Ring-Closure Reactions. 14.[1] Kinetics of Macrocyclization by the Intramolecular Acylation of Thiophene and Benzothiophene Compounds[2]

C. Galli,* G. Illuminati,* and L. Mandolini*

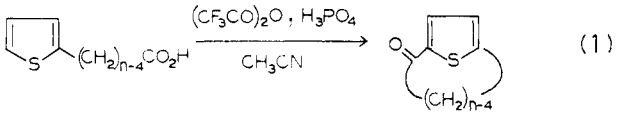
Centro C.N.R. di Studio sui Meccanismi di Reazione, Istituto di Chimica Organica dell'Università, 00185 Rome, Italy

Received July 16, 1979

The intramolecular acylation of long chain ω-(thienyl-2)alkanoic acids occurs in acetonitrile solution in the presence of trifluoroacetic anhydride and of catalytic amounts of H_3PO_4. Despite the complex nature of the reaction, sufficiently reliable rate data and effective molarities (EM) have been obtained for ring sizes 12, 13, 15, 17, and 21 for use in structure–reactivity correlations. These are the first quantitative data for large ring-forming aromatic-type substitution via C–C bond formation. They provide a measure for the effect of decreasing the length of the connecting α-oxopolymethylene chain upon the free energy of activation, which is mainly attributed to ring strain. Below the nine-membered chain length the rate is estimated to be exceedingly low. Steric hindrance of solvation in the transition state is suggested by the EM analysis and by comparison with the behavior of 14-(benzothienyl-2)tetradecanoic acid, for which steric hindrance of solvation is not expected to be important.

In our previous studies on the kinetics of ring-closure reactions,[3] cyclization was based on oxygen–carbon bond-forming reactions by intramolecular nucleophilic substitutions. It seemed desirable to move toward other reaction types, particularly those leading to carbon–carbon bond formation, in order to understand the influence of such changes on the energetics of ring closure. Syntheses of five-, six-, and seven-membered cyclic ketones by the intramolecular Friedel–Crafts acylation of aromatic substrates are well known.[4] Extensions to the synthesis of many-membered cyclic ketones incorporating a benzene or naphthalene residue in the ring have been described by Huisgen and his co-workers.[5] Similarly, Gol'dfarb and his co-workers[6] have reported the preparation of a series of macrocyclic ketones in which a thiophene ring was part of the cycle. To minimize polymerization, both groups of authors have employed conditions of extremely high dilution, namely the addition of a few grams of reactant into relatively large volumes of solvent over a period of several days. The conditions of such procedures are hardly suitable to rate measurements. Aliphatic carboxylic acids have been found[7] to smoothly acylate activated aromatic and heteroaromatic substrates in CH_3CN solution in the presence of $(CF_3CO)_2O$ and H_3PO_4. The reaction occurs under homogeneous conditions at moderate temperatures and requires fairly short reaction times.

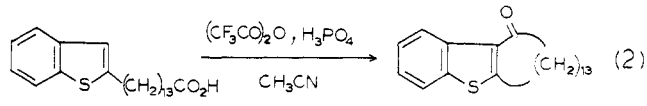
In this paper we report the application of the above reaction to the cyclization of long-chain ω-(thienyl-2)alkanoic acids (eq 1) under conditions suitable for kinetic



(1)

1 2

studies. The ring size n of the formed (2,5)thiophenophan-1-ones **2** ranges from 12 to 21. In order to compare an α-to-α′ to an α-to-β ring-closure reaction, the formation of the analogous benzothiophene macrocycle **4** has also been studied (eq 2).



(2)

3 4

Results

Since the reaction kinetics proved to be complex, a preliminary objective of the experimental work was to ascertain the reliability of the rate constants for use in the evaluation of the ring-closure tendencies of the bifunctional reactants under examination.

Reaction 1. The cyclization of compounds **1** was run in CH_3CN solution at 50.0 °C in the presence of a large excess of $(CF_3CO)_2O$ and a small amount of H_3PO_4. The progress of the reaction was followed by the increase of absorption at 295 nm, where the ketone products exhibit a strong band with ε values in the order of 10^4 M^{-1} cm^{-1}. The kinetics were followed at substrate concentrations as low as 3×10^{-5} M in order to minimize competition of the intermolecular polymerization reaction (vide infra). Other things being equal, the rate of appearance of the 295-nm band was a function of the concentration of both $(CF_3CO)_2O$ and H_3PO_4. The OD vs. time profiles showed an induction period during which no ketone was formed. After the inflection point, the reaction regularly progressed to reach a reproducible infinity value which was very close to that calculated on the basis of the initial reactant concentration and the known extinction coefficient of the expected cyclic product. At conversions as high as 30%, the kinetics approached first-order behavior, as shown in Figure 1 for the cyclization of **1**, $n = 15$. The first-order rate coefficient calculated from the linear part of the plot was found to be reproducible and independent of a fivefold change in initial substrate concentration. Similar behavior was observed for all compounds **1** under examination.

In the case of the cyclization of **1**, $n = 12$, which is the least reactive compound in the lot, the kinetics had to be carried out at extreme dilution, namely in the order of 6×10^{-6} M, to prevent polymerization which was still appreciable at 3×10^{-5} M. To improve sensitivity, a 40-mm cell was used. The concentration of $(CF_3CO)_2O$ was reduced to 0.016 M, in order to minimize the disturbance due to its absorption at 295 nm. For comparison with the

(1) Part 13. Mandolini, L.; Vontor, T., *Synth. Commun.* **1979**, *9*, 857.
(2) Work presented in part by G. Illuminati at the Friedel–Crafts Centennial Symposium, New Orleans (USA), March 23–25, 1977, and at the EUCHEM Conference on Stereochemistry, Bürgenstock, April 30–May 5 1978.
(3) Galli, C.; Giovannelli, G.; Illuminati, G.; Mandolini, L. *J. Org. Chem.* **1979**, *44*, 1258, and previous papers in the series.
(4) (a) Le Roi Nelson, K. *Ind. Eng. Chem.* **1958**, *50*, 1414. (b) Sethna, S. In "Friedel Crafts and Related Reactions"; Olah, G. A., Ed.; Interscience: New York, 1964; Vol. III, Part 2, pp 911–961.
(5) (a) Huisgen, R.; Rietz, U. *Tetrahedron* **1958**, *2*, 271. (b) Huisgen, R.; Ugi, I. *Chem. Ber.* **1960**, *93*, 2693.
(6) Gol'dfarb, Ya. L.; Taits, S. Z.; Belen'kii, L. I. *Tetrahedron* **1963**, *19*, 1851.
(7) Galli, C. *Synthesis*, **1979**, 303.

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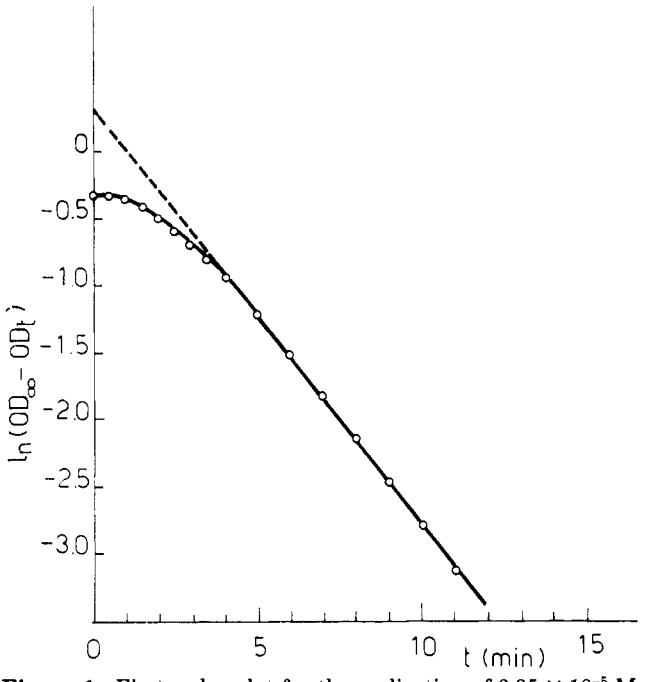

Figure 1. First-order plot for the cyclization of 3.35×10^{-5} M **1**, $n = 15$, in CH_3CN in 50.0 °C, in the presence of 0.1 M $(CF_3CO)_2O$ and 1×10^{-4} M H_3PO_4.

Table I. Kinetic Data for the Cyclization of ω-(Thienyl-2)alkanoic Acids **1**, n = 12, 13, 15, 17, and 21, in CH_3CN at 50.0 °C in the Presence of $(CF_3CO)_2O$ and H_3PO_4

n[a]	yield, %[b]	$10^3 k_{intra}$,[c] s^{-1}	$10^3 k_{intra}$,[d] s^{-1}	k_{rel}	EM, M[e]
12	85		0.23 ± 0.01	0.22	7.7×10^{-5}
13	83	1.74 ± 0.08	1.03 ± 0.06	1.0	3.5×10^{-4}
15	93	5.03 ± 0.29		2.9	1.0×10^{-3}
17	99	7.53 ± 0.07		4.3	1.5×10^{-3}
21	98	8.51 ± 0.19		4.9	1.7×10^{-3}

[a] Ring size in the ring to be formed. [b] As based on infinity spectra obtained in the kinetic runs (see text). [c] In the presence of 0.1 M $(CF_3CO)_2O$ and 1×10^{-4} M H_3PO_4. [d] In the presence of 0.016 M $(CF_3CO)_2O$ and 1×10^{-4} M H_3PO_4. [e] Calculated using a k_{inter} value of 5.0 M^{-1} s^{-1} (see text).

other substrates, a rate constant under the above conditions was also determined for **1**, $n = 13$. The kinetic results are collected in Table I. It should be noted that on changing the $(CF_3CO)_2O$ concentration from 0.016 to 0.1 M the rate of cyclization of **1**, $n = 13$, increases less than twofold.

The reaction was accelerated by increasing the amount of H_3PO_4. However, at high H_3PO_4 concentrations the kinetics are never first-order throughout. With no H_3PO_4 added, the reaction was unmeasurably slow under the given conditions. The role of H_3PO_4 is not well understood. It is unclear whether H_3PO_4 catalyzes the formation of a mixed alkanoic–trifluoroacetic anhydride, which is a possible acylating agent, or the attack of the anhydride itself onto the aromatic nucleus. Also, H_2SO_4 was found to be by far less powerful a catalyst than H_3PO_4. Although an assessment of this effect would require a knowledge of the protonating ability of the protic species present in CH_3CN solution, the catalytic role of H_3PO_4 does not seem to be simply that of a strong acid and may quite specifically be bound to the formation of a mixed alkanoic–phosphoric anhydride as the acylating agent.[8] The induction period

(8) Satchell, D. P. N. *Q. Rev., Chem. Soc.*, **1963**, *17*, 180.

Table II. Effect of Added 2-Methylthiophene (2MTH) on the Yield of Cyclic Ketone **2**, $n = 15$, Obtained in the Cyclization of 3×10^{-4} M **1**, $n = 15$, in CH_3CN at 50.0 °C in the Presence of 0.1 M $(CF_3CO)_2O$ and 1×10^{-4} M H_3PO_4

[2MTH]	yield, % found[a]	yield, % calcd[b]
none	71 ± 3	75
1.1×10^{-3}	38 ± 2	42
1.2×10^{-3}	36 ± 4	41
2.7×10^{-3}	24 ± 4	23
4.7×10^{-3}	15 ± 3	15
8.5×10^{-3}	12 ± 4	9

[a] As based on VPC analysis. [b] Calculated on the basis of an EM value of 9.0×10^{-4} M (see text).

may indicate that the accumulation of the acylating species is not instantaneous, even though it is relatively fast as compared to the acylation step. We suggest that the process takes place according to the general reaction 3,

$$R(CH_2)_{n-4}CO_2H \underset{}{\overset{(CF_3CO)_2O,\ H_3PO_4}{\rightleftharpoons}} R(CH_2)_{n-4}COY \qquad (3a)$$

$$R(CH_2)_{n-4}COY \xrightarrow[-HY]{k_{intra(slow)}} \mathbf{2} \qquad (3b)$$

where R = 2-thienyl and Y = CF_3CO_2 or $(HO)_2PO_2$, and that the observed first-order rate constant coincides with k_{intra}, i.e., the rate constant for the cyclization of the bifunctional intermediate.

The Effective Molarity. The effective molarity (EM) for a given cyclization reaction is defined by the k_{intra}/k_{inter} ratio.[9] In order to determine the k_{inter} value for the intermolecular model reaction, the acylation of 2-methylthiophene with pentanoic acid was studied under the same reaction conditions, namely $[(CF_3CO)_2O] = 0.1$ M and $[H_3PO_4] = 1 \times 10^{-4}$ M. Typical initial concentrations were 1×10^{-4} M for the heteroaromatic compound and 5×10^{-5} M for the alkanoic acid. Treatment of the OD vs. time data according to the standard second-order equation, using the calculated OD_∞ value, yielded second-order plots, which were linear from the end of the induction period up to at least 75% conversion. From the linear part of the curves a k_{inter} value of 5.0 ± 0.2 M^{-1} s^{-1} was obtained.

Similar calculations were possible for thiophene and its 3-methyl derivative. The following relative rates were obtained, after correction for the statistical factor: 2-methylthiophene (15.9); 3-methylthiophene (3.2); thiophene (1.0). These results compare very well with the ratios 16.7:3.4:1.0, as reported by Marino[10] for the acylation with mixed acetic–trifluoroacetic anhydride of the same compounds in the given order, and provide support to the reliability of the above k_{inter} value for the intermolecular model reaction. Nevertheless, due to some uncertainties in the spectral behavior of the model reaction (see Experimental Section), we have looked for a confirmation of the above results by a second procedure, as follows.

We carried out the cyclization of **1**, $n = 15$, under conditions similar to those of the kinetic experiments, except for the concentration of the substrate, i.e., 3×10^{-4} M instead of 3×10^{-5} M for analytical convenience. The yield of cyclic ketone **2**, $n = 15$, as determined by VPC analysis, is 71 ± 3%. Now, similar experiments carried out in the presence of increasing amounts of added 2-methyl-

(9) Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1977**, *99*, 6308.

(10) (a) Linda, P.; Marino, G. *Tetrahedron* **1967**, *23*, 1739. (b) Marino, G. *Adv. Heterocycl. Chem.* **1971**, *13*, 299–308.

thiophene (2MTH) give rise to decreasing yields of the cyclic product (Table II), because a portion of the bifunctional compound is used up in the intermolecular reaction with the added monofunctional reagent. A quantitative treatment of such results requires an expression for the rate of consumption of the bifunctional monomer M to be derived as shown in eq 4. The ex-

$$-\frac{d[M]}{dt} = k_{intra}[M] + k_{inter}[M][2MTH] \quad (4)$$

pression is approximate because the term in $[M]^2$ due to the self-condensation product can be neglected under the low concentrations used in our experiments. Then the ratio of the two main competing processes is given by eq 5. Since even under very high dilution as used in the

$$\frac{\%\text{ cyclic product}}{\%\text{ intermol reaction product}} = \frac{k_{intra}}{k_{inter}[2MTH]} = \frac{EM}{[2MTH]} \quad (5)$$

kinetic runs the yield is found to be slightly less than quantitative, i.e., 93% (Table I), the (% cyclic product)/(% intermolecular reaction product) ratio of eq 5 can be expressed by (% cyclic product)/(93 − % cyclic product), and eq 5 can be rearranged according to eq 6 and 7.

$$\%\text{ cyclic product} = EM\frac{93 - \%\text{ cyclic product}}{[2MTH]} \quad (6)$$

$$\%\text{ cyclic product} = 93\frac{EM}{[2MTH] + EM} \quad (7)$$

When the left-hand member of eq 6 was plotted against (93 − % cyclic product)/[2MTH], a reasonably good straight line (not shown) was obtained, from the slope of which an EM value of 9.0×10^{-4} M was calculated. The last column in Table II reports the yields predicted on the basis of eq 7 and the EM value obtained above. It is worth noting that for the run in which no 2-methylthiophene was added, eq 5 in ref 11 predicts a 75% yield of cyclic product, which compares fairly well with the experimental value of 71 ± 3%. Thus, the yield decrease due to competing intermolecular acylation is well accounted for by an EM value of 9.0×10^{-4} M. The latter, combined with the known k_{intra} value (Table I), afforded a k_{inter} value of 5.3 M^{-1} s^{-1}, in very good agreement with that derived from the kinetic experiments, i.e., 5.0 ± 0.2 M^{-1} s^{-1}.

The last column of Table I lists the EM values for all of the substrates under study. It can be easily verified that for each compound the concentrations used in the kinetic runs are at least one order of magnitude lower than the corresponding EM values. This fulfills the condition for the cyclization reactions to be essentially free from competition of polymerization processes.[11] As a consequence, the slight yield decrease as observed in the kinetic runs with the less reactive compounds (Table I) is likely to be due to competition of side reaction(s) other than polymerization.

Reaction 2. Under the same conditions as those adopted for the thiophene derivatives, the cyclization of the benzothiophene compound 3 and its intermolecular model reaction were significantly more sluggish, so that incursion of side reaction(s) interfering with the spectral behavior became more significant. The disturbance became even more serious because no prominent and intense band was observed in the UV, and a large portion of the spectrum was obscured by solvent absorption. In order to estimate the EM value for reaction 2, a set of competitive experiments was carried out, as shown in Table III. The concentration of H_3PO_4 was increased to 1.1×10^{-3} M to speed the reaction up. The decrease in the yield of the cyclic product 4 as caused by the added 2-hexylbenzothiophene (2HBT) is well accounted for by an EM value of 1.1×10^{-2} M. The latter was estimated by means of eq 8, which differs from eq 6 by the value for the limiting

$$\%\text{ cyclic product} = EM\frac{89 - \%\text{ cyclic product}}{[2HBT]} \quad (8)$$

yield (89%) as obtained spectrophotometrically at extremely high dilution.

(11) Galli, C.; Mandolini, L. *Gazz. Chim. Ital.* **1975**, *105*, 367.

Table III. Effect of Added 2-Hexylbenzothiophene (2HBT) on the Yield of Cyclic Ketone 4 Obtained in the Cyclization of 3 in CH_3CN at 50.0 °C in the Presence of 0.1 M $(CF_3CO)_2O$ and 1.1×10^{-3} M H_3PO_4

[3], M	[2HBT], M	yield, % found	yield, % calcd[a]
4.3×10^{-4}	none	88 ± 4	86
1.0×10^{-3}	none	80 ± 3	82
4.3×10^{-4}	1.00×10^{-2}	45 ± 2	47
4.3×10^{-4}	1.33×10^{-2}	40 ± 1	40

[a] Calculated on the basis of an EM value of 1.1×10^{-2} M (see text).

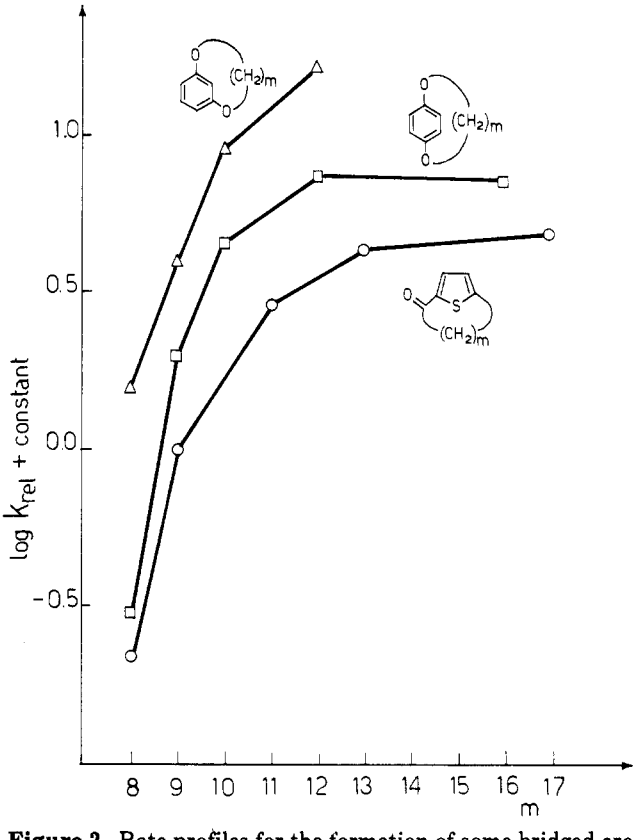

Figure 2. Rate profiles for the formation of some bridged aromatic compounds. For graphical convenience the data for *p*- and *m*-dioxacyclophanes are displaced upward along the *y* axis by 0.3 and 0.6 log units, respectively.

Discussion

The reactivity profile for the cyclization reaction 1 is shown in Figure 2 and compared with that of other reaction series. When the chain length is decreased, the reactivity also decreases and eventually drops steeply. For chains shorter than eight methylene groups, we predict

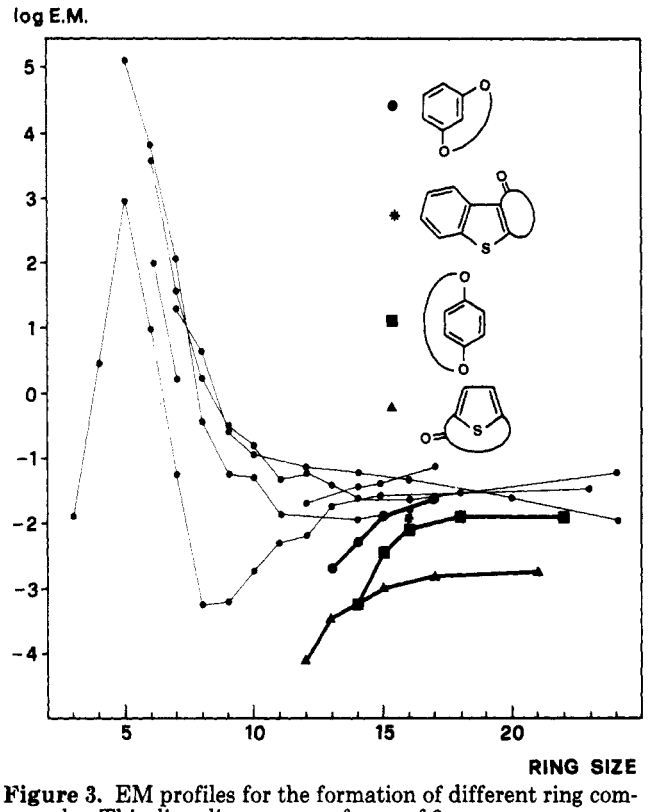

Figure 3. EM profiles for the formation of different ring compounds. Thin-line diagrams are from ref 9.

extremely low EM values, which would require prohibitively low concentrations for rate measurements. Although no parameters of activation are available, we believe that the enthalpy term is essentially responsible for this behavior because of the increasingly greater strain energy in the lower members of the series. Relief of strain in the larger rings causes the reactivity to become essentially independent of chain length.[9]

The data for the formation of two series of *m*- and *p*-dioxacyclophanes[12] from the corresponding ω-bromoalkoxyphenoxides are also shown in Figure 2. Despite the difference in reaction type, the shapes of the reactivity profile are remarkably similar. It follows that a major factor in determining the chain-length dependence of reactivity in the three series considered is a structural one, i.e., the incorporation in the bifunctional chains of rigid units by means of nonadjacent aromatic or heteroaromatic ring positions.

We have recently noted[9,13] that all available EM values for large ring formation in diverse cyclization reactions cluster in the limited range of 0.05 to 0.01 M. These data are reported in Figure 3 as thin-line diagrams. Figure 3 now shows that the data for the *m*- and *p*-dioxacyclophanes are in line with this rule, whereas the EM values for the formation of the thiophenophanones are shifted downward below the above stated range by at least one order of magnitude. The possibility that this unusual behavior is inherently linked to the particular mechanistic type of the reaction at hand is ruled out by the fact that the EM value for the benzothiophene compound (Figure 3) turns out to be "normal". We suggest that for reaction 1 desolvation occurs in the transition state, whose configuration is assumed to resemble a cationic charge-delocalized σ adduct. That solvation effects may play a role is supported by the dependence of the ring-closure reactivity on solvent. We found that the reaction is at least 60 times slower when carried out in the less polar ethylenedichloride as a solvent. Solvent stabilization of the developing positive charge, a major share of which is possibly concentrated on sulfur, might be disturbed by the bulky polymethylene chain across the thiophene ring, particularly in the surroundings of the sulfur atom itself, as suggested by molecular models. Conformational analysis is available in ring systems similar to the ring to be formed[14] for which an S inside type conformation[15] has been considered, although the conformational situation is not quite the same as the structure of the σ adduct. Since no steric inhibition of solvation is expected to affect the related intermolecular model reaction, the unusual EM value under consideration may also be viewed as resulting from the use of an inappropriate intermolecular model, whose solvation state is not perturbed, unlike the intramolecular process. No desolvation effect is expected to operate in the formation of **4**, since the methylene chain does not have to extensively cross the charged σ adduct, and the sulfur atom is clearly "outside" the ring.

Although the steric desolvation hypothesis is supported by the benzothiophene experiment, we would expect that the inhibition of solvation eventually fades out for sufficiently large rings. This change is not observed up to $n = 21$, and we are unable at present to extend the investigation to still larger rings because of severe experimental limitations (solubility).

This work offers a new example of application of the EM parameter for use in evaluating reactivity factors in ring-closure reactions. In particular, the EM parameter has been used as a reliable tool for the detection of a special effect which in no way could be revealed on the basis of reactivity data alone.

Experimental Section

Most apparatus were as previously described.[13] Elemental analyses were performed by Alfred Bernhardt, Mikroanalytisches Laboratorium, Elbach über Engelskirchen, West Germany.

Materials. Reagent grade CH_3CN (Erba RPE) was refluxed over P_2O_5 and distilled therefrom through a 20-cm Vigreux column. It was stored in an automatic buret that was protected from light and moisture. Trifluoroacetic anhydride (Merck, 99% pure), benzothiophene (Aldrich), hexyl bromide (ERBA RP), diethyl malonate (ERBA RP), and 1,12-dibromododecane (Aldrich) were used as received. Pentanoic acid (ERBA RP) and 2-methylthiophene (Aldrich) were redistilled before use. BuLi/hexane was from Aldrich. 5-Methyl-2-valeroylthiophene, available from a previous investigation,[7] had ϵ_{max} 10400 M^{-1} cm^{-1} at λ_{max} 291 nm in CH_3CN. The preparation of ω-(thienyl-2)alkanoic acids **1**, $n = 12$, 13, 15, 17, and 21, and their cyclization to the corresponding (2,5)thiophenophan-1-ones **2** was carried out as described elsewhere.[16]

2-Hexylbenzothiophene. All operations before workup were carried out under dry nitrogen. Sodium-dried diethyl ether was used throughout. A solution of benzothiophene (3 g, 22 mmol) in diethyl ether (10 mL) was added dropwise to 14.5 mL of BuLi/hexane (1.6 M) diluted with 15 mL of diethyl ether. After an hour, hexyl bromide (4 g, 23 mmol) in 7 mL of diethyl ether was added rapidly. The solvent was then distilled off and the residue heated at 120 °C for 4 h. After workup with aqueous mineral acid and diethyl ether, 6.1 g of a red liquid was obtained, which by distillation under vacuum gave, after a forerun of unreacted benzothiophene, the pure title compound (2.0 g, 12 mmol, 54% yield): bp 147–150 °C (1.5 mmHg); n^{22}_D 1.5689; ^1H NMR (CCl_4) δ 7.0–7.7 (m, 4 H, benzene ring protons), 6.8 (s, 1 H,

(12) Unpublished data from this laboratory.
(13) Mandolini, L.; Masci, B.; Roelens, S. *J. Org. Chem.* **1977**, *42*, 3733.
(14) Nozaki, H.; Koyama, T.; Mori, T. *Tetrahedron* **1969**, *25*, 5357.
(15) Prelog, V. *J. Chem. Soc.* **1950**, 420
(16) Catoni, G.; Galli, C.; Manololini, L. *J. Org. Chem.*, submitted for publication.

thiophene ring β proton), 2.8 (t, 2 H, CH_2Ar), 1.1–1.9 (broad m, 8 H, "central" methylene protons), 0.9 (t, 3 H, CH_3).

Anal. Calcd for $C_{14}H_{18}S$: C, 77.01; H, 8.31. Found: C, 76.88; H, 8.38.

14-(Benzothienyl-2)tetradecanoic Acid (3). This compound was prepared according to the following scheme (R = 2-benzothienyl).

$$RH \xrightarrow[2.\ Br(CH_2)_{12}Br]{1.\ BuLi} R(CH_2)_{12}Br \xrightarrow{(CO_2Et)_2CHNa} R(CH_2)_{12}CH(CO_2Et)_2 \xrightarrow[AcOH/H_2O]{H_2SO_4} 3$$

Alkylation of benzothiophene (6.6 g, 49 mmol) was carried out as above with BuLi (54 mmol) and 1,12-dibromododecane (16 g, 49 mmol). Since we found it difficult to separate the monobenzothienyl from the bisbenzothienyl derivative, the mixture was treated with sodium diethyl malonate in ethanol, and the resulting crude product was eluted with benzene on silica gel, to give 6.3 g (14 mmol) of 12-(benzothienyl-2)dodecylmalonate in 28% overall yield: n^{20}_D 1.5132; ^1H NMR as expected. Hydrolysis and decarboxylation of the latter with boiling 12% H_2SO_4 in an acetic acid–water mixture for 20 h gave **3** in 74% yield: mp 83–84.5 °C from MeOH; IR $\nu_{C=O}$ 1710 cm^{-1}.

Anal. Calcd for $C_{22}H_{32}O_2S$: C, 73.29; H, 8.95. Found: C, 73.06; H, 8.88.

[14](2,3)Benzothiophenophan-14-one (4). To a solution of **3** (0.40 g, 1.1 mmol) and 85% H_3PO_4 (0.26 g) in dry CH_3CN (220 mL), heated at 50 °C, was rapidly added 3.2 mL of $(CF_3CO)_2O$ under magnetic stirring. The resulting mixture was kept at 50 °C for 45 min, then worked-up with water–ether. The crude material was eluted on silica gel with benzene–light petroleum 2:1 to give 130 mg (0.38 mmol) of pure (TLC) **4** in 34% yield. For analytical purposes the compound was further purified by microdistillation with the ball tube under high vacuum. Compound **4** had: mp 21–23 °C; n^{19}_D 1.5503 (of the supercooled liquid); IR $\nu_{C=O}$ 1670 cm^{-1}; M^+ 342; ^1H NMR (CCl_4) δ 7.0–7.7 (m, 4 H, benzene ring protons), 2.85 (t, 2 H, $ArCH_2$), 2.70 (t, 2 H, CH_2COAr), 1.0–1.8 (broad m, 22 H, "central" methylene protons).

Anal. Calcd for $C_{22}H_{30}OS$: C, 77.14; H, 8.83. Found: C, 77.16; H, 8.94.

Further elution afforded 25 mg of a white crystalline material melting at 54.5–57.5 °C, to which the tentative structure of the dimeric cyclic can be assigned on the basis of the finding that its ^1H NMR spectrum is practically superposable to that of the monomeric cycle **4**.

Rate Measurements. These were carried out on a Beckman DB GT spectrophotometer fitted with a thermostated cell compartment and recorder. The kinetics solutions were prepared by placing the appropriate amounts of substrates and H_3PO_4 in CH_3CN in an all-quartz cell. After thermal equilibration at 50.0 ± 0.1 °C, the reaction was started by rapidly adding with a microsyringe a calculated amount of a standard solution of $(CF_3CO)_2O$ in CH_3CN. All operations were carried out under an argon atmosphere.

In the intermolecular model reaction between 2-methylthiophene and pentanoic acid, it was noted, in addition to the induction period, that the absorption rose significantly after the expected OD_∞ was reached. This behavior was attributed to the concurrent formation of an unknown byproduct whose strong absorption in the range of 300 to 600 nm superposed to that of the expected ketone. The addition of a drop of water at the end of the reaction caused the disappearance of the anomalous absorption and left an absorption consistent with a 75% yield of the expected ketone product. Similar behavior was also observed with thiophene and its 3-methyl derivative and with alkanoic acids other than pentanoic acid.

Product Analyses. These were carried out on scaled-up kinetic experiments. The crude materials obtained after standard workup were analyzed by VPC on a "Erba Model G" instrument, fitted with a 5% methylsilicone SE-30 on Chromosorb column. In the case of product **2**, n = 15, the column was operated at 178 °C with eicosane as the internal standard, while in the case of the compound **4**, the temperature of the column was 230 °C and octacosane was the internal standard.

Registry No. **1**, n = 12, 21010-08-2; **1**, n = 13, 21010-09-3; **1**, n = 15, 21010-10-6; **1**, n = 17, 71948-92-0; **1**, n = 21, 26359-19-3; **2**, n = 12, 71948-93-1; **2**, n = 13, 886-42-0; **2**, n = 15, 6907-25-1; **2**, n = 17, 6907-40-0; **2**, n = 21, 6907-44-4; **3**, 71948-94-2; **4**, 71948-95-3; 2-hexylbenzothiophene, 71948-96-4; benzothiophene, 95-15-8; diethyl 12-(benzothienyl-2)dodecylmalonate, 71948-97-5.

Tests for Free-Radical Intermediates in the Decarbonylation of Aldehydes by Tris(triphenylphosphine)chlororhodium(I)

J. A. Kampmeier,* S. H. Harris,[1] and D. K. Wedegaertner

Department of Chemistry, University of Rochester, Rochester, New York 14627

Received July 10, 1979

Wilkinson's catalyst [$RhCl(PPh_3)_3$ (**1**)] was reacted with phenylacetaldehyde (**5h**), phenylacetaldehyde-*d* (**5d**), *p*-methylphenylacetaldehyde (**6**), citronellal (**7**), and *exo*- and *endo*-5-norbornene-2-carboxaldehyde (**10x** and **10n**). The decarbonylation of mixtures of **5h** and **5d** shows an isotope effect (k_H/k_D) of 1.86 ± 0.07. No H–D crossover is observed when a mixture of **5d** and **6** is reacted with **1**. The reaction of citronellal (**7**) gives only 2,6-dimethyl-2-heptene. **10x** gives norbornene, and **10n** gives nortricycline; no crossover between the two systems is observed. These observations are consistent with concerted processes, intramolecular in aldehyde, for each step in the overall decarbonylation reaction; free-radical intermediates are excluded.

There is general agreement[2] on the overall mechanism (eq 1) for the decarbonylation of acid chlorides and aldehydes by tris(triphenylphosphine)chlororhodium(I) (**1**). However, the exact nature of the individual processes, i.e., oxidative addition (**1** + RCOX → **2**), acyl–alkyl migration (**2** → **3**), and reductive elimination (**3** → RX + **4**), is not clear. This reaction is a useful synthetic method and is a model for the discrete processes in other organometallic reactions. Therefore, a detailed knowledge of the mech-

$$\underset{\mathbf{1}}{RhCl(PPh_3)_3} + RCOX \rightarrow \underset{\mathbf{2}}{RCO(X)RhCl(PPh_3)_2} \rightarrow \underset{\mathbf{3}}{R(X)RhCl(CO)(PPh_3)_2} \rightarrow RX + \underset{\mathbf{4}}{RhCl(CO)(PPh_3)_2} \quad (1)$$

X = Cl, H

(1) Taken in part from the Ph.D. Thesis of Stephen H. Harris, University of Rochester, 1979; Sherman Clarke and Elon H. Hooker Fellow, University of Rochester.

(2) D. L. Egglestone, M. C. Baird, C. J. L. Lock, and G. Turner, *J. Chem. Soc., Dalton Trans.*, 1576 (1977); J. K. Stille and M. T. Regan, *J. Am. Chem. Soc.*, **96**, 1508 (1974), and references cited therein.

0022-3263/80/1945-0315$01.00/0