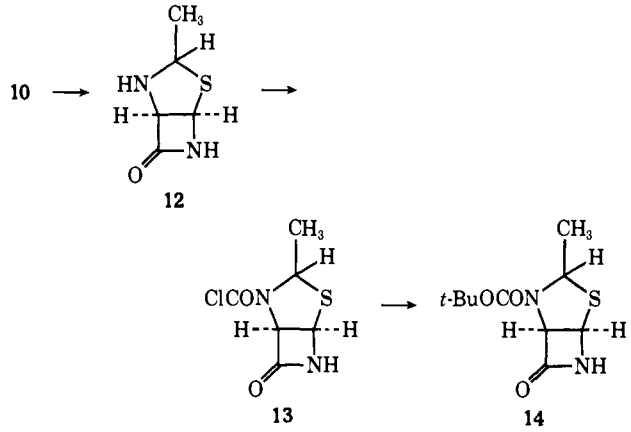
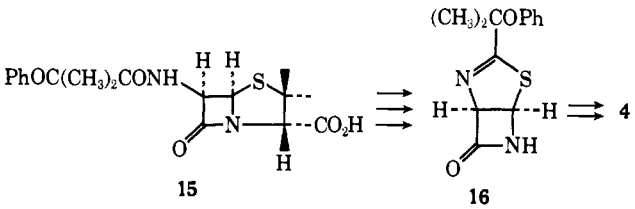
4.99 (1 H, q, J = 6 Hz), 5.33 (1 H, d, J = 4 Hz), 5.73 (1 H, q, J = 4 Hz, 2 Hz), and 7.10 (1 H, broad, exchangeable)] analogous to that previously used in the synthesis of cephalosporin C.



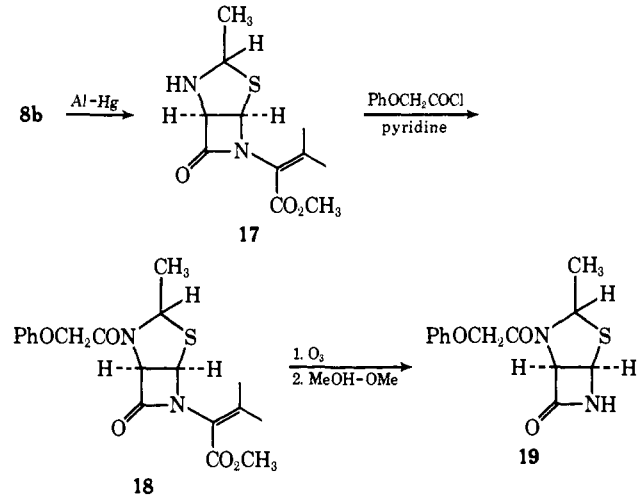
Repetition of this reaction sequence on α-methyl-α-phenoxyethylpenicillin (**15**) yielded the thiazoline **16** which on reduction and acylation yielded the thiazolidine **4** identical with that prepared by Heusler and Woodward.[2]

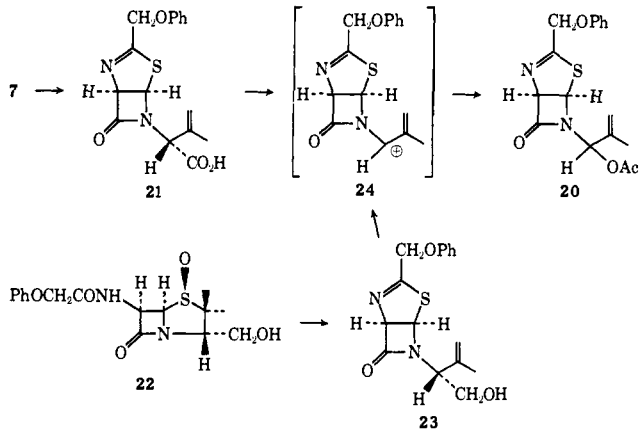


Removal of the five-carbon unit from thiazolidine–azetidinone derivatives could also be achieved. Thus aluminum–amalgam reduction of the thiazoline **8b** gave an excellent yield of the thiazolidine **17** [nmr δ ($CDCl_3$) 1.50 (3 H, d, J = 6 Hz), 1.92 (3 H, s), 2.19 (3 H, s), 3.77 (3 H, s), 4.40 (2 H, m, 1 exchangeable), 5.20 (1 H, broad, d, J = 4 Hz), and 5.73 (1 H, d, J = 4 Hz)], which could then be acylated with phenoxyacetyl chloride to yield **18** [nmr δ ($CDCl_3$) 1.65 (3 H, d, J = 6 Hz), 1.95 (3 H, s), 2.23 (3 H, s), 3.70 (3 H, s), 4.92 (2 H, s), 5.24 (1 H, q, J = 6 Hz), 5.70 (2 H, s), and 6.7–7.4 (5 H, m)].

Ozonolysis and methanolysis of **18** yielded the thiazolidine–azetidinone **19**: mp 135–137°; nmr δ ($CDCl_3$) 1.88 (3 H, d, J = 6 Hz), 4.94 (2 H, s), 4.95 (1 H, d, J = 4 Hz), 5.04 (1 H, d, J = 6 Hz), 5.93 (1 H, broad, d, J = 4 Hz), 6.9–7.4 (5 H, m), and 9.08 (1 H, broad, exchangeable); ir (mull) 1792 (β-lactam C=O) and 1700 cm^{-1} (amide C=O).

An alternate approach involving the acetoxy derivative **20** was also successful. Compound **20** [nmr δ ($CDCl_3$) 1.67 (3 H, broad, s), 2.06 (3 H, s), 4.88 (2 H, s), 5.03 (1 H, broad, s), 5.20 (1 H, broad, s), 5.54 (1 H, d, J = 4 Hz), 5.93 (1 H, d, J = 4 Hz), 6.36 (1 H, s), and 6.7–7.4 (5 H, m)] was synthesized in high overall yield by treatment of **7** with zinc in 90% acetic acid to obtain the acid **21**, followed by reaction of **21** with lead tetraacetate in benzene. An alternate route to **20** was developed from the penicillanyl alcohol sulfoxide **22** which was rearranged to the thiazoline **23** with trimethyl phosphite in benzene. Subsequent treatment of **23** with lead tetraacetate in benzene gave a quantitative yield of **20**. Formation of **20** in high yield from either **21** or **23** is not unexpected because of the stabilization of the incipient carbonium ion **24** by both the β-lactam nitrogen atom and the allylic double bond.





Hydrolysis of the acetoxy function of **20** using pH 7.6 phosphate buffer led to isolation of the thiazoline–azetidinone.[5] Unfortunately, the yield in the hydrolysis step was poor; however, we think that further work could improve this substantially.

Acknowledgment. We wish to acknowledge Mr. D. Fukuda of the Lilly Research Laboratories for experimental assistance.

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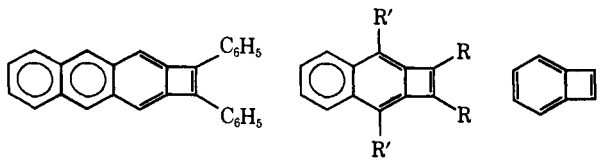
The Synthesis of 6,7-Diphenyl-3-thiabicyclo[3.2.0]heptatriene, a Thienocyclobutadiene

Sir:

Whereas 1,2-diphenylanthra[*b*]cyclobutadiene (**1**)[1] and the substituted naphtho[*b*]cyclobutadienes (**2a,b**),[2] have been isolated as relatively stable compounds, benzocyclobutadiene (**3**) and its derivatives have only

(1) M. P. Cava, *Chem. Soc., Spec. Publ.*, 21, 163 (1967).
(2) M. P. Cava, B. Y. Hwang, and J. P. van Meter, *J. Amer. Chem. Soc.*, 85, 4032 (1963); M. P. Cava and B. Y. Hwang, *Tetrahedron Lett.*, 2297 (1965).

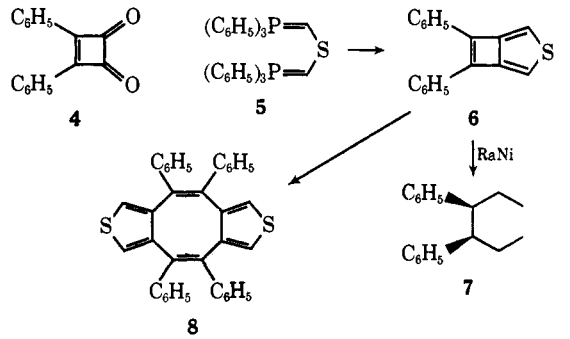
been implicated as transitory reaction intermediates.[3] The difference in stability between these systems is presumably a reflection of the fact that the compounds of type **1** and **2** can accommodate the dimethylenecyclo-



1 **2a**, R = C_6H_5; R′ = H; **b**, R = Br; R′ = C_6H_5 **3**

butene structure as the principal canonical form with less disruption of the aromatic system than can benzocyclobutadiene (**3**). Our recent preparation of 2-thianorbiphenylene,[4] in which the properties of the thiophene ring demonstrate the dominance of the dimethylenecyclobutene structure, suggested that the corresponding thienocyclobutadienes might be isolable compounds. We now report the preparation of 6,7-diphenyl-3-thiabicyclo[3.2.0]heptatriene (**6**), the first known thienocyclobutadiene.

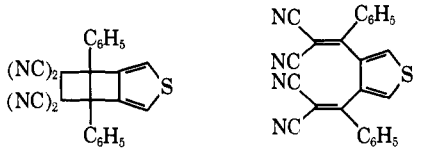
A solution of 3,4-diphenylcyclobutadienequinone (**4**)[5,6] in THF was added to an equimolar ethereal solution of the ylide **5**[8,9] at −78° under N_2, and the mixture was allowed to warm to room temperature. Chromatography on alumina gave bright red crystals of **6** (3.5%), mp 134–136° dec.[10] The structural assignment is based on the spectral and chemical properties. The mass spectrum parent ion was at *m/e* 260.068 (calcd 260.066); the nmr spectrum (220 MHz, CCl_4) had signals at τ 2.37 (dd, 4 H, J = 9, 1.5 Hz, *o*-C_6H_5), 2.70 (m, 6 H, *m,p*-C_6H_5). and 3.84 (s, 2 H, H_2, H_4). The electronic spectrum [λ_{max}^{EtOH} 266.5 (ϵ 39,800), 273.5 (38,600), 447 nm (5450)] was quite similar, though less complex, to that of **2a**.[3] Treatment of **6** with Raney nickel in boiling ethanol gave *meso*-3,4-diphenylhexane (**7**), identical with an authentic sample.[11] Reaction of **6** with 2,4,7-trinitrofluorenone gave a black-violet crystalline 1:1 complex, mp 159–160° dec.[10]



4 **5** **6** **7** **8**

When **6** is heated under N_2 at 160° for 1 hr, it melts, decolorizes, and then resolidifies. The resulting compound (87%, mp 258–260°) was assigned the dimeric structure **8** on the basis of its mass spectrum (*m/e* 520) and other spectral properties.[10] The nmr spectrum (100 MHz, CCl_4) showed signals at τ 3.00 (b s, 20 H) and 3.08 (s, 4 H) and the electronic spectrum exhibited a broad band [223 sh (ϵ 44,000), 273 sh nm (21,000)], typical of annelated cyclooctatetraenes.[3,12] The same dimer was also obtained when **6** was photoirradiated in Et_2O at −65° with a medium-pressure lamp. However, if **6** was allowed to stand at room temperature in chlorinated solvents, the resulting colorless oil was shown to be a trimer (*m/e* 780.198). When a solution of **6** in CH_2Cl_2 was frozen at −190°, examination in an esr spectrometer showed signals attributable to a triplet species.[13]

Treatment of **6** with tetracyanoethylene in benzene at room temperature for 40 hr gave a 1:1 adduct (72%), mp 259–260°.[10] The nmr spectrum (100 MHz, CD_3CN plus trace of $CDCl_3$) showed signals at τ 1.85 (s, 2 H), 2.54 (m, 6 H), and 2.96 (dd, 4 H, J = 9, 2 Hz); the electronic spectrum had absorption maxima (EtOH) at 236 (ϵ 18,000), 293 (22,600), and 322 nm (20,500); the ir spectrum had bands at 2226 and 2231 cm^{-1} (C≡N). The spectral properties, and the presently accumulated chemical evidence, do not distinguish decisively between structures **9** and **10**.



9 **10**

The high-field position of the H_2, H_4 signals in the nmr spectrum of **6** indicates the presence in this molecule of a paramagnetic ring current, arising from the four-membered ring.[14] The electronic spectrum suggests that the phenyl rings in **6** lie in the molecular plane and that extensive conjugation occurs. A similar suggestion was made to explain the electronic spectrum of **2a**.[1,3]

The compound **6** may be considered to be derived from the 8π-electron system thiepin (**11**) by formation of a 3,6-transannular bond. The anion **12**, conceptually derived in the same way from the cycloheptatrienyl anion, has been prepared,[15] but only in solution at low temperatures. Thus compound **6** is more stable than the anion **12**,[16] and this parallels the difference in

(3) For a comprehensive review, see M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

(4) P. J. Garratt and K. P. C. Vollhardt, *Chem. Commun.*, 109 (1970).

(5) A. T. Blomquist and E. A. LaLancette, *J. Amer. Chem. Soc.*, **83**, 1387 (1961).

(6) Compound **4** was prepared in 85% yield by treatment of 3,4-dichlorocyclobutadienequinone in benzene with $AlCl_3$ at 55° for 3 hr. These conditions are modified from those of De Selms, *et al.*,[7] for the preparation of 3-phenyl-4-chlorocyclobutadienequinone.

(7) R. C. De Selms, C. J. Fox, and R. C. Riordan, *Tetrahedron Lett.*, 781 (1970).

(8) K. Dimroth, H. Follmann, and G. Pohl, *Chem. Ber.*, **99**, 642 (1966).

(9) The ylide was prepared by treatment of thiodimethylene bis(triphenylphosphonium)dichloride with *n*-butyllithium in Et_2O at room temperature, and the solution was then cooled to −78°.

(10) Satisfactory analytical results were obtained for all new crystalline compounds.

(11) W. C. J. Ross, *J. Chem. Soc.*, 536 (1945).

(12) See J. A. Elix, M. V. Sargent, and F. Sondheimer, *J. Amer. Chem. Soc.*, **92**, 973 (1970).

(13) See R. Breslow, H. W. Chang, R. Hill, and E. Wasserman, *ibid.*, **89**, 1112 (1967), and references therein.

(14) Attempts to oxidize **6** into the corresponding sulfone, using the conditions previously found to convert 2-thianorbiphenylene into its sulfone,[4] were unsuccessful, and it was therefore not possible to compare the proton resonance positions with those in the sulfone. Attempts to reduce the cyclobutene double bond have so far also been unsuccessful.

(15) R. Breslow and W. Washburn, *J. Amer. Chem. Soc.*, **92**, 427 (1970).

(16) Part of the increased stability of **6** probably arises from the presence of the phenyl substituents, and comparison of the parent system with **12** would be more satisfying.

11 12

stability between 2-thianorbiphenylene[4] and the norbiphenylene anion.[17] Further studies on **6** and related systems are currently in progress.

Acknowledgments. We thank Professor H. Hellmann, Chemische Werke Hüls, for generous gifts of squaric acid, and Dr. B. P. Roberts for the esr spectrum.

(17) M. P. Cava, K. Narasimhan, W. Zeiger, L. J. Radonovich, and M. D. Glick, *J. Amer. Chem. Soc.*, **91**, 2378 (1969).

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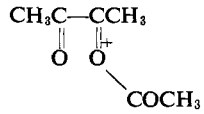
Steric Inhibition of Gaseous Ionic Acetylation

Sir:

Previously we have presented evidence for steric inhibition of certain unimolecular processes of gaseous ions.[1,2] We report now the first evidence for complete removal of reactivity in gaseous ion–molecule reactions attributable to steric inhibition.

We have already reported ion cyclotron resonance studies indicating the broad ability of the *m/e* 129 ion (presumably **1**), derived by collision of the 2,3-

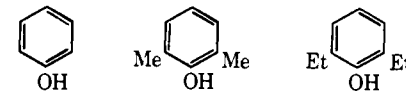


1

butanedione molecular ion with its neutral precursor, to transfer acetyl ion to a wide variety of organic compounds containing oxygen and nitrogen.[3] Lately we have observed differences in reactivity for the epimers of bicyclo[2.2.1]heptanol-2 in accepting the acetyl ion from **1**, the exo isomer producing more acetylated product than the endo isomer.[4]

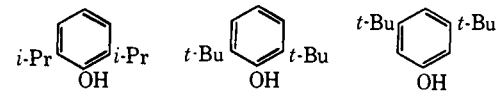
In our pursuit of substituent-effect studies on electrophilic aromatic substitution[5] reactions in the gas phase, we were distracted by consideration of multiple reaction sites, namely, the ring[5] and the substituent,[3] in compounds with electron pair donor substituents such as phenol and aniline. We find now that under conditions used for our acetylation studies (2×10^{-5} Torr $CH_3COCOCH_3$, $2\text{–}4 \times 10^{-6}$ Torr substrate, 30-eV ionizing voltage) reactions of neutral phenol with various acetylating ions from 2,3-butanedione can be reduced to below our limit of detection by increasing the size of ortho substituents. The ortho substituents chosen were alkyl groups, since the ability of alkyl groups to stabilize ions formed by attachment of protons[6] and larger groups[7] increases with increasing size of the group, as in the series methyl < ethyl < isopropyl < *tert*-butyl, so that on the basis of previously observed trends the larger substituents might be anticipated to stabilize the acetylated product.

In fact we observed that compounds **2**, **3**, and **4** are



2 **3** **4**

acetylated by the *m/e* 129 and 43 ions. The product peak intensity decreases as the ortho group becomes larger in this series, but quantitative assignments are not possible at present since there are several competing reactions which *increase* the amount of acetylated product with respect to the amount of phenol molecular ion. The substituents introduced in compounds **5** and **6** *completely* prevent the formation of the acetylated



5 **6** **7**

product, within the limits of detection of our instrumentation.[7a] To confirm the nature of the effect as a steric one, the acetylation of compound **7** was attempted and found successful, as would be expected since the hydroxyl group is accessible to the acetylating agent, and since in the absence of steric effects larger groups stabilize such ions.[6,7] The results incidentally indicate that the hydroxyl group rather than the ring is the site of addition of acetyl, for if the opposite were true **6** might acetylate at least as easily as **7**.

It has been our contention[3,4,7] that ion–molecule reactions with suitably large "reagent ions" will be found to be sensitive indicators of steric environment of reaction centers in organic molecules and therefore should be explored for their analytical utility. The present example is the first example of *complete* inhibition of an ion–molecule reaction by steric effects in an otherwise general reaction system. We are continuing further exploration of alteration of reactivity by steric environment in other aromatic and aliphatic systems.

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(1) M. M. Bursey, *J. Amer. Chem. Soc.*, **91**, 1861 (1969).
(2) M. M. Bursey and M. K. Hoffman, *ibid.*, **91**, 5023 (1969).
(3) M. M. Bursey, T. A. Elwood, M. K. Hoffman, T. A. Lehman, and J. M. Tesarek, *Anal. Chem.*, **42**, 1370 (1970).
(4) M. M. Bursey and M. K. Hoffman, *Can. J. Chem.*, **49**, 3395 (1971).
(5) S. A. Benezra, M. K. Hoffman, and M. M. Bursey, *J. Amer. Chem. Soc.*, **92**, 7501 (1970).
(6) M. S. B. Munson, *ibid.*, **87**, 2332 (1965).
(7) W. B. Nixon and M. M. Bursey, *Tetrahedron Lett.*, 4389 (1970).

(7a) NOTE ADDED IN PROOF. Quantitative assessment of icr rate data is difficult but an upper limit on the order of 10^{-7} cm^3 molecule^{-1} sec^{-1} for the rate constants of the unobserved reactions seems reasonable. We base this on our inability to detect the product ion with more than a 100-fold excess of the precursor and trapping voltages such that the product ion would be held *ca.* 1 msec.
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