Bicyclic Azoalkanes via Urazoles Derived from Cycloaddition of *N*-Phenyl-1,2,4-triazoline-3,5-dione with Strained Bicycloalkenes

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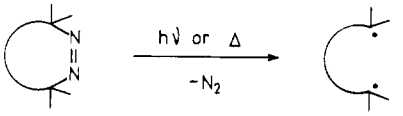
Abstract: Cycloaddition of *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD) to strained bicycloalkenes **1** leads to urazoles **2** via skeletal rearrangement of dipolar intermediates. This novel reaction appears to be general, including benzoannelated, spiroannelated, alkylidene-functionalized, and heteroatom-substituted substrates. Bicyclo[2.2.2]octene is not sufficiently strained to undergo reaction with PTAD. Ene reaction and homo-Diels–Alder addition will suppress this useful dipolar PTAD cycloaddition. Oxidative hydrolysis of the urazoles **2** provides a convenient entry into the hitherto unknown polycyclic azoalkanes **3** possessing C-type skeletons.

Introduction

Azoalkanes have occupied a central position during the last two decades in the mechanistic elucidation of diradicals. Through the thermal and photochemical extrusion of nitrogen they serve as convenient and efficient precursors to such elusive reaction intermediates (eq 1). This is amply witnessed in several excellent



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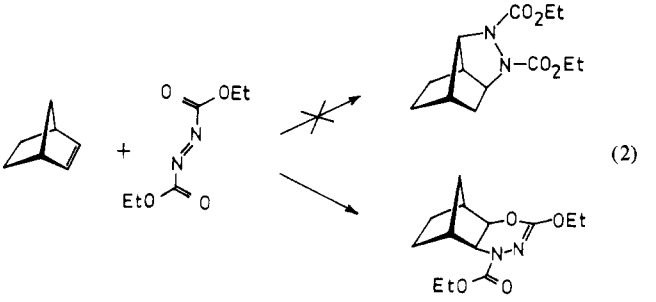
reviews on this subject.[2] Recently, some timely mechanistic studies on generating diradicals from polycyclic azoalkanes have included the substrates shown below.[3] Besides providing a wealth

of significant data on the energetics and spin-state dependence of interconverting diradicals that are postulated in photorearrangements, photocyclizations, and photofragmentations,[4] these substrates yield unusual and strained products after nitrogen extrusion. These are hard to come by via more traditional synthetic methodology.

A general preparation of polycyclic azoalkanes entails oxidative hydrolysis of diacylhydrazines or urazoles, which are readily available through Diels–Alder cycloaddition of azidoformates or 1,2,4-triazoline-3,5-diones, with the appropriate cyclodiene.[5] However, this synthetic approach can afford the polycyclic azoalkanes with generalized skeletons A and B but not C. In these structures we show the minimum structural features.

A B C

In this context, it is of interest to mention that cycloaddition of ethyl azidoformate to norbornene (eq 2) was shown to give the



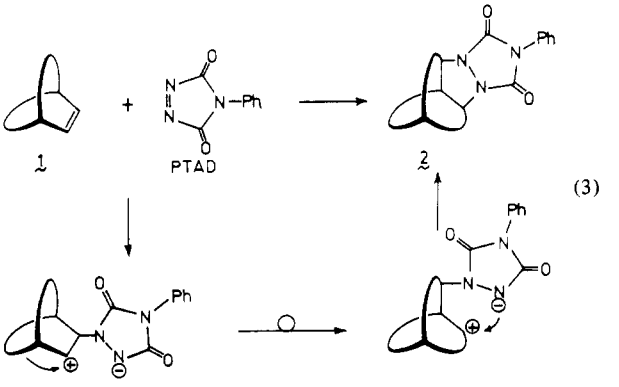
(2)

Diels–Alder product by engaging the carbonyl moiety as part of the diene component, rather than leading to the expected C-type skeleton.[6] However, by enclosing the azo linkage in a ring structure as in *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD), the undesired action of the azo dienophile as a [2 + 4]-diene substrate is discouraged in view of its locked-in cisoid geometry. Furthermore, since the propensity of PTAD to [2 + 2]-cycloadd to highly strained polycyclic alkenes such as benzvalene[7] and homobenzvalene[8] has been demonstrated and more importantly shown to afford urazoles, presumably via skeletal rearrangement of dipolar intermediates, we hoped that such cycloaddition of PTAD could provide a useful pathway to unknown C-type azoalkanes.

Indeed, the validity of this synthetic concept was initially demonstrated for the substrates **1a,c,d,i**, all affording the respective

1a 1c 1d 1i

urazoles **2** via the generalized dipolar rearrangement mechanism proposed in eq 3.[9] During the course of this investigation we



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(3)

(1) NIH Career Development Awardee (1975–1980).
(2) (a) Cherry, W.; Chow, M. F.; Ramamurthy, V.; Turro, N. J. *Mol. Photochem.* **1979**, *9*, 11. (b) Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446. (c) Meier, H.; Zeller, K.-P. *Angew. Chem.* **1977**, *89*, 876. (d) Dürr, H.; Ruge, B. *Fortschr. Chem. Forsch.* **1978**, *66*, 53. (e) Engel, P. S.; Steel, C. *Acc. Chem. Res.* **1973**, *6*, 275.
(3) (a) Zimmerman, H. E.; Boettcher, R. J.; Buehler, N. E.; Keck, G. F.; Steinmetz, M. G. *J. Am. Chem. Soc.* **1976**, *98*, 7680. (b) Turro, N. J.; Cherry, W. R.; Mirbach, M. F.; Mirbach, M. J. *Ibid.* **1977**, *99*, 7388. (c) Trost, B. M.; Scudder, P. H.; Cory, R. M.; Turro, N. J.; Ramamurthy, V.; Katz, T. J. *J. Org. Chem.* **1979**, *44*, 1264. (d) Turro, N. J.; Liu, K.-C.; Cherry, W.; Liu, J. M.; Jacobson, B. *Tetrahedron Lett.* **1978**, 555.
(4) Turro, N. J. "Modern Molecular Photochemistry"; Benjamin-Cummings Publishing Co.: Palo Alto, CA, 1978.
(5) Müller, E. *Methoden Org. Chem.* (*Houben-Weyl*) **1967**, *10*, 757.
(6) (a) Cristol, S. J.; Allred, E. L.; Wetzel, *J. Org. Chem.* **1962**, *27*, 4058. (b) Tufariello, J. J.; Mich, T. F.; Miller, R. S. *Tetrahedron Lett.* **1966**, 2293.
(7) Katz, T. J.; Acton, N. *J. Am. Chem. Soc.* **1973**, *95*, 2738.
(8) Browne, A. R.; Paquette, L. A. *J. Org. Chem.* **1978**, *43*, 4522.

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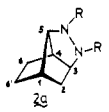
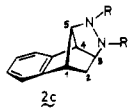
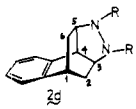
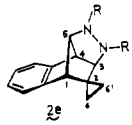
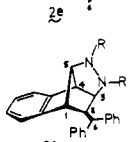
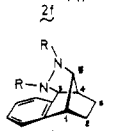
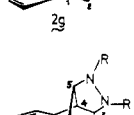
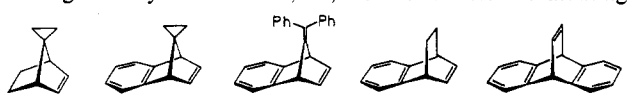
Table I. Reaction Conditions, Yields, and Physical and Spectroscopic Data of the Urazoles

urazole[a]	conditions: solvent	T, °C	t, h	amt of PTAD, mol	% yield	mp,[b] °C	^{1}H NMR ($CDCl_3$): type	H's	δ[c]	pattern	IR ($CHCl_3$) ν, cm^{-1}
 2a	CH_2Cl_2	30	14	1.3	47	144	$H_{2,6,6'}$ $H_{1,4}$ $H_{3,5}$	6 2 2	1.2–2.0 2.60 4.25	m m m	2960, 2900, 1775, 1725, 1600, 1505, 1410, 1350, 1300, 1130, 910
 2b	$CDCl_3$	30	48	2	50	184	$H_{6,6'}$ $H_{7,7'}$ H_1 H_4 H_3 H_5	4 4 1 1 1 1	0.5–1.3 1.65 2.07 2.80 3.68 4.25	m m m m m m	2975, 2880, 1765, 1710, 1600, 1500, 1407, 1250, 1130, 1025
 2c	CH_2Cl_2	30	14	1.2	76	182–183	$H_{2(endo)}$ $H_{2(exo)}$ $H_{1,4}$ $H_{3,5}$	1 1 2 2	1.53 2.28 3.75 4.61	B part AB[d] A part AB[d] m m	3020, 1785, 1715, 1600, 1500, 1412, 1320, 1280, 1220
 2d	$CHCl_3$	60	6	1.2	31	202–203	$H_{2,6}$ H_1 H_4 $H_{3,5}$	4 1 1 2	1.98 3.07 3.48 4.35	m m m m	3080, 3060, 3040, 2960, 2900, 2875, 1770, 1705, 1600, 1500, 1400, 1330, 1260, 1130
 2e	CH_2Cl_2	30	36	4	70	158–159	$H_{6,6'}$ H_1 $H_{4,3}$ H_5	4 1 2 1	0.1–1.5 2.94 3.80 4.57	m m m m	3090, 3010, 1775, 1720, 1610, 1510, 1400, 1310, 1280, 1255, 1135
 2f	CH_2Cl_2	30	18	2	31	183–184	H_1 H_4 H_3 H_5	1 1 1 1	3.78 4.18 4.70 5.07	m m m m	3080, 3060, 3025, 2980, 1775, 1715, 1600, 1500, 1400
 2g	CH_3CN	80	240	10	17	180	$H_{2,6}$ H_1 H_4 H_5 H_3	4 1 1 1 1	1.50–2.10 3.45 3.70 4.45 4.90	m m m dd[e] d[f]	3000, 1775, 1720, 1610, 1510, 1415, 1270
 2h	CD_3CN	80	16	10	63[g]	243–245 dec	$H_{1,4}$ $H_{3,5}$	2 2	4.39 4.8–5.1	m m	3060, 2980, 1775, 1715, 1660, 1470, 1415, 1250, 1140, 1100

[a] R + R = -C(O)N(Ph)C(O)-. [b] Recrystallized from ethanol or methanol; satisfactory elemental composition by combustion analysis or high-resolution mass spectral analysis. [c] In parts per million from Me_4Si. [d] J_{vic} = 12.67 Hz; $J_{1,2(exo)}$ = 5.50 Hz; $J_{2(endo),3}$ = 4.67 Hz; $J_{1,2(endo)}$ = 1.33 Hz. [e] J = 4.3 and 6.7 Hz. [f] $J_{4,6}$ = 5 Hz. [g] Yield based on substrate consumed.

became aware of the report that 2,3-benzo-7-oxabicyclo[2.2.1]-hepta-2,5-diene (**1i**) had already been submitted to such scrutiny and shown to give the corresponding urazole **2i**.[10] Subsequently we explored the generality of this unusual cycloaddition by examining the bicycloalkenes **1b**,**e**–**h**,[11] in the interest of evaluating



1b 1e 1f 1g 1h

such factors as ring strain, steric demand, benzoannealation, and functionalities. We report in this paper the full details of this study, together with the conversion of the urazoles **2** into their corresponding azoalkanes **3**. The latter are currently being intensively investigated by us for mechanistic purposes.

Results and Discussion

Urazoles 2. The experimental data for the urazoles **2a**–**h** are summarized in Tables I and II. Besides the correct elemental composition, determined either by combustion analysis or high-resolution mass spectrometry, the ^{1}H NMR, ^{13}C NMR, and IR spectral data were definitive in the structure assignment.

The resonances of the bridgehead protons were particularly characteristic (Table I). For example, the bridgehead protons H_1 and H_4 (not adjacent to the urazole nitrogens) usually fall in the δ 2.07–2.80 range for the nonbenzo system and in the δ 2.94–4.39 range for the benzo system. The bridgehead protons H_3 and H_5 (adjacent the urazole nitrogens) usually fall in the δ 3.48–5.12 range for both systems. Frequently decoupling experiments were helpful in securing the proposed structures.

Also the resonances (Table II) of the bridgehead carbons exhibited characteristic doublets in the δ 34.55–67.23 range for C_1 and C_4 (not adjacent to the urazole nitrogens) and the δ 53.79–76.84 range for C_3 and C_5 (adjacent to the urazole nitrogens). For these urazoles the C_6H_4 aromatic protons showed up as complex multiplets in the expected δ 6.5–7.5 range and the *N*-phenyl protons as a broad singlet at δ 6.9–7.4. The aromatic and urazole carbonyl carbons are located in the expected δ 120.45–156.59 and δ 144.60–156.70 ranges, respectively. In view of the difficulty and ambiguity in assigning these proton and carbon resonances, we have dispensed with listing them in Tables

(9) Adam, W.; De Lucchi, O.; Erden, I. *Angew Chem.* **1979**, *91*, 512.
(10) Sasaki, T.; Kanematsu, K.; Henide, M. *Tetrahedron Lett.* **1971**, 4855.
(11) Adam, W.; De Lucchi, O. *Tetrahedron Lett.* **1979**, 4367.

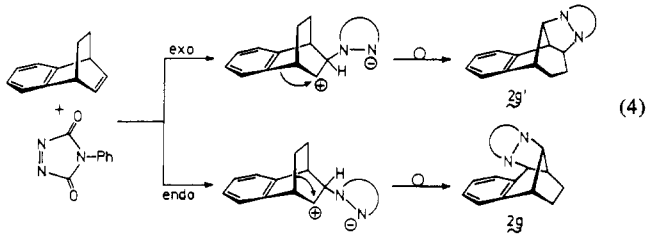
Table II. ^{13}C NMR Shifts[a] of the Urazoles

carbon[b]	2a[c]	2c[c]	2d[c,e]	2e[e]	2f[c,e]	2h[d]
1	39.08	46.12	34.55	54.15	52.63	50.73
2	31.96	34.53	31.63	3.30	*f*	
3	62.11	58.64	55.71	66.84	62.76	62.79
4	46.97	53.43	46.33	56.15	54.19	53.79
5	66.89	76.84	55.71	76.17	*f*	67.23
6,6′	18.50–28.85		31.63	8.97–10.16	*f*	

[a] δ in parts per million relative to $CDCl_3$. [b] Index refers to the numbering shown for each structure in Table I. [c] Kindly recorded by Professor A. de Meijere (University of Hamburg, West Germany). [d] Kindly recorded and interpreted by Dr. D. Scheutzow (University of Würzburg, West Germany); financial support by the DFG is gratefully acknowledged. [e] Kindly recorded by Professor N. A. Porter (Duke University, Durham, NC). [f] Hidden by solvent resonances ($CDCl_3$).

I and II. The IR spectra showed the characteristic carbonyl doublets of the urazole moiety at ca. 1775 and 1720 cm^{-1}, besides the expected aromatic and aliphatic C–H stretching frequencies.

A potential structural ambiguity was encountered with the PTAD adduct of 2,3-benzobicyclo[2.2.2]octa-2,5-diene (**1g**),[12] i.e., urazoles **2g** and **2g'** (eq 4). Via exo attack the resulting dipolar



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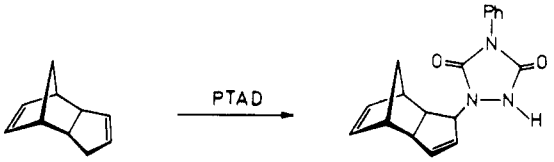
intermediate should suffer aryl (benzo bridge) migration, affording after cyclization the urazole structure **2g'**. On the other hand, via endo attack the resulting dipolar intermediate should undergo alkyl (dimethylene bridge) migration, giving after cyclization the urazole structure **2g**. Through double-resonance experiments we confirmed that the bridgehead protons H_3 and H_5 are, respectively, a doublet and a doublet of doublets, suggesting that **2g** (endo attack) is the more consistent structure for this urazole. An X-ray structure determination is under way for rigorous assignment. Besides, endo attack is more likely than exo attack since the flat benzo ring provides easier access to the double bond than the dimethylene chain.

Concerning the reactivity of the bicyclic olefins **1** toward PTAD cycloaddition, we conclude that it depends greatly on the structural features of the substrate. Although we only have qualitative data, e.g., percent yields and changes in reaction conditions such as time, temperature, and polarity of solvent (Table I), it is clear that the more strained and the more exposed the double bond, the more effective the initial cycloaddition step to afford the essential dipolar intermediate. For example, benzonorbornadiene (**1c**) is among the most effective, while with 2,3-benzobicyclo[2.2.2]octa-2,5-diene (**1g**) the reaction is sluggish, requiring elevated temperature, polar solvent, long reaction times, and a large excess of PTAD. The large excess of PTAD is necessary in this case due to its extensive decomposition under these reaction conditions. In this respect it is important to mention the bicyclo[2.2.2]oct-2-ene failed to react with PTAD. Still more drastic conditions than those used for **1g** led only to PTAD destruction.

On the other hand, introduction of a spiro moiety into the benzonorbornadiene as in **1e** diminishes the olefin reactivity. Although the ring strain is enhanced through such spiroannealation, presumably steric factors are important for an unencumbered exo approach of PTAD. Furthermore, benzoannelation tends to enhance the reactivity of the olefin. Apparently stabilization of the cationic center in the initial dipolar intermediate by the benzo group provides additional incentive for [2 + 2] cycloaddition. Similarly, stabilization by the benzhydryl functions in **1f** promotes enhanced reactivity in these substrates.

It should be emphasized, however, that ene reaction and homo-Diels–Alder reaction can dominate the course of action by PTAD. For example, the cyclopentadiene dimer gave quantitatively the ene product (eq 5).[13] On the other hand, benzo-



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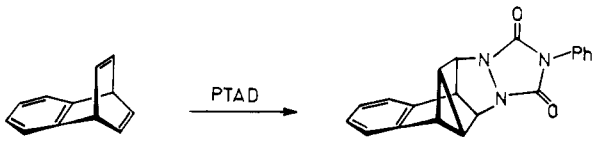
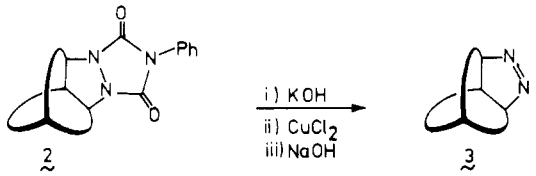
barrelene[14] gave quantitatively the homo-Diels–Alder adduct (eq 6).[9,3a] Therefore, when PTAD encounters substrate molecules



(6)

which have the opportunity to ene or homo react, it is quite likely that [2 + 2] cycloaddition with dipolar rearrangement to afford C-type skeletons will be suppressed.

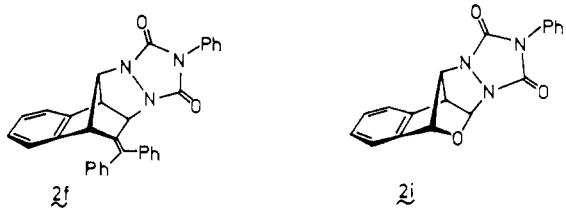
Azoalkanes 3. Base-catalyzed hydrolysis of the urazoles **2** and subsequent oxidation afforded the tricyclic azoalkanes **3** (eq 7).



(7)

The yields, physical constants, and spectral data are summarized in Table III. Correct elemental composition was secured by combustion analysis. The assignment of the bridgehead protons $H_{1,4}$ and $H_{3,5}$ (same numbering is shown for the urazole structures in Table I) is tentative because it was not possible to conduct decoupling experiments. An attempt to use chemical shift reagents,[15] specifically $Eu(fod)_3$, was also not helpful. The bridgehead proton resonances shifted irregularly upfield and downfield with increasing concentration of the $Eu(fod)_3$.

Much to our dismay, the urazoles **2f** and **2i** could not be



converted into their respective azoalkanes **3f** and **3i** with the existing hydrolytic methods.[5] The conditions are too drastic, leading to undefined products in which it appears that the nitrogen heterocyclic ring has been sacrificed. Much milder and specific

(12) The bicycloalkadiene **1g** was prepared according to Simmons. (Simmons, H. E. *J. Am. Chem. Soc.* **1961**, *83*, 1657). In view of the complex product mixture obtained in the preparation of **1g**, isolation was aided by treating the crude product mixture with PTAD until persistance of the red PTAD color. The undesired PTAD adducts were precipitated with pentane and removed by filtration. The residue was chromatographed on silica gel (pentane eluent) to afford **1g**: yield 12%, n^{25}_D 1.5663 (lit. n^{25}_D 1.5657).

(13) Unpublished results: mp 155 °C, colorless needles from EtOH; ^1H NMR ($CDCl_3$) δ (δ_{Me_4Si} = 0) 1.4 (2 H, m), 2.4–2.8 (2 H, m), 2.95 (1 H, m), 3.23 (1 H, m), 4.38 (1 H, m), 5.2 (1 H, m), 5.7 (1H, m), 7.17 (5 H, m); IR ($CDCl_3$) ν 3840–2600, 3380, 3165, 3075, 2995, 1770, 1710, 1605, 1505, 1435, 1340, 1250, and 1135 cm^{-1}.

(14) We are grateful to Professor J. W. Jefford (University of Geneva) for a gift sample of benzobarrelene.

(15) Wilson, S. R.; Turner, R. B. *J. Chem. Soc., Chem. Commun.* **1973**, 557.

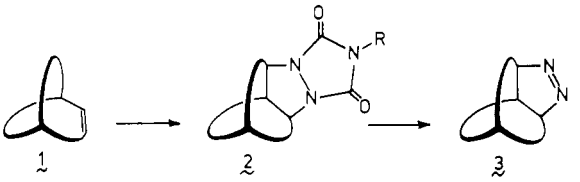
Table III. Yields, Physical Constants, and Spectral Data of Azoalkanes

azoalkane	% yield	mp, °C	^{1}H NMR (CCl_4) type[a]	H's	δ	pattern[b]	IR (CCl_4) ν, cm^{-1}
3a	32	147–149 (sublimed at ca. 60 °C (1.5 mmHg))	$H_{1,2,4,6,6'}$	8	0.45–2.10	m	3000, 2975, 2880, 1500, 1455, 1312,
			H_4	1	2.20	br s	1287, 1100, 910
			H_3	1	4.82	br s	
			H_5	1	5.00	br s	
3c	74	74–75 (hexane)	H_2	2	1.20	m	3100, 3070, 3040, 3020, 2985, 2960,
			H_1	1	2.78	nm	2895, 1495, 1470, 1383, 1267,
			H_4	1	3.21	nm	1220, 1190, 1165, 1135, 1020,
			H_3	1	4.63	nm	1000, 950
			H_5	1	5.26	nm	
			C_6H_4	4	6.88	m	
3d	45	124–125 (hexane)	$H_{2,6}$	4	1.40	m	3080, 3060, 3030, 2980, 2940, 2860,
			H_1	1	3.10	m	1480, 1450, 1320, 1230, 1180,
			H_4	1	3.30	m	1150, 1020, 920
			$H_{5,3}$	2	4.50	m	
			C_6H_4	4	7.20	m	
3e	72	85–86 (hexane)	$H_{6,6'}$	4	0–1.37	m	3080, 3010, 1495, 1470, 1450, 1430,
			H_1	1	2.30	br s	1260, 1210, 1175, 1150, 1140, 1022
			H_4	1	3.33	br s	940, 905
			H_3	1	4.00	br s	
			H_5	1	5.45	br s	
			C_6H_4	4	6.95	m	

[a] Subscript refers to the numbering shown for each structure in Table I; the assignments of the bridgehead protons are uncertain. Europium shift reagents were not helpful. [b] m = multiplet; nm = narrow multiplet; br s = broad singlet.

methods will be necessary to convert such sensitive urazoles into their corresponding azoalkanes. Efforts are in progress for developing such methods in order to broaden the potential and scope of azoalkane chemistry.

In conclusion, we feel that the recently discovered dipolar addition of PTAD to strained bicycloalkenes **1** is a convenient and general entry into the hitherto unknown polycyclic azoalkanes **3** with C-type skeletons via the intermediary urazoles **2** (eq 8). The



(8)

synthetic and mechanistic utility of these azoalkanes make them valuable target molecules. The pyrolysis and photolysis of the azoalkanes **3** reported here are under intensive investigation for the mechanistic elucidation of the diradical intermediates postulated in the di-π-methane rearrangement of the corresponding bicycloalkenes **1**.

Experimental Section

All melting points are uncorrected. Solvents and starting materials, the latter either purchased from standard chemical suppliers or prepared according to known literature procedures, were purified to match the reported physical constants and spectral data. The infrared spectra were taken on a Perkin-Elmer Model 283 spectrophotometer and the ^{1}H NMR spectra on an Hitachi Perkin-Elmer R-24B spectrometer. Elemental analyses were carried out by Atlantic Analytical Laboratories. Room-temperature was ca. 30 °C unless otherwise specified. Rotoevaporation of the solvent was conducted at room temperature and ca. 15–20 mmHg unless otherwise specified. The yields, physical constants, and spectral data of the urazoles **2** are collected in Tables I and II and those of the azoalkanes **3** are given in Table III.

General Procedure for the Preparation of the Azoalkanes 3. A 50-mL, round-bottomed, two-necked flask, equipped with a reflux condenser, gas inlet and outlet tubes, and magnetic spinbar, was charged with 20 mmol of KOH and **3** mmol of urazole **2** in 10 mL of isopropyl alcohol. The mixture was refluxed under a N_2 atmosphere for 2 h while it was stirred magnetically and heated with an oil bath. After the solution cooled to room temperature ca. 5 g of crushed ice was added and the mixture was acidified to pH ~2 with concentrated HCl (gas evolution). The mixture was warmed to 40 °C for 5 min and neutralized with 5 M NH_4OH, and then, with gentle stirring, a 3 M aqueous solution of $CuCl_2 \cdot 2H_2O$ was added dropwise, leading to precipitation of the brick red copper complex. The latter was collected by filtration and the filtrate again adjusted to pH ~5–6 with 5 M NH_4OH. The process was repeated until the brick red product failed to precipitate (usually two cycles were sufficient). The combined precipitates were washed once each with 5 mL of brine (10%), 5 mL of EtOH, and 5 mL of H_2O. After treatment with 4 M NaOH and liberation of the azoalkane **3**, the reaction mixture was extracted with 3 × 30 mL of Et_2O, washed with 3 × 50 mL of H_2O, and dried over anhydrous $MgSO_4$ and the solvent was rotoevaporated. The azoalkane **3** was isolated by chromatography (CH_2Cl_2 eluent) on 70–230 mesh silica gel (ca. 15:1 weight ratio of adsorbant to substrate) and purified by recrystallization from the appropriate solvent (cf. Table III) and/or sublimation at 60–70 °C and (0.1 mmHg).

General Procedures for the Preparation of the Urazoles 2. To a magnetically stirred solution of the bicycloalkene or bicycloalkadiene **1** (ca. 0.5 M) in the appropriate solvent was added, in small portions, the specified quantity of PTAD, and the flask was protected from light and the mixture stirred at the specified temperature for the required period of time (cf. Table I for specific reaction conditions). When the characteristic intense red of PTAD had discharged to pale yellow, more PTAD was added until TLC showed complete consumption of the olefin **1**. The insoluble matter was removed by decantation, the solvent rotoevaporated, and the residue chromatographed (CH_2Cl_2 eluent) on 70–230 mesh silica gel (ca. 15:1 weight ratio of adsorbant to substrate). Final purification was achieved by recrystallization from the appropriate solvent (cf. Table I).

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