of phenacyl bromide and thiourea by the method of Hurd, *et al.*[24] The compound melted at 148° (lit.[23] mp 147°).

The solvents used were of AnalaR B. D. H. variety. They had the following characteristics: nitrobenzene, bp 210–211°; *sec*-butyl alcohol, bp 99°; *n*-butyl alcohol, bp 118°; *tert*-butyl alcohol, bp 83°.

Kinetic Measurements.—The rate of reaction of the thiazoles with methyl iodide was studied in nitrobenzene at different temperatures in a thermostat (±0.1°) by monitoring the change in electrical conductivity with a Phillips model conductivity bridge at 1000 Hz. The platinum electrodes of the conductivity cell were coated with platinum black. Pseudo-first-order kinetics were maintained during the course of a kinetic run where [thiazole] was 0.01 *M* and [CH_3I] was 0.2 *M* (20-fold excess). Pseudo-first-order rate plots of log $R_t/R_t - R_\infty$ *vs.* time, where R_t and R_∞ are the electrical resistances at time t and at infinite time, respectively, were linear. The pseudo-first-order rate constants were calculated from the slopes of these linear plots and were reproducible to within ±0.2 units.

(24) C. D. Hurd and H. L. Herhrmeister, *J. Amer. Chem. Soc.*, **71**, 4007 (1949).

Registry No.—1, 1826-16-0; 2, 39541-91-8; 3, 24840-75-3; 4, 33102-81-7; 5, 120-75-2; 6, 95-21-6; 7, 2941-62-0; 8, 2010-06-2; 9, 3755-83-7; 10, 91-63-4; 11, 491-35-0; 12, 615-15-6; methyl iodide, 74-88-4.

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Reactions of 3-Carboxyacryloylhydrazines. II.[1] Acid-Induced Rearrangement of Isomaleimides

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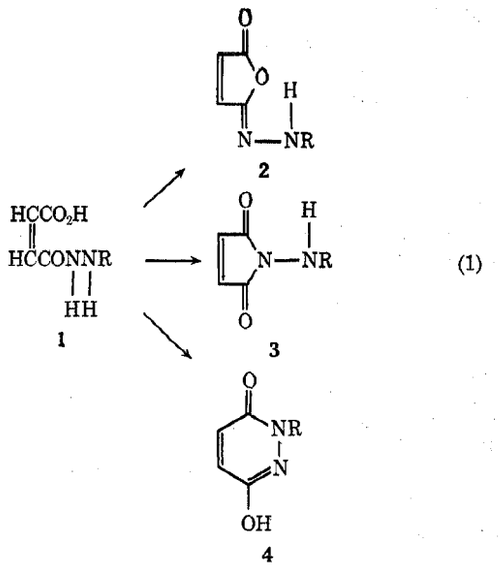
3-Carboxyacryloyl derivatives of several nitrophenylhydrazines undergo cyclization in acetic anhydride to the corresponding aminoisomaleimides. The latter in acid solutions rearrange to aminomaleimides or pyridazinones. Contrary to reports in the literature, these aminomaleimides do not rearrange to pyridazinones in acid media but are recovered unchanged.

Recently, Rubinstein, Skarbek, and Feuer[1] have discussed conditions under which 3-carboxyacryloylhydrazines **1** undergo cyclization to aminoisomaleimides **2**, aminomaleimides **3**, or pyridazinones **4** (eq 1).



They have also presented criteria for distinguishing between these structures.

In 1968, Baloniak[2] reported that the dehydration with acetic anhydride of various nitrophenyl-2-(3-carboxyacryloyl)hydrazines **1** led to the corresponding nitrophenylaminomaleimides **3**. It was further reported that these compounds were converted to pyridazinones **4** on treatment with sulfuric acid or with a mixture of sulfuric and acetic acids.[2–8]

These results, as well as previous reports in the literature[9,10] on ring formation and rearrangement, seemed incongruous when examined by the newly established criteria[1] and other recent work.[11,12] In light of the many discrepancies, it seemed important to reexamine the formation and interconversion of the various ring compounds formed by cyclization of **1** in acid solutions, and to reconcile the results obtained by previous workers.[2–10]

Results

Various aminoisomaleimide derivatives **2a–f** were prepared from the corresponding 3-carboxyacryloylhydrazines on treatment with acetic anhydride or thionyl chloride.[1] On treatment with acetic acid *N*-acetylaminoisomaleimide (**2a**), *N*-benzenesulfonylaminoisomaleimide (**2b**), 1-(2-nitrophenyl)aminoisomaleimide (**2c**), and 1-(2,4-dinitrophenyl)aminoisomaleimide (**2f**) rearranged to the corresponding aminomaleimides **3**. However, 1-(3-nitrophenyl)aminoisomaleimide (**2d**) was converted to the pyridazinone **4d**, while 1-(4-nitro-

(1) H. Rubinstein, J. Skarbek, and H. Feuer, *J. Org. Chem.*, **36**, 3372 (1971).

(2) S. Baloniak, *Rocz. Chem.*, **42**, 1231 (1968).

(3) S. Baloniak, Abstracts, Third International Congress of Heterocyclic Chemistry, Sendai, Japan, 1971, p 323.

(4) S. Baloniak, *Rocz. Chem.*, **43**, 1187 (1969).

(5) S. Baloniak, *ibid.*, **42**, 1867 (1968).

(6) S. Baloniak, *ibid.*, **43**, 315 (1969).

(7) S. Baloniak and U. Wrzeciono, *ibid.*, **45**, 567 (1971).

(8) S. Baloniak and A. Mroczkiewicz, *ibid.*, **45**, 659 (1971).

(9) H. Feuer and H. Rubinstein, *J. Amer. Chem. Soc.*, **80**, 5873 (1958).

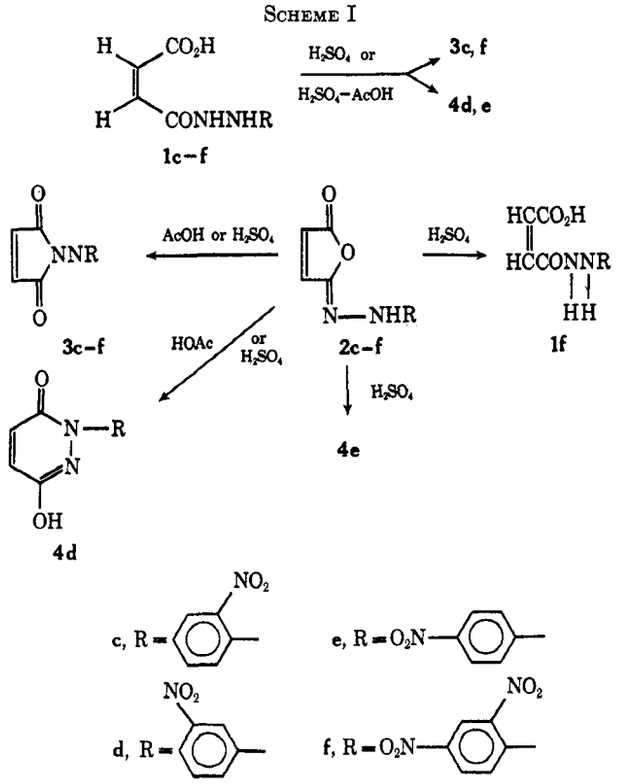
(10) H. Feuer and J. Asunskis, *J. Org. Chem.*, **27**, 4684 (1962).

(11) E. Hedaya, R. L. Hinman, and S. Theodoropulos, *ibid.*, **31**, 1311 (1966).

(12) A. Le Berre, J. Godin, and R. Garreau, *C. R. Acad. Sci., Ser. C*, **265**, 570 (1967).

phenyl)aminoisomaleimide (2e) was recovered unchanged (Scheme I).

SCHEME I



When the nitrophenylaminoisomaleimides were treated with sulfuric acid according to the procedure of Baloniak,[2,5,6] 2c was converted to the aminomaleimide 3c, 2d and 2e to the corresponding pyridazinones 4d and 4e, but 2f to a mixture composed of 1f and 3f (Scheme I).

That the rearrangements shown in Scheme I were those of aminoisomaleimides 2 and not of aminomaleimides 3 was established by the fact that samples of 3 were recovered unchanged when subjected to similar reaction conditions.

When the nitrophenyl-3-carboxyacryloylhydrazines 1c–f were treated with sulfuric acid or with mixtures of sulfuric–acetic acids according to the procedure reported by Baloniak,[2] 1c and 1f were converted to the aminomaleimides 3c and 3f, while 1d and 1e gave the pyridazinones 4d and 4e (Scheme I).

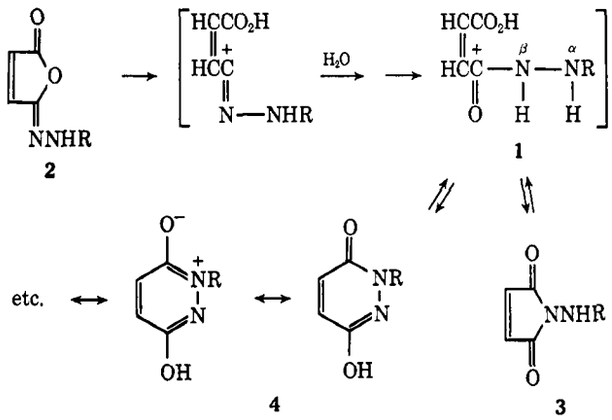
A summary of the physical properties of the compounds isolated from these experiments is presented in Table I.

Discussion

The data presented in this paper indicate that our previously reported substituted aminomaleimide rearrangements[9,10] are instead aminoisomaleimide rearrangements. Furthermore, the data show that the starting materials which Baloniak[2,3] considered to be nitrophenylaminomaleimides were all nitrophenylaminoisomaleimides.

Rearrangement of the aminoisomaleimides does not lead exclusively to the formation of aminomaleimides or to pyridazinones. Rather it is dependent on the acidity of the medium used to effect the rearrangement and on the electronegativity of the group attached to the α nitrogen (Scheme II). Thus, the less electronegative 1-(3-nitrophenyl)aminoisomaleimide (2d) is converted to the pyridazinone 4d and the more electronegative aminoisomaleimides 2c and 2f give the aminomaleimides 3c and 3f. The 4-nitrophenyl compound 2e, which lies in electronegativity between 2d and 2c or 2f, gives no reaction in acetic acid but is converted to the pyridazinone 4e in sulfuric acid. It is of interest to note that the open-chain compound 1e undergoes ring closure to the aminomaleimide 3e in acetic acid.

SCHEME II



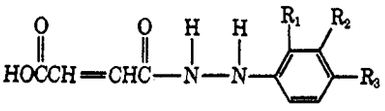
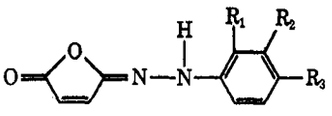
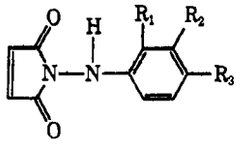
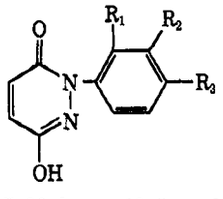
The course of the rearrangement of 2 which is illustrated in Scheme II presumes the formation of 1 as an intermediate through the addition of water to the immonium center as proposed by Ernst[13] and demonstrated by Sauers[14,15] for the isoimide system. It is reasonable to expect that ring formation from 1 (or some related intermediate) then proceeds by nucleophilic attack of the α or β nitrogen atom, leading to the six- or five-membered ring compound. Electron-withdrawing substituents on the α nitrogen favor aminomaleimide formation by inhibiting attack at the α nitrogen. The results obtained on dehydration of 1 with acetic or sulfuric acid give further evidence for the mechanism proposed in Scheme II. The results were similar to those observed in the rearrangement reactions except that cyclization of 1e in acetic acid gave the aminomaleimide 3e while in sulfuric acid it was converted to the pyridazinone 4e. The difference observed in acetic and sulfuric acid with 1e can be ascribed to the stabilization of the pyridazinone ring (through its resonance forms) which would be expected to be favored in a strongly acidic polar medium.

The rearrangement and product formation which have been observed in this investigation can readily be used to explain some of the anomalous results reported[4] in the literature. For example, it has been stated, "In contrast with some reactions of 4-nitrophenyl- and 3-nitrophenyl-, the corresponding reactions of 2-nitrophenyl- and 2,4-dinitrophenylpyridazinones with acetic anhydride, dimethyl sulfate, and phosphorus oxychloride and pentachloride failed." These differences, as well as differences in the ir and uv spectra,

(13) M. L. Ernst and G. L. Schmir, *J. Amer. Chem. Soc.*, **88**, 5001 (1966).
(14) C. K. Sauers, *Tetrahedron Lett.*, 1149 (1970).
(15) C. K. Sauers, C. L. Gould, and E. S. Ivannou, *J. Org. Chem.*, **36**, 1941 (1971).

TABLE I

PHYSICAL AND SPECTRAL PROPERTIES OF NITROPHENYLHYDRAZINE DERIVATIVES

R_1	R_2	R_3	Ir, cm^{-1},[a] obsd	CO stretch, lit.[i]	Nmr[b-d] Olefinic protons, δ	J, Hz	Aromatic protons, δ	Mp, °C obsd	Mp, °C lit.[j]
			3-Carboxyacryloylhydrazines 						
NO_2	H	H (1c)	1705		6.53 d, 6.26 d	12	8.29–6.27 m	163–164	158–159
H	NO_2	H (1d)	1703		6.68 d, 6.34 d[e]	13	6.68–7.28 m	147.5–148	145–146
H	H	NO_2 (1e)	1694		6.32 d, 6.26 d	12	7.92 d–6.78 d	172.5–173	165–166
NO_2	H	NO_2 (1f)	1706		6.57 d, 6.32 d[f]	13	8.95–7.49 m	192.5–193	189–190
			Aminoisomaleimides 						
NO_2	H	H (2c)	1780		8.10 d, 7.00 d	6.0	8.40–7.14 m	129–131	155–157[g]
H	NO_2	H (2d)	1774, 1748		7.83 d, 6.63 d	5.5	7.74–7.52 m	213.5–214.5	213–214[g]
H	H	NO_2 (2e)	1790		7.76 d, 6.68 d	6.0	8.16 d–7.36 d	277–278	260[g]
NO_2	H	NO_2 (2f)	1792		7.99 d, 6.99 d	6.0	8.84–7.33 m	182.5–183.5	184–186[g]
			Aminomaleimides 						
NO_2	H	H (3c)	1730, 1715	1750	7.19 s		8.24–6.68 m	136–137.5	140–142[h]
H	H	NO_2 (3e)	1704		7.19 s		8.10 d–6.88 d	179–180.5	
NO_2	H	NO_2 (3f)	1714	1750	7.30 s		8.97–7.37 m	232.5–233	230–232[h]
			Pyridazinones 						
H	NO_2	H (4d)	1662	1672	7.28 d, 7.06 d	10.5	8.61–7.63 m	272–273 d	269–270
H	H	NO_2 (4e)	1665	1675	7.26 d, 7.08 d	9.5	8.36 d–8.00 d	308–310 d	302–303

[a] Run as a Nujol mull. [b] Parts per million. [c] All spectra were run in DMSO-d_6 using P.E. R-20 unless indicated otherwise. [d] d = doublet, m = multiplet, s = singlet. [e] Run in acetone-d_6. [f] Run using P.E. R-24. [g] Assumed by authors to be aminomaleimides. [h] Assumed by authors to be pyridazinones. [i] References 4–6. [j] Reference 2.

were attributed to the fact that some of these compounds are in the diketo form while others are in the enol form of the pyridazinone. However, our results indicate that the reported differences are those expected between pyridazinones and aminomaleimides. The former would be expected to react with the above reagents[16] while the latter would not. The observed spectral differences can be explained by the same reasoning. Furthermore, the many anomalous bromination reactions and rearrangements reported in the literature[3-8] can now be understood in the light of structure assignments in this paper and should be reinvestigated.

Experimental Section

All infrared spectra were obtained on a Beckman IR-10 instrument using sodium chloride cells and Nujol mulls. The nmr spectra were obtained on Perkin-Elmer R-20 and R-24 spectrometers. Melting points were obtained using a Thomas-Hoover melting point apparatus, and are corrected.

Hydrazines.—All hydrazines were purchased commercially or prepared by previously described procedures,[1,9] except for *m*-nitrophenylhydrazine, which was prepared by an adaptation of a method described in the literature.[17]

3-Carboxyacryloylhydrazines (1).—The 3-carboxyacryloylhydrazines were prepared by the methods indicated in the literature: 1-acetyl-2-(3-carboxyacryloyl)hydrazine,[9] 1,1-dimethyl-2-(3-carboxyacryloyl)hydrazine,[18] 1-benzenesulfonyl-2-(3-carboxyacryloyl)hydrazine,[9] 1,2-bis(3-carboxyacryloyl)hydrazine,[9] 1-(2-nitrophenyl)-2-(3-carboxyacryloyl)hydrazine,[2] 1-(3-nitrophenyl)-2-(3-carboxyacryloyl)hydrazine,[2] 1-(4-nitrophenyl)-2-(3-carboxyacryloyl)hydrazine,[2] and 1-(2,4-dinitro)-2-(3-carboxyacryloyl)-hydrazine.[10]

Aminoisomaleimides (2).—The aminoisomaleimides were prepared according to methods published in the literature for the formation of aminomaleimides, except in the case of the dimethyl-substituted compound, which was reported as the aminoisomaleimide, 1-acetylaminoisomaleimide,[10] 1,1-dimethylaminoisomaleimide,[1] 1-benzenesulfonylaminoisomaleimide,[10] 1,2-biisomaleimide,[9] and 1-(2,4-dinitrophenyl)aminoisomaleimide.[10]

1-(2-Nitrophenyl)aminoisomaleimide[2] (2c).—Acetic anhydride (120 ml) was added to 6.0 g of 1-(2-nitrophenyl)-2-(3-carboxyacryloyl)hydrazine and the mixture was stirred at room temperature. Upon solution of the hydrazine, 18 ml of water was added and stirring was continued. The solvent was removed *in vacuo*, leaving a red solid which upon recrystallization from acetic acid

(16) S. Druey, *et al.*, *Helv. Chim. Acta*, **37**, 510 (1954).

(17) (a) A. Bischler and S. Bradsky, *Chem. Ber.*, **22**, 2809 (1889); (b) A. W. vander Haar Utrecht, *Chem. Weekbl.*, **14**, 147 (1917).

(18) H. H. Hagemann and W. L. Hubbard, Belgian Patent 613,799 (Feb 28, 1962).

gave 5.56 g of product, mp 129.5–131.0° (lit.[2] mp 155–157°). We cannot account for the difference in the melting points, but all of our physical data confirm the structure of **2c**.

Anal. Calcd for $C_{10}H_7N_3O_4$: C, 51.51; H, 3.03; N, 18.02. Found: C, 51.28; H, 3.07; N, 18.09.

Aminomaleimides (3).—The aminomaleimides were prepared according to methods reported in the literature for the preparation of pyridazinones, except for the dimethyl derivative, which was reported as the aminomaleimide, 1-acetylaminomaleimide,[9] 1,1-dimethylaminomaleimide,[1] 1-benzenesulfonylaminomaleimide,[9] and 1-(2,4-dinitrophenyl)aminomaleimide.[10]

1-(2-Nitrophenyl)aminomaleimide (3c).—Glacial acetic acid (100 ml) was added to 4.0 g of 1-(2-nitrophenyl)-2-(3-carboxyacryloyl)hydrazine. The resulting dark red solution was refluxed for 3 hr and the solvent was removed *in vacuo* to give a red-orange solid. Recrystallization from 95% ethanol produced 0.64 g of the aminomaleimide, mp 136.0–137.5°.

Anal. Calcd for $C_{10}H_7N_3O_4$: C, 51.51; H, 3.03; N, 18.02. Found: C, 51.47; H, 3.08; N, 17.94.

1-(4-Nitrophenyl)aminomaleimide (3e).—The experiment was performed as described for the preparation of **3c**. 1-(4-Nitrophenyl)-2-(3-carboxyacryloyl)hydrazine gave 1.3 g of dark orange **3e**, mp 179.0–180.5° (EtOH).

Anal. Calcd for $C_{10}H_7N_3O_4$: C, 51.51; H, 3.03; N, 18.02. Found: 51.69; H, 3.22; N, 17.74.

Rearrangement of Aminoisomaleimides (2). A. In Acetic Acid.—Glacial acetic acid was added to 0.006 mol of the aminoisomaleimide and the mixture was refluxed for the time indicated with each compound. The solvent was removed *in vacuo* and the product was purified by recrystallization: 1-acetylaminoisomaleimide, 5 hr; 1,1-dimethylaminoisomaleimide, 2 hr; 1-benzenesulfonylaminoisomaleimide, 6 hr; 1-(2,4-dinitrophenyl)-aminoisomaleimide, 4 days; 1-(2-nitrophenyl)aminoisomaleimide, 18 hr; 1-(3-nitrophenyl)aminoisomaleimide, 6 days; and 1-(4-nitrophenyl)aminoisomaleimide, 2 days (no transformation took place).

In all but one case, the product formed was found to be identical with the corresponding aminomaleimide. The exception was the 3-nitrophenyl derivative, which rearranged to the pyridazinone.

B. In Sulfuric Acid.—The various nitrophenylaminoisomaleimides **2c–f** were treated with sulfuric acid according to the methods described by Baloniak.[2] **2d** and **2e** formed the corresponding pyridazinones **4d** and **4e** and **2c** gave the aminomaleimide **3c**. The 2,4-dinitrophenyl derivative **2f** was converted to a mixture consisting of the aminomaleimide **3f** and 3-carboxyacryloylhydrazine **1f**. The nmr spectrum of this mixture was identical with the spectrum of a 1:1 mixture of authentic **3f** and **1f**.

Reaction of 3-Carboxyacryloylhydrazines with Sulfuric Acid or Sulfuric–Acetic Acid Mixture.—The various nitrophenyl 3-carboxyacryloylhydrazines were treated according to methods reported by Baloniak.[2] The 3-nitrophenyl- and 4-nitrophenyl-substituted hydrazines **1d** and **1e** formed the corresponding pyridazinones **4d** and **4e**. The 2-nitrophenyl and 2,4-dinitrophenyl derivatives **1c** and **1f** gave the corresponding aminomaleimides **3c** and **3f**.

In the case of **1d** treatment with refluxing acetic acid also produced the corresponding pyridazinone **4d**.

Attempted Rearrangement of Aminomaleimides with Sulfuric Acid or Sulfuric–Acetic Acid. A. Sulfuric Acid.—A 0.5-g sample of the 2-nitro- and a 0.42-g sample of the 4-nitrophenylaminomaleimides were dissolved in 2.5 and 2 ml of concentrated sulfuric acid, respectively. The solutions obtained were added to 10 and 8 ml of distilled water to produce 0.46 and 0.40 g of recovered starting material.

B. Sulfuric–Acetic Acid.—Glacial acetic acid (50 ml) was added to 50 ml of concentrated sulfuric acid and the resulting solution was cooled to room temperature. A 1.64-g sample of 1-(2,4-dinitrophenyl)aminomaleimide was dissolved in the acid mixture and the mixture was stirred for 24 hr. On addition of water a solid (1.30 g) precipitated which was identified as starting material.

Registry No.—**1c**, 39704-29-5; **1d**, 39704-30-8; **1e**, 39704-31-9; **1f**, 31413-88-4; **2a**, 6903-87-3; **2b**, 30986-27-7; **2c**, 39704-35-3; **2d**, 39838-39-6; **2e**, 39704-36-4; **2f**, 31413-91-9; **3c**, 14938-99-9; **3e**, 20970-39-2; **3f**, 20970-35-8; **4d**, 39704-40-0; **4e**, 39704-41-1.

Acknowledgment.—We are indebted to Mr. Michael Wuerthele of Scott Graphics Inc., Holyoke, Mass., for the microanalyses.

Rates of Intramolecular Diels–Alder Reactions of Pentadienylacrylamides

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Among the substrates derived from 4,5-diphenylpentadienylamines **4**, prepared for a study of the intramolecular Diels–Alder reaction, the highly reactive N–CH_3 amide of fumaric acid ethyl ester **7a** directly produces the endo cycloadduct **8a** at 0°, whereas the *N*-demethyl derivative **7b** is far less reactive. The N–CH_3 cinnamamide **9** and *N*-allylamine **11** give predominantly the cycloadducts *trans*-**10** at 90° and *cis*-**12** at 140°, respectively, while the acrylamide **13a** produces an equal mixture of *trans*-*cis*-**14a**. The structures and relative configurations of the cycloadducts are discussed and elaborated. The kinetic parameters for the intramolecular cycloadditions of **13a–d** reveal that $\Delta G^{\ddagger}$ decreases from 28.7 kcal/mol for **13a** by increments of $\Delta\Delta G^{\ddagger} \cong 1.2$ kcal/mol for the homologs **13b** and **13c** to 25.3 kcal/mol for **13d**. This phenomenon is discussed in terms of a conformational equilibrium on part of the substrate, as evinced by nmr studies.

The marked rate-increasing or -decreasing effects of alkyl substituents in the [4 + 2] cycloaddition of dienes with dienophiles has been observed in numerous cases and is well documented.[1–3] The reactivity of a diene increases if appropriate alkyl substituents, such as in the 2 and 3 positions of butadiene, move the conformational equilibrium to the s-cis form, the prerequisite diene conformation for the Diels–Alder reaction. Conversely, bulky substituents at the dienophile generally have a rate-decreasing effect. The present study of the intramolecular Diels–Alder reaction with amides of α,β-unsaturated acids reveals still another phenomenon: the rate-accelerating influence of a bulky substituent attached neither to the diene nor to the dienophile component but to an atom linking the two together.

(1) S. Seltzer in "Advances in Alicyclic Chemistry," Vol. 2, Academic Press, New York, N. Y., 1968, pp 17–32.

(2) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Wiley-Interscience, New York, N. Y., 1964, pp 878–929.

(3) J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).