Flash Vacuum Pyrolysis of 3-*t*-Butylindeno[1,2-*c*]isoxazol-4-one. Formation of 2-Carbonyl-1,3-indandione 2-Azine

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Flash Vacuum Pyrolysis (FVP) of 3-*t*-Butylindeno[1,2-*c*]isoxazol-4-one (**1**) and 3-*t*-Butylspiro[2*H*-azirine-2,2'-(2*H*)indene]-1',3'-dione (**2**) were carried out. Reaction of **1** from 300-400° afford **2** and 2-carbonyl-1,3-indandione 2-azine (**3**) as the major products, whereas 2-*t*-Butylindeno[1,3-*c*]oxazol-4-one (**4**) was the main products in FVP of **2** together with minor amounts of **3**.

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Introduction.

We have been interested in the synthesis of novel tricyclic heterocycles as synthons for the preparation of biologically active compounds. Recently, we reported the synthesis and reactivity of isomeric indeno[1,2-*c*]isoxazolones [1]. In addition, the thermal isomerization of isoxazoles has been investigated [2] and a general mechanism for the isomerization of isoxazoles into azirines, oxazoles and α-carbonyl derivatives of acetonitriles [3-5], using the donor-acceptor model suggested by Epiotis has been proposed [6-7].

The previous studies have involved isoxazole derivatives with electron-releasing sustituents at the five position; therefore, we carried out the FVP of 3-*t*-butylindeno[1,2-*c*]-isoxazol-4-one (**1**) looking for additional evidence to establish the scope of reliability of the general reaction mechanism previously proposed. Additionally, we report the synthesis and results of FVP of 3-*t*-butylspiro-[2*H*-azirine-2,2'-(2*H*)indene]-1',3'-dione (**2**). A reaction mechanism consistent with the experimental evidences is discussed.

Results and Discussion.

The reaction of **1** at 300-400° and 10^{-2} torr gave **2** and **3** as the only products (Table I). According to these results, it might be expected that the reaction proceeds either by route A-B or C shown in Scheme I. Route A-B involves isomerization of **1** to **2** and subsequent C-C homolytic cleavage to give the imine free radical which dimerizes to form **3**. On the other hand, route C involves also an equilibrium between **1** and **2**, but **3** is formed directly from the starting isoxazole through the same free radical.

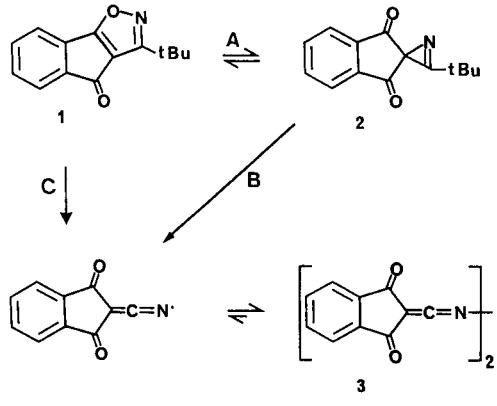
Considering the results shown in Table I, **2** would appear to be the kinetic product and **3** the thermodynamic one. In order to get additional evidences on the reaction

Table I

Reaction of 3-*t*-Butylindeno[1,2-*c*]isoxazol-4-one (**1**)

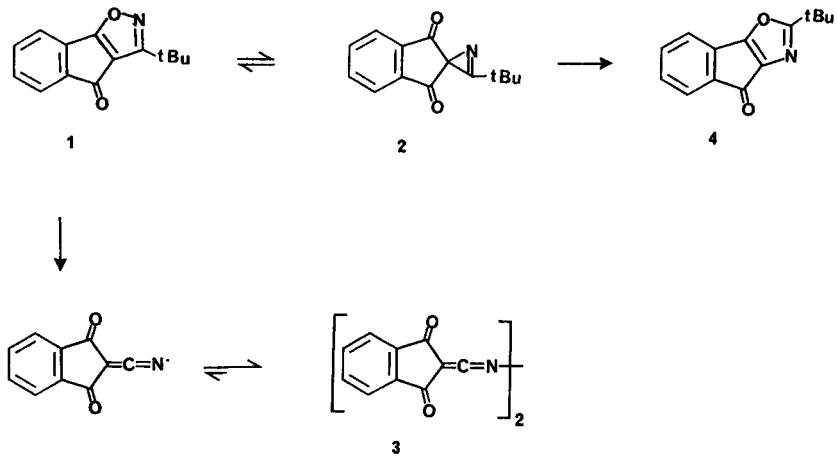
Temp °C	% Products [13]			
	1	**2**	**3**	**4**
300	60	22	18	–
350	4	47	49	–
400	–	35	65	–
500	–	–	70	30

Scheme I



route, we carried out the synthesis of **2** and performed the reactions at 300-400° and 10^{-2} torr (results are shown in Table II). The higher thermal stability of **2** compared with **1** (no reaction is observed at 300°) and the isomerization to **4**, led us to reject the route A-B of Scheme I and propose the reaction mechanism shown in Scheme II. Furthermore, the product compositions at different temperatures allow us to suggest the reaction coordinate of Figure I. This scheme requires that **4** must be observed when **1**

Scheme II



reacts at higher temperatures or longer residence times within the furnace. In order to confirm this fact, we carried out the FVP of **1** at 500° and **4** was obtained in 30% yield (Table I).

Table II

Reaction of 3-*t*-Butylspiro[2*H*-azirine-2,2'-(2*H*)-indene]-1',3'-dione (**2**)

Temp °C	% Products [13]		
	2	**3**	**4**
300	100	–	–
400	–	17	83

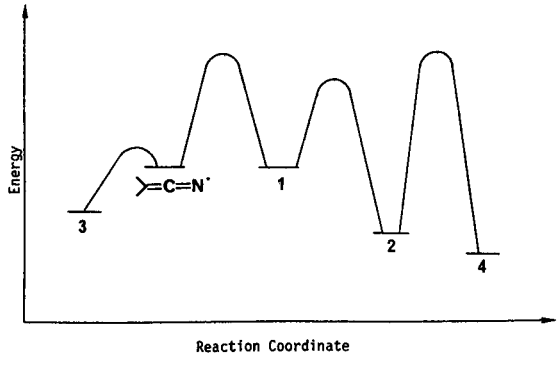


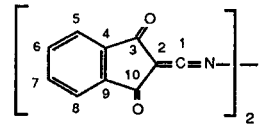
Figure I

In addition to using **1** as a mean of expanding the scope of the isoxazole-azirine-oxazole isomerization, **1** affords a novel reaction route to **3** which is an interesting compound in view of its unusual structure and properties. The structure of **3** was confirmed by elemental and spectral analysis. The first spectral data obtained from **3** led us to think in assigning to this compound the structure of 2-cyanoindan-1,3-dione; but it was rejected because the synthesis spectral analysis and physical properties (mp) of this nitrile have been recently reported [8] and they are different from those of **3**. The characteristic chemical shifts for the ketene imine carbons in **3** (C = C = N-) appear at δ 211.9 and 79.4 ppm which are in agreement with previously reported chemical shifts for ketene imines of δ 188-195 and 55-79 ppm [9-11]. The IR absorption at 2190 cm^{-1} also is very characteristic of the ketene imine structure.

In addition this nitrile does not explain the ^1H and ^{13}C nmr spectra obtained from **3** neither for the keto nor for the enolic form. This fact was confirmed by theoretical calculation of ^{13}C chemical shifts (Table III).

Table III

^{13}C Chemical Shifts for 2-Carbonyl-1,3-indandione 2-Azine (**3**)



	Found	Calcd. (BASF)
C-1	211.9	182.0 ± 12.7
C-2	79.4	110.8 ± 17.8
C-3,10	193.4	179.2 ± 9.0
C-4,9	139.2	140.5 ± 0.7
C-5,8	120.8	123.3 ± 0.5
C-6,7	133.4	133.8 ± 0.7

Although we were not able to obtain the molecular weight of **3** by ms (normal, FD, LD), it was estimated by ^1H nmr using several internal standards; the values obtained

support the proposed structure of **3** within the method precision (± 10%); the elemental analysis agree with those expected for **3**.

Conclusion.

The isomerization reactions agree with the reactivity model previously suggested using the donor-acceptor approach [4-7]. The derivatives previously studied demonstrated that electron donating groups attached to the heterocyclic ring caused a decrease in the activation energy. The electron-withdrawing substituents of **1** could change the reactivity pattern from III AX to I AX (as classified by Epiotis) [7]. Although we were not able to measure the kinetic parameters, it can be seen that the temperatures involved in these reactions are lower than those necessary for isomerization of the aminomethyl derivatives [4].

In addition, these derivatives showed an unusual reaction pathway with loss of a substituent attached to the isoxazole ring.

EXPERIMENTAL

The ^{1}H nmr were recorded on a Varian T-60 or Bruker FT-80 spectrometer and chemical shifts are reported in ppm downfield from tetramethylsilane. The ^{13}C nmr were recorded on a Bruker FT-80 spectrometer. Infrared spectra were recorded on a Beckman IR-12 and ultraviolet spectra were run on a Beckman DBG or Model 24 spectrophotometer. Mass spectra were determined on a Finnigan 3300 with a 1500 INCOS data system. Column chromatography was performed on silica gel 60 (35-70 mesh ASTM) with solvents that were analytical reagents. Melting points were determined on a Buchi 510 and are uncorrected.

General Procedure for Flash Vacuum Pyrolysis FVP.

FVP reactions were carried out in a "seasoned" pyrex glass reactor (40 cm length and 1.2 cm internal diameter) using oxygen free dry nitrogen as the carrier [4]. Heating was performed in a Lindberg Heavi-Duty model 55035 tube furnace. The sample was vaporized by heating with an external resistance. It was necessary to place an external resistance at the end of the furnace in order to prevent product condensation near the heating zone, which could induce products decomposition. The more volatile products were trapped at liquid air temperature in a "U" pyrex glass trap.

In FVP of **2** it was also necessary to wrap the trap and reactor at the end of the furnace with aluminum foil to prevent photochemical decomposition of **4**.

The system pressure was 10^{-3} torr without carrier and sample and 10^{-2} torr with carrier and sample. The time of residence into the furnace was about about 10^{-2} sec.

Synthesis of 3-*t*-Butylspiro[2*H*-azirine-2,2'-(2*H*)-indene]-1',3'-dione (**2**).

To a suspension of 1.2 g (5 mmoles) of 2-pivaloyl-1,3-indandione oxime [1] in 30 ml of toluene was added 0.3 g (5 mmoles) of methyl isocyanate. The reaction mixture was stirred at 25° for 48 hours at which time an additional 0.3 g (5 mmoles) of methyl isocyanate was added and stirring was continued an additional 12 hours. The reaction mixture was concentrated *in vacuo* and the residue was chromatographed on 100 g of silica gel eluting with ethyl acetate-toluene (1:19). The major component isolated consisted of 0.7 g of **2** which was recrystallized from cyclohexane, mp 68-70°; ir (potassium bromide): 2980, 1740, 1725, 1610, 1625, 745 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.37 (s, 9H), 7.8 (s, 4H); uv (ethanol): nm (log ε), 239 (4.67); ms: 70 eV m/z (%), 227 (75), 212 (65), 171 (100), 104 (14), 76 (8), 57 (6).

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 74.02; H, 5.77; N, 6.17. Found: C, 73.99; H, 5.78; N, 6.12.

A second compound recovered from the column consisted of starting material 0.3 g.

FVP of 3-*t*-Butylindeno[1,2-*c*]isoxazol-4-one (**1**).

Between 300-400° the reaction products were eluted from the reaction apparatus with acetone/methanol (2:1), and after the solvent was evaporated *in vacuo*, the mixture was chromatographed on silica gel with a normal elutropic array.

From the first eluate compound **1** was obtained and identified by comparison (nmr, ir, ms, uv) with an authentic sample. The azirine **2** was obtained from the second eluate (carbon tetrachloride eluting solvent) and identified by comparison with an authentic sample. A yellow crystalline product was obtained from the last eluate (ethanol eluting solvent) which decomposed without melting >300° and was identified as 2-carbonyl-1,3-indandione 2-azine (**3**); ir (potassium bromide): 2190 (strong), 1650, 1620, 1570, 720 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 7.4 (m); ^{13}C nmr (DMSO-d_6): δ 120.8, 133.4, 139.2, 193.4, 79.4, 211.9 (see Table III for assignations), in good agreement with similar allenic structures [9-11] uv (ethanol): nm (log ε), 254 (4.66) (sh), 262 (4.77), 272 (4.80).

Anal. Calcd. for $C_{20}H_8N_2O_4$: C, 70.59; H, 2.37; N, 8.23. Found: C, 70.17; H, 2.34; N, 8.25.

It was not possible to obtain neither normal nor field desorcion or Laser Desorcion mass spectrum of **3**; we were also not able to obtain an X-Ray crystallography of **3** due to its microcrystalline structure.

Molecular weight was estimated by ^{1}H nmr using nitromethane, acetone or 4-nitro-3,5-dimethylisoxazol as internal standards [12]; the result support the dimeric structure of **3**.

FVP of **1** at 500° gave two products, one of them condensed at the end of the reactor tube and the other one condensed in the "U" trap. The compound which condensed in the trap was removed with acetone in the absence of light to prevent photochemical decomposition. The solvent was evaporated *in vacuo* in the absence of light giving a yellow crystalline product mp 97-98°. This material was identified as 2-*t*-butylindeno[1,3-*c*]oxazol-4-one (**4**); ir (potassium bromide): 2750, 1745, 1710, 1620, 1590, 1210, 875, 795, 725 cm^{-1}; ^{1}H nmr (carbon tetrachloride): δ 1.41 (s, 9H), 7.1-7.3 (m, 4H); ms: (70 eV) m/z (%), 227 (52), 212 (35), 171 (58), 104 (30), 76 (25), 57 (100), 41 (10). This product decomposed in the presence of light.

The second reaction product was eluted from the reactor with acetone/methanol (2:1) and identified as **3** by comparison with an authentic sample.

FVP of 3-*t*-Butylspiro[2*H*-azirine-2,2'-(2*H*)-indene]-1',3'-dione (**2**).

The reaction was quantified only at 400° when one of the products condensed at the end of the reactor tube and the other one on the "U" trap as on FVP of **1** at 500°. The products were the same as in the latter case and they were isolated and identified in a similar way.

Although a mixture of **2** and **4** was detected by ^{1}H nmr in FVP of **2** at 350°, we were not able to quantify the products because **2** and **4** condensed in the "U" trap and **4** decomposed when we tried to isolate it from the crude reaction mixture.

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REFERENCES AND NOTES

[1] T. L. Lemke, K. N. Sawhney, and B. K. Lemke, *J. Heterocyclic Chem.*, **19**, 363 (1982).

[2] C. Wentrup, *Adv. Heterocyclic Chem.*, **28**, 248 (1981).

[3] D. Murature, J. D. Pérez, M. M. de Bertorello, and H. E. Bertorello, *An. Asoc. Quim. Argent.*, **64**, 337 (1976).

[4] J. D. Pérez, R. G. Díaz, and G. I. Yranzo, *J. Org. Chem.*, **46**, 3505 (1981).

[5] J. D. Pérez, G. I. Yranzo, and D. A. Wunderlin, *J. Org. Chem.*, **47**, 982 (1982).

[6] J. D. Pérez, *An. Asoc. Quím. Argent.*, **71**, 99 (1983).

[7a] N. D. Epiotis, *J. Am. Chem. Soc.*, **95**, 1191 (1973); [b] N. D. Epiotis, "Theory of Organic Reactions", Springer-Verlag, New York, 1978.

[8] E. Gudrinietse, P. V. Pastors, and V. V. Prieele, *Zh. Org. Khim.*, **9**, 1307 (1973).

[9] Leavy-Nelson, "^{13}C NMR for the Organic Chemist", John Wiley & Sons, 1972.

[10] C. Collier and G. A. Webb, *Org. Magn. Reson.*, **12**, 659 (1979).

[11] W. Runge, *Org. Magn. Reson.*, **14**, 25 (1980).

[12] P. J. Nathan and E. Díaz, "Introduccion a la RMN", Limusa, ed, México, 1970.

[13] **1** + **2** + **3** + **4** = 100% (Table I); **2** + **3** + **4** = 100% (Table II). The mass balance was higher than 90% in all runs. Percentages are averaged over at least three runs.