

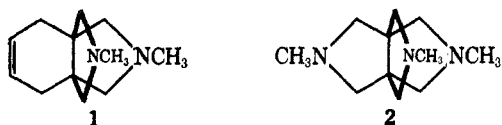
# Carbocyclic and Heterocyclic Propellanes

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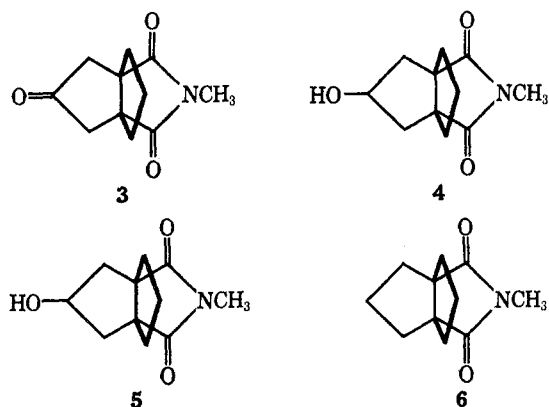
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We entered the field of propellane chemistry through the back door. After the appearance of a series of papers describing the efficacy of tetracyanoethylene as a dienophile,<sup>1</sup> we thought that the adducts with butadiene and other dienes might serve as intermediates for further synthesis of potential pharmaceuticals such as **1** and **2**.<sup>2,3</sup> Although these compounds did not



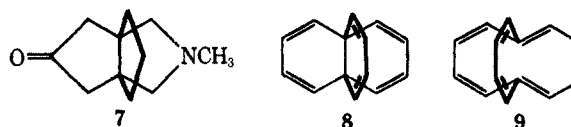
justify this hope, it became clear that such molecules, being relatively rigid, were worth investigating because of the existence of interaction between rings in these Y-shaped molecules.

The first such case concerned the behavior of **3** during catalytic reduction. We wanted to obtain the two corresponding epimeric alcohols, **4** and **5**, and applied various reduction methods to **3**. Reduction of **3** with



sodium borohydride yielded **5** exclusively, as evidenced by the fact that the product contained an intramolecular hydrogen bond, resulting from interaction of the hydroxyl function with the imide ring. No such interaction could be entertained with the saturated (cyclopentane) ring. It turned out that we could obtain the other epimeric alcohol, **4**, by inverting the configuration in **5** by percolating a solution of the tosylate of the latter through a column of basic alumina. But we also used, among other methods for obtaining the alcohol from **3**, Adams catalyst, in acetic acid as solvent. Neither **4** nor **5** was obtained; the carbonyl group was completely hydrogenolyzed and the exclusive product was **6**.

This was unexpected as it is unusual for alicyclic ketones to undergo hydrogenolysis to the corresponding cyclic hydrocarbon. Such ketones do not behave, for example, like acetophenones, where catalytic hydrogenolysis can be effected due to the presence of an aromatic nucleus adjacent to the carbonyl group. It must therefore be assumed that the existence of the imide ring in **3** is influencing its reductive behavior. Indeed, the amino ketone **7** under the same conditions yields a mixture of the corresponding epimeric amino alcohols. It was established, incidentally, that **4** and **5** are not intermediates in the reaction **3** → **6** as they are recovered unchanged when their hydrogenolysis was attempted in acetic acid solution in the presence of Adams catalyst.<sup>4</sup>



As we searched the literature for the existence of simple tricyclic systems conjoined in a carbon-carbon bond, we found to our amazement that, although a few rather more complex systems of this type had been prepared, simple systems had not been reported. Because of our long interest in nonbenzenoid aromatic compounds, we wanted to prepare compounds such as **8** which in itself might exhibit extraordinary interaction between the three rings and perhaps, if the bond common to the three rings could be induced to realign itself with concurrent realignment of additional bonds and yield **9** (and its resonance forms), we would have specifically a kind of three-dimensional cyclodecapentaene and more generally we would find ourselves involved in a study of electrocyclic reactions.

The molecular shape of **8** led to the suggestion of the "propellane" nomenclature for these tricyclic systems. This is less cumbersome than that proposed in the IUPAC rules which are still followed as to detail; it has been discussed<sup>4</sup> and has been accepted by most workers in the field. Indeed, the dictum "And there is nothing new under the sun"<sup>5</sup> has been proved correct for propellanes, for within 6 months after the beginning of our work on alicyclic propellanes, two papers appeared describing the same type of system that we had undertaken to prepare.<sup>6</sup> More and more workers have be-

(1) W. J. Middleton, R. E. Heckert, E. L. Little, and C. G. Krespan, *J. Am. Chem. Soc.*, **80**, 2783 (1958).

(2) S. Welner and D. Ginsburg, *Israel J. Chem.*, **4**, 39 (1966).

(3) J. Altman, E. Babad, J. Pucknat, N. Reshef, and D. Ginsburg, *Tetrahedron*, **24**, 975 (1968).

(4) J. Altman, E. Babad, J. Itzhaki, and D. Ginsburg, *Tetrahedron Suppl.*, **8**, Part 1 279 (1966).

(5) "Ecclesiasticus," Chapter 1, Verse 9.

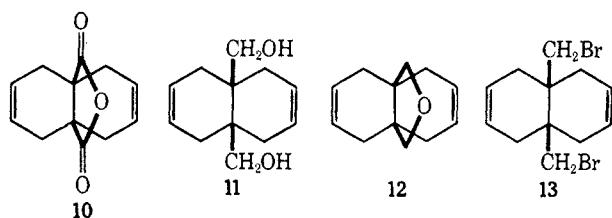
(6) (a) G. Snatzke and G. Zanati, *Liebigs Ann.*, **684**, 62 (1965); (b) F. Nerdel, K. Janowsky, and D. Frank, *Tetrahedron Letters*, 2979 (1965).

come involved in this field because of its great potential interest.<sup>7</sup> It is this interest which I hope to justify in this Account.

It is nevertheless surprising that propellanes began to attract the attention of organic chemists in 1966 and not, *e.g.*, in 1936. The major synthetic method leading to propellanes, the Diels-Alder reaction, was available at the earlier date. The stereochemical interest in alicyclic systems was certainly strong during the past three decades. Yet it is a fact that the combination of these interests came to fruition for propellanes only a very short time ago.

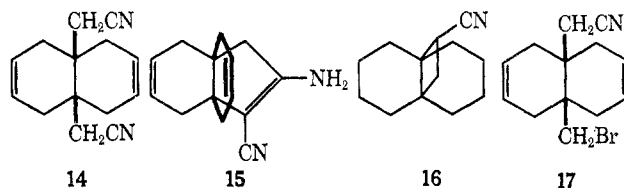
It occurred to others and to ourselves to use very similar starting materials for the synthesis of alicyclic propellanes. During one of my frequent visits to Zürich I gave Prelog a description of some of our work on propellanes. He walked over to one of his files and politely presented me with several (unpublished) reports on work which had anticipated ours and that of others by a decade. The aim had been to prepare substituted cyclodecapentaenes.<sup>8</sup>

The starting materials were simply butadiene and acetylenedicarboxylic acid. This reaction was first carried out by Alder.<sup>9</sup> The adduct **10** was reduced with lithium aluminium hydride to yield the diol **11** which could be cyclized to the oxapropellane **12** by means of *p*-toluenesulfonic acid. Treatment of the latter with triphenylphosphine dibromide afforded the (dineopentylidene) dibromide **13**. Now, although

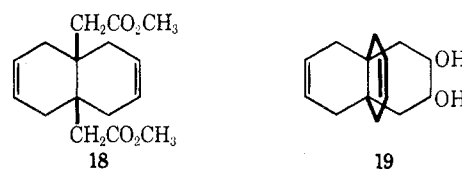


Dostrovsky, Hughes, and Ingold<sup>10</sup> have taught us many years ago about the relative sluggishness of neopentylidene halides in nucleophilic substitution reactions, we have at our disposal solvents of higher dielectric constant, and in the case of **13** we have the angular substituents in *cis* disposition with respect to each other. Thus, when **13** is heated with cyanide ion in dimethyl sulfoxide, the over-all conversion into products is high, but the product mixture contains three components, **14**, **15**, and **17**.

If we assume that **17** is formed *en route* to **14** we can understand the formation of **16** in the alkaline milieu of the analogous reaction of tetrahydro-**13**. Similarly we can understand the formation of **15** from **14** through a Thorpe-Ziegler cyclization. The course of the cyclization may be reversed by employing sodamide in liquid ammonia.

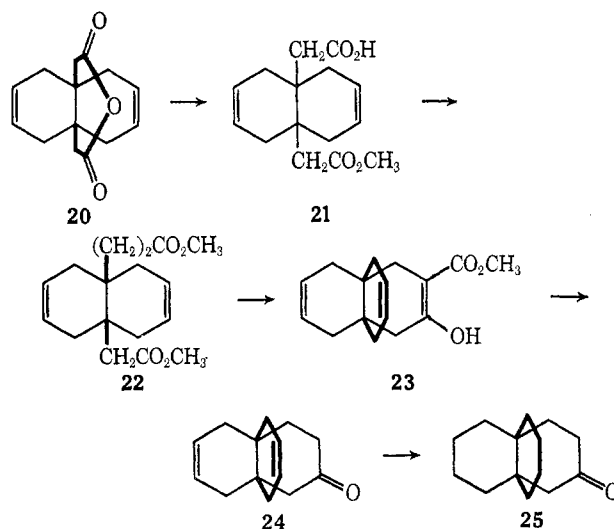


Although one usually likes to get a good yield of one product in a given reaction, we were particularly delighted with the composition of the above reaction mixture. One common starting material, **13**, permitted us to obtain entry into the [4.4.4]-, the [4.4.3]-, and the [4.4.2]propellane systems. Saponification of **14** to the diacid and esterification yielded the dimethyl ester **18**. Acyloin condensation thereof permitted the isolation of the [4.4.4]propellane derivative **19**. **15** and **16** are already derivatives of the [4.4.3]- and [4.4.2]propellane systems, respectively. The details



of the conversion of these derivatives into the corresponding parent propellanes are given in the original papers.<sup>3,4</sup>

It turned out, however, that [4.4.4]propellane itself could be prepared in higher over-all yield through the intermediacy of the seven-membered anhydride **20**. Methanolysis to the half-ester **21**, followed by Arndt-Eistert homologation, yielded the diester **22**. Dieckmann condensation afforded the totally enolic  $\beta$ -keto ester **23** which upon saponification (and decarboxylation) gave the dienic ketone **24**. This was reduced to the saturated ketone **25**.



As a result of a seminar given by Dr. Altman on her work, including the above reaction scheme, Dan Becker, one of my colleague Loewenthal's graduate students, whose thesis involved the intramolecular addition of keto carbenes generated in one part of a molecule to double bonds in another part of the molecule, devised

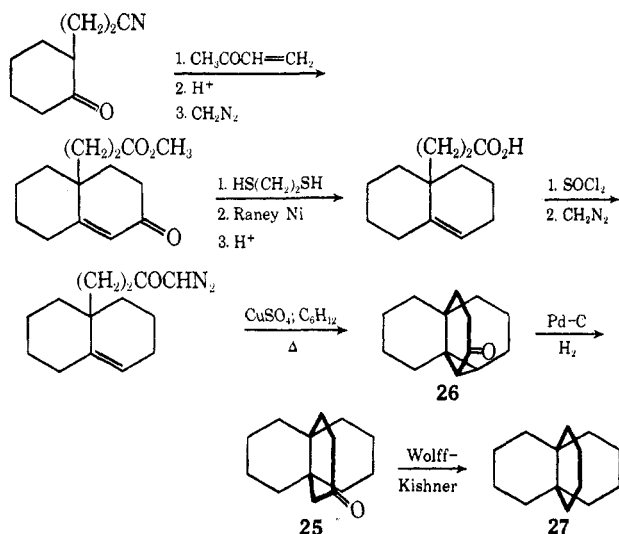
(7) See ref 3, footnotes 2a-o.

(8) V. Prelog, W. H. Laarhoven, and M. F. Lynch, private communication from Professor V. Prelog.

(9) K. Alder and K. H. Backendorf, *Ber.*, **71**, 2199 (1938).

(10) I. Dostrovsky, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 173 (1946).

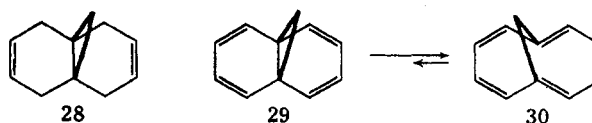
and subsequently carried out the following synthesis of ketone **25**.<sup>11a</sup> Hydrogenation of the cyclopropyl



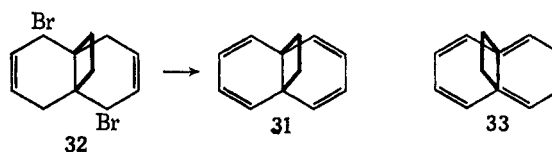
ketone **26** led selectively in 90% yield to ketone **25**. Wolff-Kishner reduction gave [4.4.4]propellane (**27**). Dunitz and Ermer<sup>11b</sup> showed that the three six-membered rings in **27** are somewhat flattened cyclohexane chairs. The molecule has  $D_3$  symmetry and is chiral.

Since we had in our hands a goodly number of 9,10-disubstituted *cis*-decalin derivatives we determined the activation energy of ring inversion in these compounds. Gerig and Roberts,<sup>12</sup> using potential energy calculations and assuming a particular model for transition path and equilibrium, have estimated that the barrier for inversion should be about 17 kcal/mol. Our results<sup>13</sup> are in good agreement with their estimate and model. It would appear from this that the barrier for inversion of [4.4.4]propellane would be too low to permit the actual resolution of one of its derivatives, although we may nevertheless attempt this if manpower and time permit.

Snatzke and Zanati<sup>6a</sup> as well as Nerdel and co-workers<sup>6b</sup> have prepared a number of alicyclic propellanes, the former in the [4.4.4]- and [4.4.3]propellane series and the latter in the [4.4.3]propellane series. When Vogel and his coworkers attempted the preparation of the tetraenic [4.4.1]propellane **29** by bromination of **28** followed by dehydrobromination, methanocyclodecapentaene **30** was obtained, presumably *via* the intermediacy of **29**.<sup>14</sup> Subsequently Vogel investigated the situation in the case of the tetraenic [4.4.2]propellane **31**. In this case **31** was relatively stable and could be isolated, albeit in low yield. On heating, **31** gives naphthalene in high yield, and this is presumably the

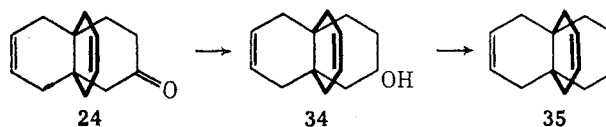


reason for the low yield of **31** as it is reported that dehydrobromination of **32** by heating with quinoline at 140° affords **31** in *ca.* 10% yield, accompanied by naphthalene.<sup>14b</sup>



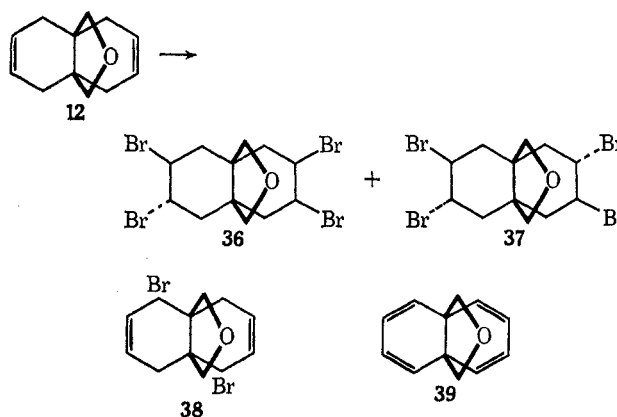
Altman has managed to prepare **31** in considerably higher yield and confirmed the ready thermal formation of naphthalene from it. But since Babad required a highly purified sample of **31** for her photochemical work (see below), purification was effected by gas-liquid partition chromatography, the column temperature never being allowed to rise above 90°. The purer sample of **31** thus obtained from a much purified sample of **31** was always accompanied by a yellow product which also accompanies **31** when prepared by dehydrobromination of **32** by heating in dimethylformamide at 90°. This may well be the fugitive **33**, but additional time will be necessary to prove this conclusively.

Doubtless there exist more efficient methods for the preparation of naphthalene than the one now to be described. So far we have not succeeded in preparing the potentially interesting hexaenic [4.4.4]propellane **8**, already mentioned above. We glibly attempted to



reach it *via* the following route. The trienic [4.4.4]propellane **35** was readily obtained. We had previously carried out "model" experiments starting from **12** and obtained the tetraenic oxapropellane **39** in good yield whether *via* the tetrabromides **36** or **37** or the diallylic dibromide **38**. We shall later discuss the photochemistry of **39**.

The symmetry of the system permits the existence of two hexabromides arising by addition of bromine to



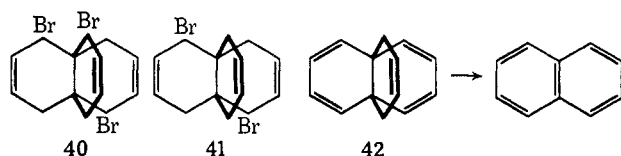
(11) (a) J. Altman, D. Becker, D. Ginsburg, and H. J. E. Loewenthal, *Tetrahedron Letters*, 757 (1967); (b) letter from Professor J. D. Dunitz, Nov 13, 1967.

(12) J. T. Gerig and J. D. Roberts, *J. Am. Chem. Soc.*, **88**, 2791 (1966).

(13) J. Altman, H. Gilboa, D. Ginsburg, and A. Loewenstein, *Tetrahedron Letters*, 1329 (1967).

(14) (a) E. Vogel and H. D. Roth, *Angew. Chem.*, **76**, 145 (1964); (b) E. Vogel, W. Maier, and J. Eimer, *Tetrahedron Letters*, 655 (1966).

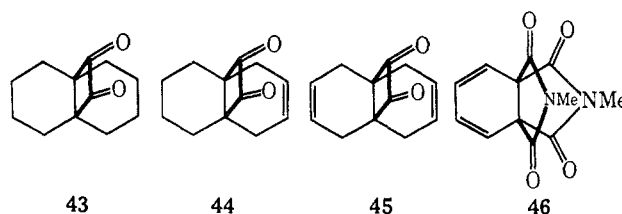
**35**, again assuming *trans* addition of the bromine to each of the double bonds. In this case, however, we isolated only one of the possible isomers. Since dehydrobromination of this led to an intractable mixture of products and we began to doubt the applicability of our "model" experiments, we nonetheless decided to try our luck with the triallylic tribromide **40**. Altman treated **35** with 3 equiv of N-bromosuccinimide. It appeared as though the major part (2 equiv?) of the reagent reacted within minutes but the last equivalent reacted sluggishly; in time hydrogen bromide appeared to split out and again an intractable reaction mixture was obtained. It was obvious, and this can readily be seen in models, that there would be a bad steric interaction between a pair of bromine atoms in **40**. The distance is about that between 1,3-diaxial bromines in a cyclohexane chair. My brilliantly simple idea



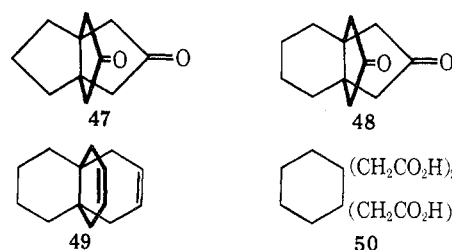
followed. Let us treat the triene **35** with 2 equiv of N-bromosuccinimide, dehydrobrominate the resulting dibromide **41**, and obtain **42**; no bromine atoms will be present in **42** to interfere with the introduction of a further bromine atom allylic to the one double bond in the third ring and . . . . And the reaction went beautifully according to prediction, but only up to a point. The pentaenic propellane **42** was undoubtedly formed in high yield but the "brilliant" predictor should have realized that **42** is well aware of its possibility to undergo a retro-Diels-Alder reaction. Naphthalene was synthesized in rather good yield!<sup>13</sup>

More routes are available to synthesize the hitherto elusive **8**. We shall return to these after a well-earned respite from these abortive attempts, but perhaps others will succeed before us.<sup>15</sup> The successful and dramatic work of Dr. Babad, to be described below, necessitated the mobilization of manpower for preparation of tetraenic propellanes for photochemical studies.

Before we turn to this, we should report some of the interesting work of others on alicyclic propellanes. Bloomfield, to whom we owe an exciting discovery which will be reported below, has prepared four-membered ring acyloins in high yield and has prepared from these the  $\alpha$ -diketones **43**, **44**, and **45**.<sup>16</sup> One does not need a spectrophotometer to observe the inter-ring interaction in these compounds. **43** is light yellow, **44** is light pink, and **45** is deep pink, clearly showing the same type of interaction as we have observed in the ultraviolet absorption spectra of compounds such as **46**, although in our case a spectrophotometer is necessary for observation.<sup>4</sup>

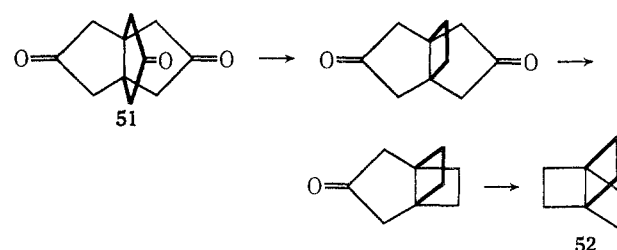


Weiss and Edwards have attempted a reaction between cyclopentane-1,2-dione or cyclohexane-1,2-dione, acetonedicarboxylic ester, and a third component, but have obtained condensation of the first two to yield **47** and **48**, respectively, without isolation of the resulting tetraesters.<sup>17</sup> Since Altman had the dienic ketone **24** in hand, she converted it into **49** by Wolff-Kishner reduction and ozonized the latter to yield **50**.

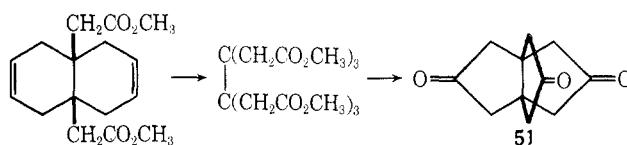


Cyclization of **50** with acetic anhydride followed by pyrolysis afforded **48** and proved the structure thereof.<sup>18</sup>

The triketone **51** is of interest as it may provide a route to [2.2.2]propellane (**52**). We are, of course, interested in determining the scope and limitations of ring size in alicyclic propellanes. There appears to be no reason why one could not synthesize larger ring propellanes than those discussed above. It is more interesting to delineate the ring size in the other direction. Perhaps mercury-sensitized decarbonylation of **51** might afford, stepwise, [2.2.2]propellane (**52**). The



starting material has been prepared as follows.<sup>18</sup>



Model photochemical decarbonylation experiments are in progress with the diketone **53**.<sup>18</sup>

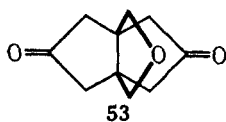
At the San Francisco meeting of the American Chemical Society in April 1968 Eaton reported elegant syntheses of [4.2.2]propellane (**55**) and [3.2.2]propel-

(15) Professor G. B. Butler of the University of Florida is also interested in this synthesis (letter to Dr. J. Altman, March 19, 1968).

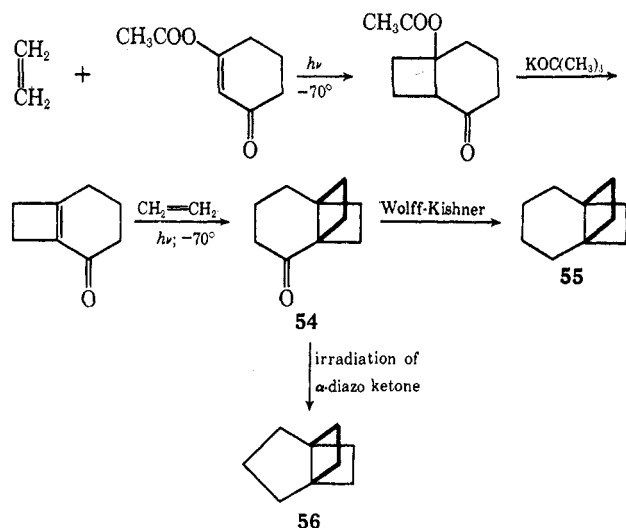
(16) Private communication from Dr. J. J. Bloomfield; J. J. Bloomfield and R. E. Moser, *J. Am. Chem. Soc.*, **90**, 5625 (1968).

(17) Private communication from Drs. U. Weiss and J. M. Edwards; U. Weiss and J. M. Edwards, *Tetrahedron Letters*, 4885 (1968).

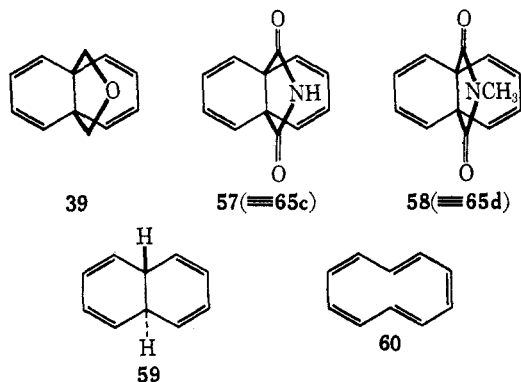
(18) Unpublished results from this laboratory.



lane (**56**), *via* a common intermediate, ketone **54**.<sup>19</sup>



We think that the most dramatic result of our work on propellanes to date has stemmed from irradiation of a number of tetraenic propellanes, the ether **39**, the imide **57**, and the methylimide **58**. Let us go off on what may appear momentarily to be a tangent and briefly summarize the electrocyclic reactions of  $(CH)__{10}$ . van Tamelen has irradiated *trans*-9,10-dihydronaphthalene (**59**) and has shown the existence of cyclodecapentaene (**60**) in solution at low temperature.<sup>20</sup> But



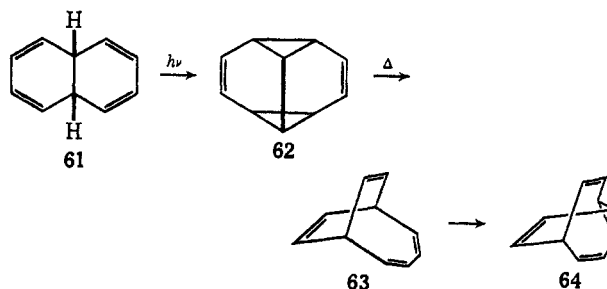
propellanes are derivatives of *cis*-9,10-dihydronaphthalene (**61**), and the variegated species related to **61** include bullvalene (**64**), tricyclo[5.3.0.0<sup>4,8</sup>]deca-2,5,9-triene, tricyclo[4.2.2.0<sup>2,5</sup>]deca-3,7,9-triene ("Nenitzescu's hydrocarbon"), bicyclo[4.2.2]deca-2,4,7,9-tetraene ("prebullvalene," **63**), tetracyclo[4.4.0.0<sup>1,5</sup>.0<sup>2,8</sup>]deca-3,9-diene, and various substituted derivatives.<sup>21</sup>

(19) P. E. Eaton, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, P1.

(20) E. E. van Tamelen and T. L. Burkoth, *J. Am. Chem. Soc.*, **89**, 151 (1967).

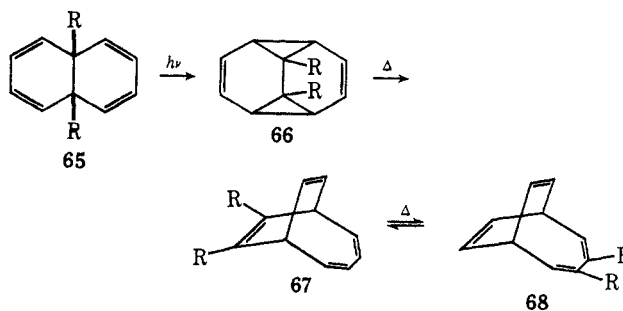
(21) (a) For a recent review see G. Schröder and J. F. M. Oth, *Angew. Chem. Intern. Ed. Engl.*, **6**, 414 (1967); (b) M. Avram, E. Sliam, and C. D. Nenitzescu, *Liebigs Ann.*, **636**, 184 (1960); (c) W. von E. Doering and J. W. Rosenthal, *J. Am. Chem. Soc.*, **88**, 2078 (1966).

The missing link in this series of fluxional isomers had been the oft-cited but ne'er isolated tetracyclo[4.4.0.0<sup>2,10</sup>.0<sup>5,7</sup>]deca-3,8-diene (**62**).<sup>22</sup>



Our photochemical intentions were realized when our new colleague and collaborator Rubin came to the Technion. After a photochemical survey of many propellane derivatives<sup>23</sup> Babad chose to begin with **39** and **58**.

Irradiation of the ether **39** (= **65a**) at 2537 Å afforded a derivative of **62** in about 95% yield. On the basis of its remarkably simple nmr spectrum ( $CDCl_3$ ; 60 MHz) determined at  $-25^\circ$ , its structure was formulated as **66a**. There were three lines of equal intensity at 361 ( $W_{1/2} = 4$  Hz; vinylic protons), 255 ( $W_{1/2} = 1.5$  Hz;  $CH_2O$ ), and 88 Hz ( $W_{1/2} = 4$  Hz; allylic cyclopropyl protons). Irradiation at 88 Hz resulted in appreciable sharpening of the line at 361 Hz ( $W_{1/2} = 1.5$  Hz) and *vice versa*. Catalytic hydrogenation of **66a** ( $PtO_2$  in  $CH_3OH$ ) quantitatively afforded the known octahydro derivative of **39**. Upon



R, R: a,  $-CH_2OCH_2-$ ; b,  $-CONMeCO-$ ; c,  $-CONHCO-$ ; d,  $-COOCO-$ ; e,  $-COOCH_2-$

standing at room temperature in deuteriochloroform or in methanol solution, **66a** was quantitatively converted into a compound believed to be **67a**, a derivative of **63**. Here again the nmr spectrum and double-resonance studies appeared to support this formulation for **67a**. The half-life for the conversion **66a**  $\rightarrow$  **67a** in methanol solution at  $22^\circ$  was *ca.* 2 hr.

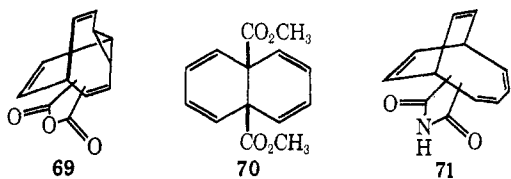
Even more dramatic than this case was the fact that the product **66b** of irradiation of the methylimide **65b** could be purified by column chromatography at room temperature and could be isolated. The half-life of

(22) It has been obtained at low temperature and its structure proved by degradation (letter from Professor S. Masamune to Professor M. B. Rubin, Aug 19, 1968). Cf. S. Masamune, R. T. Seidner, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *J. Am. Chem. Soc.*, **90**, 5286 (1968).

(23) Carried out by Mrs. Ziva Weiss.

the thermal conversion **66b**  $\rightarrow$  **67b** was *ca.* 3 hr at 60° in methanol solution. Here, too, **67b** was formulated as shown, on the basis of the spectroscopic evidence (nmr and uv).<sup>24</sup> We were not particularly happy about the extinction values in the uv spectrum of **67b** (uv in methanol:  $\lambda_{\max}$  293 (sh), 248 nm ( $\epsilon_{\max}$  2600, 13,200)), but since similar values were obtained for the analogous anhydride,<sup>25</sup> these values were considered reasonable.

Vogel and his coworkers had irradiated the tetraenic anhydride **65d** and did not isolate an analog of **66b** but reported the isolation of two products, **67d** (an analog of **67b**) and the bullvalene anhydride **69**.<sup>25</sup> As already

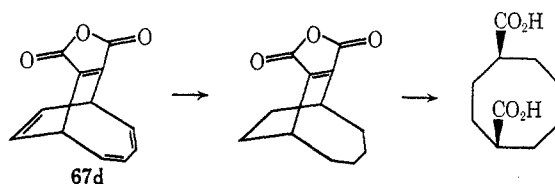


stated, the spectroscopic properties reported for **67d** were analogous to those we later obtained for **67b**, and those for **69** were reasonable for a bullvalene derivative. Furthermore, irradiation of **70** by Vogel permitted isolation of a bullvalene dimethyl ester and treatment of **69** with methanolic HCl gave the same nmr spectrum as obtained for the bullvalene dimethyl ester.

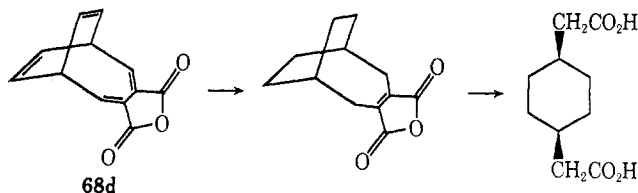
The photointermediate **66d** was not isolated. Its thermal isomerization proceeded while irradiation of **65d** was still going on. Thus, a compound formulated as **67d** was formed and later isolated from the reaction mixture. Part of this compound was converted, during further irradiation, into **69**.

Although we attempted to isolate the first intermediate of irradiation of **65d**, we were also unsuccessful, although we could observe its presence at -50°. Irradiation at -78° in methanol followed by removal of solvent under vacuum at -55° did not suffice to isolate the intermediate; only **67d**, the product of subsequent thermal reaction, was isolated. However, irradiation of the imide **65c** afforded **66c**, again as a stable compound, the half-life for its thermal conversion into **71** being *ca.* 3 hr at 60°.<sup>18</sup>

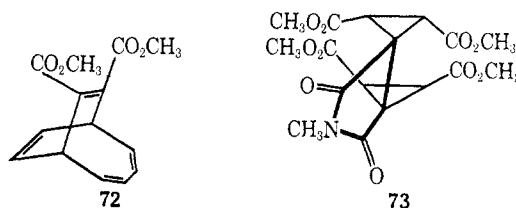
At this point it will be noted that **71** is not formulated as clearly as, *e.g.*, **67a**, **67b**, or **67c** and with good reason! Dr. Bloomfield has informed us<sup>26</sup> that he too has irradiated **65d** and that he too did not isolate the first intermediate of the irradiation and obtained the product of its thermal interconversion. But he was forced to question the structure of **67d** as formulated above. This arose from his desire to obtain cyclooctane-*cis*-1,4-dicarboxylic acid by reduction of **67d** followed by oxidation of the product. He obtained, however, cyclohexane-*cis*-1,4-diacetic acid! By hindsight he felt that the nmr spectrum of **67d** is best interpreted on the basis of its formulation as **68d**, a structure which also explains



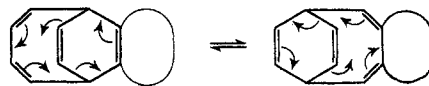
the results of its reduction-oxidation sequence.



This, of course, opens to question the formulations **67a-d**, as well as that of any other derivatives of **67**. Bloomfield suggests<sup>26</sup> that fluxional isomerism exists at the "prebullvalene" stage (**63**) in addition to the well-known bullvalene case. He has informed us, for example, that the diester formed from the anhydride **68d** is **72**, indicating that the equilibrium position in such systems is sensitive to very delicate changes in structure.



The structures of **66a-c** are not in question. In fact, we have ozonized **66b** and isolated **73**, thus affording chemical proof for the structure of **66b**. But those of their thermal conversions are indeed open to question, and it is necessary to prove their structures in each case. The mechanism of interconversion may be formulated as



In rapid succession three groups have presented evidence for the existence of fluxional isomerism in prebullvalene (**63**).<sup>22, 27, 28</sup>

But the plot thickens insofar as prebullvalene derivatives are concerned. After receiving Bloomfield's information,<sup>26</sup> Altman attempted to reduce prebullvalene derivatives so that a decision might be reached on their disposition between the **67** and the **68** series.<sup>29</sup>

Room temperature reduction of the methylimide which is either **67b** or **68b**, using Adams catalyst in ethyl acetate, afforded a mixture of two isomeric hexahydro compounds in the ratio 8:2. These were

(24) E. Babad, D. Ginsburg, and M. B. Rubin, *Tetrahedron Letters*, 2361 (1968).

(25) E. Vogel, W. Grimme, W. Meckel, H. J. Riebel, and J. F. M. Oth, *Angew. Chem. Intern. Ed. Engl.*, **5**, 590 (1966).

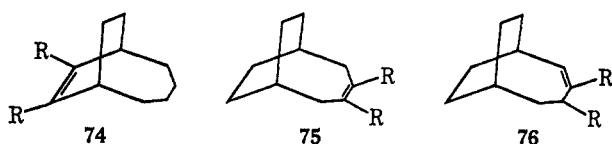
(26) Letter from J. J. Bloomfield, July 12, 1968.

(27) M. Jones, Jr., and B. Fairless, *Tetrahedron Letters*, 4881 (1968).

(28) W. Grimme, H. J. Riebel, and E. Vogel, *Angew. Chem.*, **80**, 803 (1968).

(29) J. Altman, E. Babad, M. B. Rubin, and D. Ginsburg, *Tetrahedron Letters*, in press.

first believed to be **74b** and **75b**, respectively. Assignment should be both safe and simple at this oxidation state since fluxional isomerism is no longer possible and nmr spectroscopy permits one to distinguish the presence of two or four allylic protons, respectively. It was also found that the product ratio is temperature dependent. It turned out, however, that one series of hexahydro derivatives indeed belonged to the **75** family, but the other series had the same skeleton as **75** and corresponded to **76b-d**, double bond isomers of **75b-d**.



R, R: b,  $-\text{CON}(\text{CH}_3)\text{CO}-$ ; c,  $-\text{CONHCO}-$ ; d,  $-\text{COOCO}-$

Similar reduction of the anhydride which is either **67d** or **68d** afforded a mixture of two hexahydroanhydrides, this time, however, in the ratio of 1 : 9. The numerical order in the corresponding ratio bears noting as chemical interrelations (no fluxional isomerism possible) between the various reduction products led to the following summary.

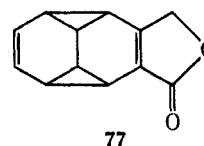


The reduction products **75c** and **76c** were also fitted into the above scheme.

These results show conclusively that structural assignments to the **67** series or to the **68** series may be based upon chemical reactions such as the above reductions, but it is not really necessary to have recourse to such means of proof. Nmr spectroscopy, when used correctly (100-MHz instrument) and when the spectra are interpreted correctly, lead to correct structural assignment for either the **67** or to the **68** series. We are indebted to Professor W. von Philipsborn with respect to the fulfillment of both these conditions. The 100-MHz spectra prove unequivocally that structures **67a**<sup>24</sup> and **67b**<sup>24</sup> as well as **67d**<sup>25,30</sup> should indeed be corrected to **68a**, **68b**, and **68d**, respectively. The imide **71** is also unequivocally formulated as **68c**.<sup>18</sup>

Only one member of this series of prebullvalene derivatives, the lactone which is either **67e** or **68e**, exhibits an ambiguous 100-MHz nmr spectrum in  $\text{CDCl}_3$ . This did not come as a complete surprise as Babad had observed its 60-MHz spectrum at temperatures ranging from  $-42$  to  $120^\circ$ . After irradiation of propellanes of type **65** the photointermediates **66** were often observed at low temperature (e.g.,  $-55^\circ$ ) when **65** had been fully

converted and thermal isomerization had not yet fully proceeded to **68**. Once the compounds of the **68** series had been obtained, **66** or **67** could no longer be observed in their respective nmr spectra. Only the lactone was an exception to this rule. It appears from its better resolved 100-MHz spectrum that at room temperature the solution contains roughly equal molar amounts of **67e**, **68e**, and a cyclopropane-containing intermediate which we tentatively dare to hope might be **77**. This is, of course, different from and is an

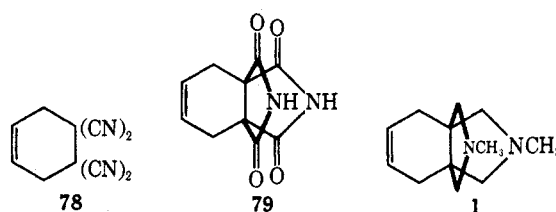


isomer of the unisolated **66e**.<sup>18</sup>

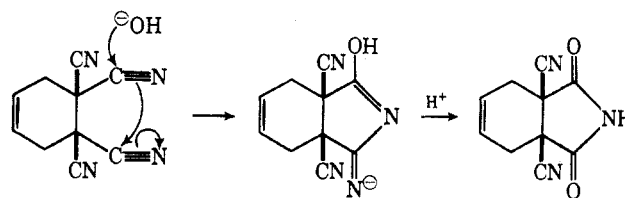
I hope that the point has been made that rather interesting discoveries in the field of fluxional isomerism have occurred as a result of the interest in the reactions of propellanes. Let us now turn to a discussion of syntheses of heterocyclic propellanes.

Here too the starting materials are obtained through Diels-Alder reactions. The dienophiles of choice were tetracyanoethylene and tetracarbethoxyethylene. Since in each of the adducts, e.g., with butadiene, there are two sets of *cis*-disposed substituents, their utility for the formation of two additional rings is obvious.

The *cis*-diimide **78** had already been obtained from the corresponding adduct of butadiene and tetracyanoethylene by treatment with concentrated sulfuric acid.<sup>1</sup> However, a higher yield of purer product could be obtained by treating **78** with concentrated sodium hy-



dride solution or with sodium methoxide, as shown for just one set of *cis*-cyano groups.

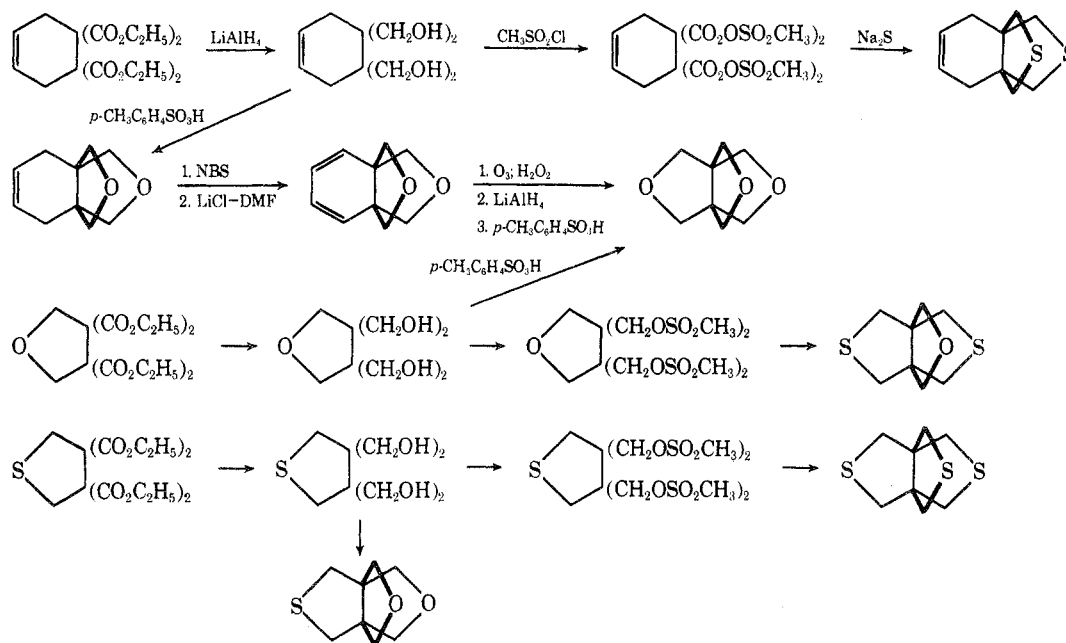


The same attack occurs on the second set of cyano groups, and after acidification the *cis*-diimide **79** is obtained. Methylation followed by lithium aluminum hydride reduction affords the diamine **1**.

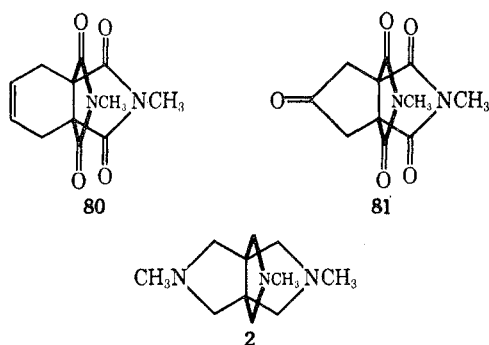
Ozonization of **80** followed by treatment with acetic

(30) A few comments must be made about one of the recent contributions<sup>28</sup> to this field. In this paper **67d**<sup>25</sup> is corrected to **68d** without, however, explicitly drawing attention to the incorrectness of the structure in the previous paper. Confusion is bound to arise since **67d** is nevertheless reported<sup>28</sup> as arising from **65d** under different conditions from those (incorrectly) reported previously.<sup>28</sup> Although the first-order rate equation is given<sup>28</sup> for the thermal isomerization of the relatively unstable **67d** to the stable **68d**, the absence of physical data in this paper makes it difficult to afford it the full appreciation that it deserves.

Scheme I



anhydride gave in a Dieckmann-like reaction the ketone diimide **81**, which in a straightforward reaction



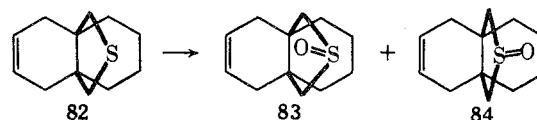
sequence gave the highly symmetrical triamine **2**.<sup>3</sup>

Propellane imides may, of course, be obtained by heating the corresponding anhydrides with ammonium hydroxide.

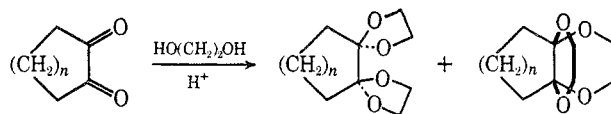
When tetracarbethoxyethylene is condensed with butadiene, the resulting tetraester may be used to prepare oxa- and thiapropellanes. Mixed oxathia compounds can also be prepared, as shown in Scheme I.<sup>31</sup>

Other propellanes containing oxygen or sulfur rings have also been prepared.<sup>3</sup> The first oxapropellane, already discussed above, was first prepared by Prelog,<sup>8</sup> and the first thiapropellane by Buchta and Billenstein.<sup>32</sup>

Sulfones and sulfoxides may be prepared from thiapropellanes in the usual way.<sup>3</sup> The sulfoxide prepared from **82**, for example, appeared from its chromatographic behavior to be a possible mixture, **83** and **84**. We intend to study this and similar reactions in more detail as well as the stereochemistry of the products.



Dr. Ben-Zion Fuchs of Tel Aviv University has discovered that cyclic  $\alpha$ -diketones upon ketalization with ethylene glycol afford mixtures of the diketal and the corresponding tetraoxapropellanes.



In the case where  $n = 2$ , the corresponding tetraoxapropellane is formed almost exclusively. Dr. Fuchs is also studying the corresponding tetrathia- and tetraazapropellanes which may be formed from  $\alpha$ -diketones with ethanedithiol and ethylenediamine, respectively.<sup>33</sup>

*It is a pleasure to express my gratitude to all of my coworkers and collaborators for the fun and stimulation arising from our common research adventure. Chaim Amit, Dr. Esther Babad, Mrs. Judith Itzhaki, and Samuel Welner have dealt with various stages of the work on azapropellanes. Nitzza Reshef worked on oxapropellanes and John B. Petersen and Dr. J. Pucknat on various aspects of the work on thiapropellanes. Dr. Janina Altman carried out most of the work on alicyclic propellanes and generally contributed a great deal to all aspects of propellane chemistry. In specific aspects of the work we have had the pleasure of collaborating with Hagai Gilboa and Professor Aaron Loewenstein, with Dan Becker and Professor H. J. E. Loewenthal, and with Professor Mordecai B. Rubin. A minor portion of this work has been supported by the Israel National Council for Research and Development.*

(31) J. B. Petersen and D. Ginsburg, *Israel J. Chem.*, in press.

(32) E. Buchta and S. Billenstein, *Liebigs Ann.*, **702**, 38 (1967).

(33) Private communication from Dr. B. Fuchs.