an unequivocal synthesis. Acylation reactions of the enamine gave only N-acylation followed by an intramolecular condensation to form pyrimidone derivatives. Steric effects on the cyclization of arylidenemalononitriles and their saturated analogs are discussed.

The formation of five- and six-membered rings by the cyclization of ylidenemalononitriles has been reported in previous papers.[1,3] It was noted that a bulky group R was essential in cyclizations forming five-membered rings (**1** → **2**).[3b] Benzylidenemalono- (PPA), whereas α-cyano-β-phenylcinnamonitrile (**1**, nitrile (**1**, R = H) did not yield cyclized products from concentrated sulfuric acid or polyphosphoric acid R = phenyl) cyclized to form 2-cyano-3-phenyl-1-indenone (**2**, R = phenyl, Z = CN) in an 80% yield. Since **1** contains a conjugated system, it was suggested that a bulky group was necessary to provide distortion of this ring-deactivating resonance system, thus facilitating electrophilic attack by the protonated nitrile group.[3c]

A bulky group was apparently not necessary in the formation of six-membered rings (**3** → **4**),[1] since good

(1) Previous paper, III: E. Campaigne, D. R. Maulding, and W. L. Roelofs, *J. Org. Chem.*, **29**, 1543 (1964).

(2) Contribution No. 1253: (a) supported in part by a Public Health Service Fellowship No. GPM-18,661 and in part by Public Health Service Research Grant GM-10366-02; (b) Public Health Service Predoctoral Research Fellow of the Division of General Medical Sciences.

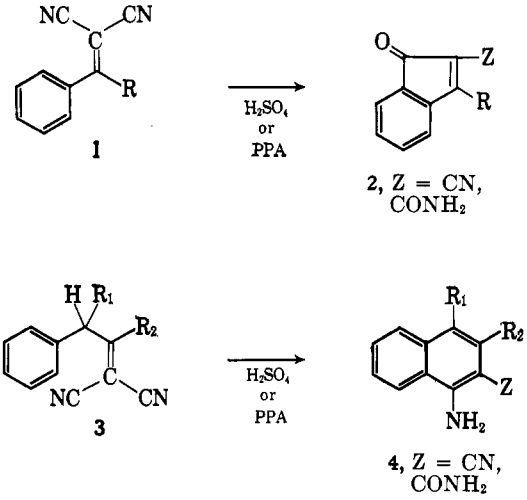
(3) (a) E. Campaigne and G. F. Bulbenko, *J. Org. Chem.*, **26**, 4703 (1961); (b) E. Campaigne, G. F. Bulbenko, W. E. Kreighbaum, and D. R. Maulding, *ibid.*, **27**, 4428 (1962); (c) E. Campaigne, R. Subramanya, and D. R. Maulding, *ibid.*, **28**, 623 (1963); E. Campaigne and D. R. Maulding, *ibid.*, **28**, 1391 (1963).

TABLE I

PREPARATION AND PROPERTIES OF REDUCED YLIDENEMALONONITRILES

Product	% yield[a]	B.p. (mm.) or m.p., °C.	$n^{30}D$	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	N.m.r. values,[b] H_x	N.m.r. values,[b] H_y	ν_{max}, cm.$^{-1}$[c]
5	86	130-135 (0.1)	1.5150	$C_{13}H_{14}N_2$	78.73	7.12	14.13	78.92	7.00	14.32	7.8-8.2 (m)	6.45 (d) (5)	2220, 2290
6a	84	91-92[d]		$C_{10}H_8N_2$							6.78 (d) (6)	6.13 (t) (6)	2280
6b	91	120-125 (0.15)	1.5220	$C_{12}H_{12}N_2$	78.23	6.57	15.21	78.08	6.86	14.94	6.92 (q) (7)	6.09 (d) (7)	2190, 2230
6c	85	115-120 (0.05)	1.5161	$C_{13}H_{14}N_2$	78.73	7.12	14.13	78.59	7.39	14.10	7.28 (t) (8)	5.81 (broad)	2200, 2270
6d	34[e]	81-82[f]		$C_{16}H_{12}N_2$	82.72	5.21	12.06	82.99	5.56	11.67	5.42 (d) (7)	5.60 (d) (7)	2200, 2290
6e	89	54-54.5		$C_{14}H_{16}N_2$	79.22	7.60	13.20	79.48	7.82	13.24	7.10 (d) (5)	5.81 (d) (5)	2200, 2280
7	95	71.5-72.5		$C_{13}H_{12}N_2$	79.54	6.16	14.28	79.70	5.93	14.04	5.40 (q) (6)	5.92 (d) (6)	2220, 2250

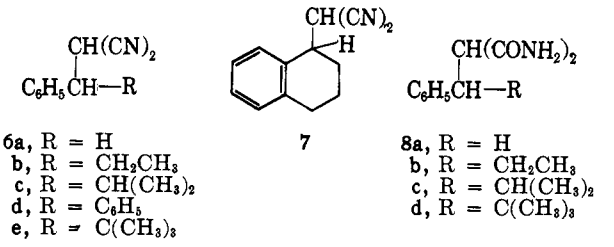
[a] Prepared by hydrogenation at 45 p.s.i. over platinum oxide. [b] Taken in deuteriochloroform with tetramethylsilane as an internal standard. Peaks other than singlets are designated as d = doublet, t = triplet, q = quartet, and m = multiplet. J-values in cycles per second are given in parentheses below the chemical shift. [c] Solids taken as potassium bromide mulls and liquids as liquid films. [d] J. C. Hessler [*Am. Chem. J.*, **22**, 185 (1899)] reported m.p. 91°. [e] Prepared by sodium borohydride reduction of the double bond; J. A. Meschino and C. H. Bond, *J. Org. Chem.*, **28**, 3129 (1963). [f] H. Le Mool, R. Carrie, and M. Bargain [*Compt. rend.*, **251**, 2541 (1960)] reported 84° and S. D. Gupte and S. V. Sunthanker [*J. Org. Chem.*, **24**, 1334 (1959)] reported 87° for the melting point of **6d**.



yields of cyclized products were obtained from ylidenemalononitriles (**3**) where R_1 and R_2 were either H or CH_3. This would be expected since the double bond is not conjugated with the aromatic ring. However, in a system such as 1-(α-naphthyl)ethylidenemalononitrile, where the double bond is again conjugated with the aromatic system, cyclization to the 8-position to form a six-membered ring did not occur and only small yields were obtained of products produced by cyclization to the 2-position to form a five-membered ring.

While cyclization to a six-membered ring occurred with a β-phenethylmalononitrile, having a saturated side chain, it was not observed with α-naphthylmethylmalononitrile, which could cyclize to form either a five- or six-membered ring.[1] Cyclization to a seven-membered ring was not observed when the saturated 2-cyano-3-methyl-5-phenylpentanonitrile (**5**) or the corresponding cinnamylidenemalononitrile[4] was treated under ring-closure conditions.

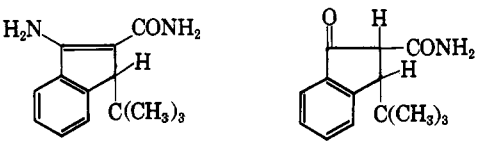
Certain inconsistencies in the above observations indicated the need to determine whether benzylmalononitriles could be cyclized to indanone derivatives, and what the steric effect of a bulky group at the β-position might be in this case. Accordingly, benzylmalononitrile (**6a**) and certain derivative (**6b–e** and **7**) were prepared by hydrogenation of the corresponding ylidene malononitriles **1** (See Table I).



The products were most readily characterized by their n.m.r. spectra, which showed peaks characteristic of the protons added across the double bond. The added protons not only give additional peaks, but also give rise to additional splitting of the original proton peaks. The chemical shifts and spin-spin splitting patterns of the added protons are summarized in Table I.

Treatment of the reduced ylidenemalononitriles **6a–d** and **7** with concentrated sulfuric acid or polyphosphoric acid did not yield cyclized products, but rather the corresponding diamides **8a–c** or water-soluble sulfonated products. A summary of the attempted cyclizations is found in Table II, and a summary of the physical properties of the diamides produced, **8**, is found in Table III.

Treatment of the *t*-butyl derivative **6e** with concentrated sulfuric acid produced a mixture of the cyclized products **9** and **10** along with the diamide **8d**. The reaction must involve an imine intermediate similar to that formed in the cyclization of ylidenemalononitriles,[1] with hydrolysis to the ketone producing the ketoamide **10** and a tautomeric shift of the double bond producing the enamine **9**.



(4) D. R. Maulding, Ph.D. Dissertation, Indiana University, 1962, p. 48.

TABLE II

ATTEMPTED CYCLIZATIONS OF REDUCED YLIDENEMALONONITRILES

Starting material	Reaction time, hr.	Temp., °C.	Product	Yield, %
5	2[a]	25	*c*	..
	0.15[a]	90	*c*	..
	0.25[b]	120	Diamide[d]	88
6a	4[a]	25	Diamide **8a**	61
	1[a]	5	Starting mat.	
	24[a]	5	Diamide **8a**	71
6b	0.25[a]	90	*c*	..
	1[a]	50	Diamide **8b**	81
6c	1[a]	50	Diamide **8c**	53
6d	0.33[a]	5	*c*	..
	1[a]	50	*c*	..
	0.25[b]	120	*e*	..
7	0.33[a]	90	*c*	..
	4[a]	25	*c*	..
	0.25[b]	120	*e*	..

[a] One gram of compound in 10 ml. of concentrated sulfuric acid was used. [b] One gram of compound in 10 ml. of polyphosphoric acid was used. [c] Only water-soluble products were formed. [d] 2-Carboxamido-3-methyl-5-phenylpentanamide. [e] Tarry product was formed.

enol tautomerization. A solid state infrared spectrum showed a broad band at 3.2–3.3 μ for hydroxyl, a peak at 4.56 μ for nitrile, a sharp peak of low intensity at 5.86 μ for the ketone carbonyl, and three intense peaks at 6.19, 6.28, and 6.37 μ for conjugated phenyl C=C absorption. An infrared spectrum in chloroform, however, did not exhibit hydroxyl absorption and gave a large ketone absorption peak at 5.80 μ. The n.m.r. spectrum of **11** in deuteriochloroform did not show resonance for the two protons of the five-membered ring as it did with the ketoamide **10**, but rather showed only a singlet at τ 6.3 similar to that of the enamine **9**. The ultraviolet spectrum of **11** was also different from that of an indanone. The ketoamide produced from the hydration of **11** was proved to be **10** by identical infrared spectra and an undepressed mixture melting point.

When **9** was heated in dilute acid for 15 min. and the solution allowed to stand for several days, the ketoamide **10** was formed. The conversion was more rapid using common reaction conditions for acetylating amines.[5]

TABLE III

PHYSICAL PROPERTIES OF MALONAMIDES

Compd.	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
a	226–228[b]	$C_{13}H_{18}N_2O_2$	66.63	7.74	11.96	66.55	7.88	12.14
8a	224–226[c,d]	$C_{10}H_{12}N_2O_2$						
8b	199–200[b]	$C_{12}H_{16}N_2O_2$	65.43	7.32	12.72	65.26	7.48	12.91
8c	251–252[c]	$C_{13}H_{18}N_2O_2$	66.63	7.74	11.96	66.65	7.76	12.05
8d	261–262[b]	$C_{14}H_{20}N_2O_2$	67.71	8.12	11.29	67.45	8.16	11.41

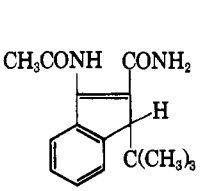
[a] 2-Carboxamido-3-methyl-5-phenylpentanamide. [b] Recrystallized from 95% ethanol. [c] Recrystallized from methanol. [d] C. A. Bischoff and H. Siebert [*Ann.*, **239**, 96 (1887)] reported m.p. 225° and P. Russell [*J. Am. Chem. Soc.*, **72**, 1853 (1950)] reported m.p. 224–226°.

It is apparent from the above data that ring closure occurs much less readily in the reduced series than in the corresponding ylidenemalononitrile series. Although the aromatic ring is not deactivated by a resonance system in the reduced compound, neither is the nitrile group rigidly held in the proximity of the aromatic ring; therefore hydration is favored over cyclization. When R becomes sufficiently large on the malononitriles **6**, for example when R is *t*-butyl, a nitrile group is forced closer to the aromatic ring than in the normal *gauche* configuration and thus the cyclization reaction is favored. When R is isopropyl or smaller, there is no internal compression, and hydration of the nitrile groups is favored. The corresponding ylidenemalononitriles cyclized because the conjugated double bond tended to keep the compound nearly planar and thus maintained the nitrile group close to the aromatic system. The relatively smaller steric effects of ethyl, isopropyl and phenyl are sufficient to favor cyclization in these cases.[3b]

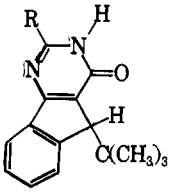
The cyclized products **9** and **10** were characterized by infrared, ultraviolet and n.m.r. spectra. The unequivocal synthesis of **10** was accomplished by reduction of 2-cyano-3-*t*-butyl-1-indenone (**2**, R = *t*-butyl; Z = CN) to 2-cyano-3-*t*-butyl-1-indanone (**11**), followed by hydration of the nitrile moiety to obtain the ketoamide **10**.

It was interesting to note that the product **11** did not produce spectra characteristic of an indanone as did the ketoamide **10**, but rather appeared to exhibit keto-

In further attempts to characterize **9**, it was subjected to conditions for the acylation of enamines as given by Stork.[6] Only nitrogen acylation was obtained when **9** was treated with acetic anhydride or benzoyl chloride in dioxane at room temperature. Reaction with acetic anhydride gave the acetylated product **12**. Treatment of **12** with dilute acid effected an intramolecular condensation to yield the pyrimidone derivative **13a**,[7] characterized by infrared, ultraviolet and n.m.r. spectra. The reaction of **9** with benzoyl chloride did not yield a benzoyl analog of **12**, but rather gave a mixture of the ketoamide **10** and the pyrimidone derivative **13b**.



12



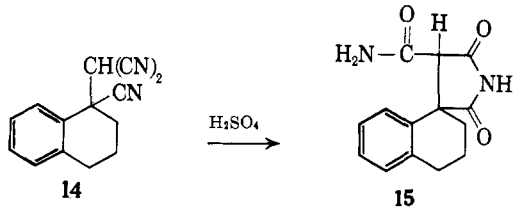
13a, R = CH_3
b, R = C_6H_5

(5) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Investigation of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 226.

(6) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(7) J. R. Marshall and J. Walker, *J. Chem. Soc.*, 1004 (1951); D. J. Brown, E. Hoerger, and S. F. Mason, *ibid.*, 211 (1955); L. N. Short and H. W. Thompson, *ibid.*, 168 (1952); D. J. Brown and L. N. Short, *ibid.*, 331 (1953); S. F. Mason, *ibid.*, 4874 (1957); D. J. Brown, "The Pyrimidines," Interscience Publishers, Inc., New York, N.Y., 1962, Chapter XIII.

In another attempt to cyclize saturated malononitrile derivatives, the cyanide Michael adduct, 1-cyano-1-tetralylmalononitrile (**14**), was treated with concentrated sulfuric acid, but only the spiro succinimide derivative **15**, resulting from hydration and interaction of the cyano groups, could be isolated.



14 **15**

Experimental[8]

Reduction of Ylidenemalononitriles.—With one exception, the malononitriles listed in Table I were prepared as in the following example. A solution of 20 g. of α-cyano-β-*t*-butylcinnamonitrile[3b] (**1**, R = *t*-butyl) in 250 ml. of absolute ethanol was shaken under hydrogen at 45 p.s.i. with 0.4 g. of platinum oxide in a Parr low-pressure hydrogenation apparatus for 2 hr. The catalyst was filtered, the solvent was evaporated *in vacuo*, and the oily residue was distilled under reduced pressure to give 18 g. (89%) of a colorless solid, m.p. 54–54.5°.

A procedure described by Meschino and Bond[9] was followed for the preparation of **6d**. To a solution of 4.9 g. (0.13 mole) of sodium borohydride in 25 ml. of isopropyl alcohol was added over a 5-min. period a solution of 10 g. (0.043 mole) of **1** (R = phenyl) in 100 ml. of isopropyl alcohol. After stirring the mixture for 8 hr., dilute acetic acid was added to destroy excess sodium borohydride and the solvent was removed *in vacuo*. Water was added and the aqueous residue was extracted with ether. The combined ether extracts were washed with 2 *N* hydrochloric acid and finally with water, then dried over magnesium sulfate, and evaporated to leave a colorless oil. Distillation under reduced pressure yielded 3.42 g. (34%) of a colorless liquid, b.p. 150–155° (0.2 mm.). Cooling caused the oil to solidify to produce a colorless solid, **6d**, m.p. 81–82°.

Attempted Cyclizations of Saturated Malononitrile Derivatives.—Cyclization of the saturated malononitriles **6** was attempted in concentrated sulfuric acid or, if water-soluble products indicated sulfonation, polyphosphoric acid. The temperatures and times of the reactions as well as the products obtained are summarized in Table II. The physical properties of the products obtained are summarized in Table III. Typical examples are as follows.

A.—A solution of 1 g. of benzylmalononitrile (**6a**) in 10 ml. of concentrated sulfuric acid was allowed to stand at room temperature for 4 hr. and then poured over ice. The precipitate was collected to give 0.75 g. of **8a**, m.p. 220–223°. Recrystallization from 95% ethanol gave a sample melting at 224–226°.

B.—A solution of 1 g. of **5** in 10 g. of polyphosphoric acid was heated at 120° for 15 min. and then poured over ice. The precipitate was collected and washed with a saturated solution of potassium carbonate before recrystallizing from 95% ethanol to give 1.03 g. (88%) of 2-carboxamido-3-methyl-5-phenylpentanamide, m.p. 226–228°.

Cyclization of 2-Cyano-4,4-dimethyl-3-phenylpentanonitrile (6e).—Five grams of **6e** was dissolved in 45 ml. of concentrated sulfuric acid and the solution was heated at 50–60° for 1 hr. The dark red solution was then poured over ice and the yellow product (0.90 g.) was collected by filtration. Extraction of the mother liquor with chloroform yielded an additional 1.34 g. of product after the chloroform extracts were dried over magnesium sulfate and evaporated. The combined products were extracted with ether, and the ether extract was evaporated to produce 0.73 g. of an orange sticky solid. Recrystallization of this solid from 95% ethanol afforded 0.43 g. (8.1%) of 2-carboxamido-3-*t*-butyl-1-indanone (**10**), m.p. 127–129°. Further recrystallizations gave a pure sample with m.p. 137–138°; λ_{max}^{KBr} 2.95 and 3.15 (NH_2), 5.85 (CO), 5.97 μ (amide CO); $\lambda_{max}^{CHCl_3}$ 2.90 and 3.0 (NH_2), 5.95 μ (CO and amide CO); $\lambda_{max}^{95\%\ C_2H_5OH}$ 250 mμ (ε 15,500), 298 mμ (ε 2330). The n.m.r. spectrum exhibited peaks at τ 6.56 (d) and 6.07 (d, *J* = 3 c.p.s.) (1 proton each) and 9.03 (9 protons).

Anal. Calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.57; H, 7.29; N, 6.23.

The residue from the ether extracts could not be recrystallized and appeared to be sulfonated product as indicated by infrared absorption peaks between 8.0 and 10.0 μ. Basification of the mother liquor caused 2.44 g. (46%) of 2-carboxamido-3-*t*-butyl-1-inden-1-amine (**9**), m.p. 179–181°, to precipitate. Recrystallization from ethanol–water gave a pure sample: m.p. 186–187°; λ_{max}^{KBr} 2.9 and 3.06 (NH_2), 6.09 and 6.18 μ (amide carbonyl); $\lambda_{max}^{CHCl_3}$ 2.88, 2.95, and 2.99 (NH_2), 6.1 μ (amide CO); $\lambda_{max}^{95\%\ C_2H_5OH}$ 243 mμ (ε 9780), 330 mμ (ε 12,700); n.m.r. τ 6.6 (1 proton) and 9.06 (9 protons).

Anal. Calcd. for $C_{14}H_{18}N_2O$: C, 73.02; H, 7.88; N, 12.12. Found: C, 72.19; H, 7.85; N, 11.93.

Extraction of the alkaline liquor with ethyl acetate produced 0.66 g. (11.6%) of the diamide **8d**. Recrystallization from 95% ethanol gave an analytical sample with m.p. 261–262°; λ_{max}^{KBr} 2.95–3.05, 3.15 (NH_2), 6.0 (broad, amide CO) (see Table IV).

2-Cyano-3-*t*-butyl-1-indanone (11).—To a solution of 0.83 g. (0.0039 mole) of 2-cyano-3-*t*-butyl-1-indenone[3b] (**2**, R = *t*-butyl; Z = CN) in 10 ml. of methanol was added dropwise a solution of 0.037 g. (0.97 mmole) of sodium borohydride in 2 ml. of 1% aqueous sodium hydroxide. After stirring for 1 hr., 0.27 g. of crude starting material was collected by filtration, the methanol filtrate was evaporated *in vacuo* and 5 ml. of 20% sulfuric acid was added to the residue. The resulting solid was collected to yield 0.36 g. (43%) of **11**: m.p. 116–117°; λ_{max}^{KBr} 3.2–3.3 (broad) (OH), 4.56 (CN), 5.86 (small, CO), 6.19, 6.28 and 6.37 μ (conj. C=C); $\lambda_{max}^{CHCl_3}$ 4.55 (CN), 5.80 μ (CO); $\lambda_{max}^{95\%\ C_2H_5OH}$ 234 mμ (ε 9100), 242 (8800), 293 (9100); n.m.r. (deuterioacetone) τ 6.3 (1 proton) and 8.89 (9 protons).

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.83; H, 7.09. Found: C, 78.63; H, 6.90.

2-Carboxamido-3-*t*-butyl-1-indanone (10). A.—A solution of 0.1 g. of **11** in 1 ml. of concentrated sulfuric acid was heated on a steam bath for 0.5 hr. before it was poured over ice. The white solid was collected by filtration to give 0.08 g. (73%) of **10**, melting at 128–129°. Further recrystallizations gave a pure sample which did not depress the melting point of a sample prepared by the previously described cyclization.

B.—A solution of the enamine **9** in 10% hydrochloric acid was heated on the steam bath for 15 min. and then placed in a refrigerator. The ketoamide **10** slowly crystallized over a period of several days. **10** was also obtained when an attempt was made to acetylate **9** in aqueous acid, as described by Shriner, Fuson, and Curtin.[5]

Acylation of the Enamine (9). A. With Acetic Anhydride.—A solution of 0.5 g. of **9**, 1 ml. of acetic anhydride and 5 ml. of dioxane was allowed to stand at room temperature. The precipitate, which formed after standing overnight, was collected to give 0.44 g., m.p. 199–200°, of the acylated product **12**. The solvent was evaporated and the residue recrystallized from 95% ethanol to give 0.09 g. of **12** for a total yield of 0.53 g. (88.3%). Further recrystallizations from 95% ethanol gave a sample with m.p. 203–204°; λ_{max}^{KBr} 2.95, 3.1 and 3.15 (NH_2), 6.0 and 6.08 μ (amide CO); $\lambda_{max}^{95\%\ C_2H_5OH}$ 225 mμ (ε 14,200), 282 mμ (ε 7820); n.m.r. τ 6.12 (1 proton), 7.82 (3 protons), 9.00 (9 protons).

Anal. Calcd. for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.41; N, 10.30. Found: C, 69.93; H, 7.43; N, 10.22.

A solution of 0.2 g. of the acylated product **12** in 5 ml. of a buffer solution containing acetic acid–sodium acetate–water (2:2:1) was heated to reflux for 15 min. Addition of water caused 0.14 g. (75%) of the pyrimidone derivative **13a**, m.p. 208–209°, to precipitate. Recrystallization from 95% ethanol gave a sample with m.p. 210–211°; λ_{max}^{KBr} 6.08 μ; $\lambda_{max}^{95\%\ C_2H_5OH}$ 245 mμ (ε 26,300), 290 (sh) (7880), 298 (8970), 312 (sh) (7700); n.m.r. τ 6.07 (1 proton), 7.4 (3 protons), 8.92 (9 protons).

B. With Benzoyl Chloride.—A mixture of 0.5 g. of **9**, 1 ml. of benzoyl chloride and 5 ml. of dioxane was allowed to stand at room temperature overnight. Recrystallization of 0.25 g. of precipitate gave the ketoamide **10**, m.p. 138–139°. The mother

(8) All melting points were determined in open capillary tubes with a Mel-Temp heating block apparatus and are corrected. Elemental analysis were performed by Midwest Microlab, Inc., Indianapolis, Ind. Ultraviolet spectra were taken with a Cary Model 14 recording spectrophotometer using 95% ethanol as the solvent. Infrared spectra were obtained on a Perkin-Elmer Model 137-B Infracord spectrophotometer. N.m.r. spectra were taken with a Varian A-60 instrument in deuteriochloroform solution using tetramethylsilane as an internal standard.

(9) J. A. Meschino and C. H. Bond, *J. Org. Chem.*, **28**, 3129 (1963).

liquor was evaporated to yield a residue which was then washed with dilute sodium hydroxide and recrystallized from 95% ethanol to give 0.17 g. (25%) of the pyrimidone derivative **13b**: m.p. 258–259°; λ_{max}^{KBr} 6.06 μ; $\lambda_{max}^{95\%\ C_2H_5OH}$ 265 mμ (ϵ 52,500), 289 (17,100), 300 (16,400), 322 (12,860); n.m.r. τ 6.01 (1 proton) and 8.87 (9 protons).

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.70; H, 6.37; N, 8.86. Found: C, 79.38; H, 6.43; N, 8.70.

Preparation of 1-Cyano-1-tetralylmalononitrile (14).—A solution of α-tetrylidenemalononitrile, 6 ml. of *t*-butyl alcohol and 1 g. of sodium cyanide was stirred for 4 hr. The resulting red solution was poured over ice and acidified with dilute sulfuric acid, precipitating 3.57 g. of sticky orange solid melting at 128–130°. Recrystallization from 95% ethanol gave 2.69 g. (81%) of colorless crystals of **14**, m.p. 131–132.5°, λ_{max}^{KBr} 4.5 μ (CN), n.m.r. τ 5.52 (1 proton).

Anal. Calcd. for $C_{14}H_{11}N_3$: C, 76.00; H, 5.01; N, 18.99. Found: C, 76.11; H, 5.22; N, 18.76.

Cyclization of 1-Cyano-1-tetralylmalononitrile (14).—A solution of 2 g. of **14** in 20 ml. of concentrated sulfuric acid was allowed to stand at room temperature for 3 hr., poured into 200 ml. of water, and boiled for 10 min. After several days, the dilute acidic solution yielded 1.91 g. (83%) of colorless crystals of the succinimido derivative **15**, m.p. 226–228°. Recrystallization from 95% ethanol gave colorless crystals: m.p. 233–235°; λ_{max}^{KBr} 2.95 (NH), 5.68 and 5.8 (CO–N–CO), 6.05 μ (amide CO).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85. Found: C, 65.37; H, 5.50; N, 11.04.

β-Substituent Stabilization of Carbanion Intermediates

J. D. PARK, J. R. DICK, AND J. H. ADAMS

Chemistry Department, University of Colorado, Boulder, Colorado

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Nucleophilic attack by an ethoxide ion on 1,2-dichlorocyclobutenes yielded mixtures of products in ratios that substantiates the presence of a "β-effect." The β-substituents were found to stabilize a carbanion intermediate in this order: *gem*-dichloro > *gem*-ethoxychloro > *gem*-fluorochloro > *gem*-diethoxy ≥ *gem*-difluoro.

The question of the β-substituent effect on the stabilization of a carbanion intermediate has been described to be unresolved.[1] Hine[2] and Roberts[3] found that β-fluorine stabilized an intermediate carbanion better than a β-chlorine and a β-methoxy in their benzenoid systems. Their results supported the supposition that carbanions would best be stabilized by induction by the most electronegative substituent in the β-position.

Hine[2] also reported seemingly contradictory results in a base elimination study of pentahaloethanes. He found that CF_2HCCl_3 dehydrohalogenated 55 times as fast as CF_3CCl_2H. As an explanation, it was thought that perhaps this elimination went by a concerted mechanism rather than through the carbanion. Some reconsideration of this statement must now be made in view of Andreades' recent proof[4] of carbanion intermediates in the reaction of monohydrofluorinated compounds with base.

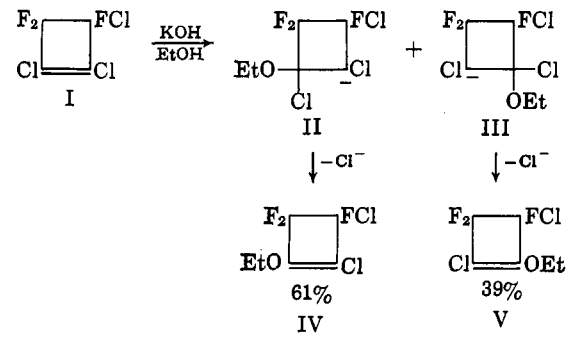
Tiers[5] reported n.m.r. data on linear fluorinated molecules that indicated that electron withdrawal toward the halogen in question increased with bulkier halogens. The ability to disperse or delocalize the negative charge over the larger volume of the atom appeared to overcome the lesser electronegativity. From this data, one could conclude that a carbanion would be stabilized better by bulkier halogens in the β-position.

A study was undertaken to examine the effects of β-substituents as applied to a halogenated cyclobutene system, which has recently been shown[1] to have carbanion intermediate character upon nucleophilic attack by ethoxide ion.

Results and Discussion

A series of 1,2-dichloro-3,3-difluorocyclobutenes was treated with potassium hydroxide dissolved in absolute ethanol at 0°. The resulting ether product distribution showed the relative effect of β-ethoxy and β-chlorine in comparison with β-fluorine in stabilizing the intermediate carbanion. The α-substituent was chlorine for ethoxide attack at either end of the double bond. The product ratios, with the exception of the first case, were determined by calibrated gas–liquid chromatograph integration with an accuracy of ±2%.

1,2,3-Trichloro-3,4,4-trifluorocyclobutene (I) yielded two inseparable isomers detected only by n.m.r. The ethoxy group was in a slightly different environment in each isomer so the methylene quartets and methyl triplets were centered at different τ-values. One isomer was later prepared by an unequivocal synthesis so the proper n.m.r. assignments could be made for each isomer. The ratio of the two products was calculated by measuring the area under each of the expanded methylene quartets by a planometer. This measurement showed 1-ethoxy-2,3-dichloro-3,4,4-trifluorocyclobutene (IV) predominating over 2-ethoxy-1,3-dichloro-3,4,4-trifluorocyclobutene (V) by a 61 to 39 ratio and thereby demonstrated that the carbanion intermediate favored the β-*gem*-fluorochloro group over the β-*gem*-difluoro group.



1-Bromo-2-chloro-3,3,4,4-tetrafluorocyclobutene (VI) has been found[6] to give both the bromo ether (VII) and chloro ether (VIII) in a 75 to 25 ratio, respectively,

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