1730, 1500, 1410 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (t, J = 7.2 Hz, 3 H), 2.46 (s, 3 H), 4.46 (q, J = 7.2 Hz, 2 H), 7.37–7.49 (m, 10 H), 7.76 (br s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.58 (q), 25.18 (q), 65.31 (t), 86.07 (s), 126.03 (d), 129.06 (d), 129.38 (d), 130.02 (s), 153.29 (s), 154.73 (s), 162.14 (s), 190.75 (s); mass spectrum, m/z 305 (M^+ – PTAD); MSCI, 481 (MH^+).

Procedure B. A solution of ethyl 3-oxobutanoate (1.99 g, 15.3 mmol) and trifluoroacetic acid (8 μL, 0.11 mmol) in 7 mL of dichloromethane was stirred for 10 min. PTAD (103 mg, 0.59 mmol) in 2 mL of dichloromethane was added, the flask wrapped in aluminum foil, and the reaction stirred for 1 h. Following removal of solvent under reduced pressure, 1.80 g of unreacted starting material was recovered by distillation at room temperature under reduced pressure. Purification as described in the previous section afforded 153.4 mg (0.50 mmol, 86%) of **13**. None of the diurazole adduct **14** was observed in this procedure.

2-(4-Phenylurazolyl)-1,3-diphenyl-1,3-propanedione (15). To a stirred solution of 1,3-diphenyl-1,3-propanedione (2.52 g, 11.23 mmol) in 5 mL of dichloromethane was added PTAD (252 mg, 1.44 mmol) in 5 mL of dichloromethane. The red color of PTAD was discharged within 2 min. The solution was allowed to stand at 5 °C overnight, during which time **15** crystallized from the solution. Recovery of two crops of crystalline product by filtration afforded 490 mg (1.23 mmol, 85%) of **15** as colorless needles, mp 172.0–174.0 °C (lit.[5b] mp 189–191 °C); IR ($CHCl_3$) 3320, 1775, 1720, 1695, 1600, 1500 cm^{-1}. Both keto and enol tautomers are present in the proton and carbon NMR spectra. Therefore, the integration values cited should be taken as relative ratios only; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (s, 0.3 H), 7.18 (d, J = 7.5 Hz, 0.8 H), 7.33–7.54 (m, 10.5 H), 7.65 (dd, J = 7.2 and 7.2 Hz, 1 H), 7.75 (d, J = 7.2 Hz, 1.5 H), 8.01 (d, J = 7.5 Hz, 1.8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.73 (d), 107.98 (s), 124.82 (d), 124.95 (d), 126.24 (d), 126.56 (d), 127.20 (d), 127.53 (d), 127.99 (d), 130.40 (s), 131.09 (d), 133.29 (d), 133.69 (s), 133.88 (s), 149.82 (s), 152.45 (s), 153.62 (s), 190.17 (s), 191.02 (s); HRMS, m/z calcd for $C_{23}H_{17}N_3O_4$ (M^+) 399.1219, found 399.1238.

2,2-Bis(4-phenylurazolyl)-1,3-diphenyl-1,3-propanedione (16). To a stirred solution of 2-(4-phenylurazolyl)-1,3-diphenyl-1,3-propanedione (**15**, 400 mg, 1.0 mmol) in 15 mL of dichloromethane was added PTAD (175 mg, 1.0 mmol) in 7 mL of dichloromethane. The red color of the PTAD was discharged within 6 days. This reaction mixture was allowed to stand at 5 °C overnight, during which time **16** precipitated from the solution. Recrystallization from dichloromethane/ethyl acetate afforded **16** (400 mg, 0.69 mmol, 69%) as colorless plates, mp 182.0–184.0 °C (dec) (lit.[5b] mp 160–162 °C); IR (KBr) 3226, 1695 (vb), 1563, 1369 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.3–7.6 (m, 18 H), 8.03 (d, J = 8.1 Hz, 4 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 93.4 (s), 127.5 (s), 129.3 (s), 129.5 (d), 129.9 (d), 130.4 (d), 132.2 (s), 134.6 (d), 135.5 (s), 154.9 (s), 156.8 (s), 186.4 (s); FAB mass spectrum, m/z 575 (MH^+).

Acknowledgment. The financial support of the National Science Foundation (CHE-8312691) and the University of Cincinnati for the award of a fellowship to A.C.H. is gratefully acknowledged. In addition we thank the National Science Foundation for grants used to purchase the NMR (CHE-8102974) and mass spectrometry (PCM-8219912) facilities used in this research. We would also like to thank Dr. Palitha Wichkramanayake for his assistance in obtaining FAB mass spectral data.

Registry No. **1**, 123675-91-2; **2**, 123675-92-3; **3**, 98186-09-5; **4**, 123209-06-3; **5**, 123675-93-4; **6**, 123675-94-5; **7**, 123675-95-6; **8**, 98186-11-9; **9**, 123209-00-7; **10**, 123209-01-8; **11**, 123209-02-9; **12**, 123675-96-7; **13**, 67818-00-2; **14**, 72708-75-9; **15**, 72708-78-2; **16**, 72708-79-3; **17**, 123675-97-8; PTAD, 4233-33-4; $CH_2(CO_2Me)_2$, 108-59-8; $EtO_2CN{=}NCO_2Et$, 1972-28-7; cyclohexanone, 108-94-1; cyclooctanone, 502-49-8; 2-octanone, 111-13-7; 4-heptanone, 123-19-3; acetophenone, 98-86-2; oxindole, 59-48-3; deoxybenzoin, 451-40-1; 1,3-diphenyl-2-propanone, 102-04-5; dimedone, 3471-13-4; ethyl acetoacetate, 141-97-9; dibenzoylmethane, 120-46-7; Meldrum's acid, 2033-24-1.

Supplementary Material Available: Experimental procedures and spectroscopic data including infrared spectra, ^{1}H NMR spectra (300 MHz), ^{13}C NMR spectra (75 MHz), mass spectra (HRMS, CI, or FAB) available for compounds **4**, **7–12**, and **17** (6 pages). Ordering information is given on any current masthead page.

Synthesis and Chemistry of Acyltriazolinedione Ylides and Related Intermediates: New Methods for the Preparation of Di- and Tricarbonyl Compounds

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Received April 29, 1988

α-Urazolylcarbonyl compounds can be easily oxidized to the corresponding ylides, and these ylides hydrolyzed to the corresponding carbonyl compounds. In addition these same urazole precursors can be converted to carbonyl compounds via a novel version of the Swern oxidation. These two methods not only are of synthetic value in the preparation of 1,2-dicarbonyl and 1,2,3-tricarbonyl compounds but also serve as useful probes for the formation of triazolinedione ylides and the related urazolium species.

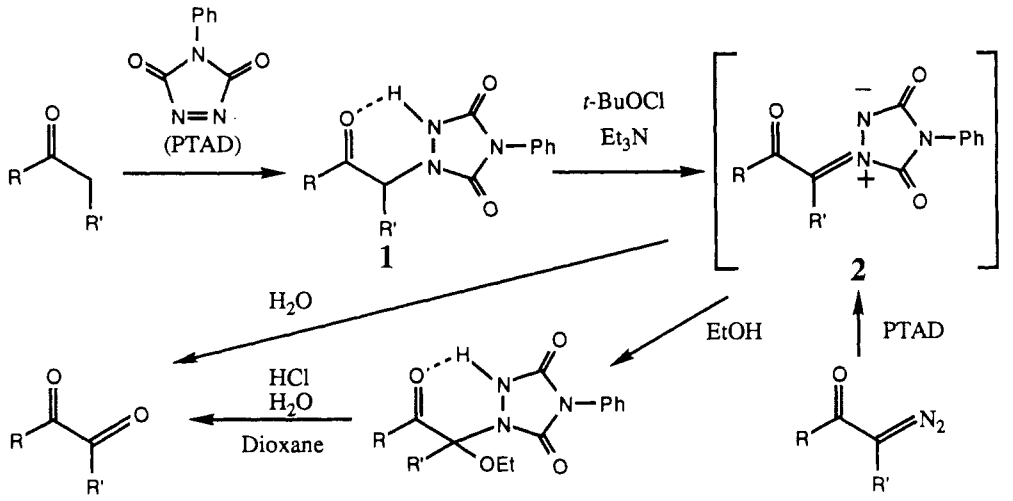
A number of methods for the oxidation of carbonyl compounds with α-methylene groups have been developed for the preparation of 1,2-dicarbonyl compounds. The reagent in the most widespread use for this purpose is SeO_2.[1] However, this reagent frequently affords quite complex reaction mixtures and products contaminated with toxic selenium impurities that are difficult to remove. Dimethyl sulfoxide has been applied in Swern oxidations of α-halo ketones.[2] While this method can provide quite high yields of the diketones, the starting halo ketones are quiet sensitive substances and must be used shortly after their preparation to ensure high overall yields. β-Keto sulfides have been oxidized to 1,2-diketones and their

(1) (a) Rabjohn, N. *Org. React. (N.Y.)* **1977**, *24*, 261. (b) Hach, C. C.; Banks, C. V.; Diehl, H. *Organic Syntheses*; Wiley: New York, 1963; Coll. Vol. 4, p 229.

(2) March, J. *Advanced Organic Chemistry*; Wiley: New York, 1985; p 1081. Iacona, R. N.; Rowland, A. T.; Nace, H. R. *J. Org. Chem.* **1964**, *29*, 3495. Nace, H. R.; Iacona, R. N. *J. Org. Chem.* **1964**, *29*, 3498. Bauer, D. P.; Macomber, R. S. *J. Org. Chem.* **1975**, *40*, 1990.

0022-3263/90/1955-0197$02.50/0

Scheme I

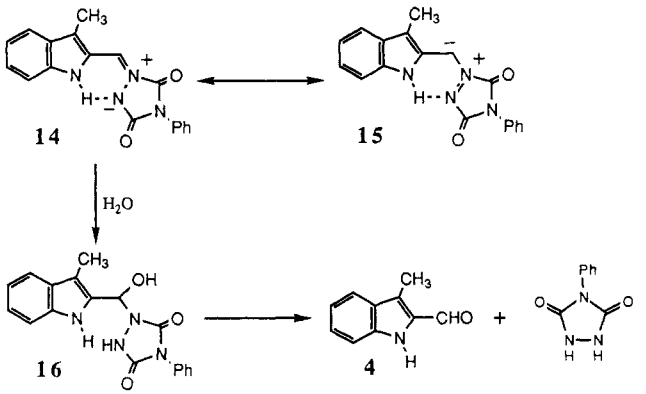


derivatives with a number of oxidizing agents such as $Pb(OAc)_4$[3] and $CuCl_2$.[4] The generation of α-hydroperoxy ketones through the reaction of enolates with molecular oxygen and the subsequent decomposition of the hydroperoxides also leads to diketones, albeit generally in poor yields.[5] Furthermore, this method is particularly prone to produce aldol condensation products, a problem that can be encountered with the other methods as well. Finally 1,3-dicarbonyl compounds can be transformed into 1,2,3-tricarbonyl compounds by using various nitrogen oxides,[6] but this method appears to have very limited applicability. Consequently, there remains a need for convenient, low-cost methods for the conversion of carbonyl compounds to their dicarbonyl analogues under mild conditions.

Regitz and co-workers have shown that triazolinedione ylides formed in the reaction of 4-phenyltriazolinedione (PTAD) with α-diazo ketones can be trapped by ethanol, and the resulting adducts subsequently hydrolyzed to 1,2-diketones with aqueous HCl (Scheme I).[7] We have recently observed that the oxidation of urazolyl compounds provides a particularly facile entry to similar highly reactive triazolinedione ylides[8] and that one of the reaction modes of these species which often occurs in very high yields is their direct hydrolysis to the corresponding carbonyl compounds. With the recent availability of α-urazolyl carbonyl compounds (1[9] in Scheme I), we have undertaken an investigation of this class of compounds as a potential source of novel acyltriazolinedione ylides (**2**). In this report we describe the generation of this class of ylide and two methods by which these ylides and the related urazolium species may be converted to carbonyl functional groups in synthetically useful yields.

In earlier work, it was observed that oxidation of the urazolylindole **3** with *tert*-butyl hypochlorite followed by formation of the triazolinedione ylide with triethylamine and hydrolysis of this stable ylide with a few drops of water afforded the aldehyde **4** in nearly quantitative yield (Table I).[8] Similar treatment of *N*-benzyl-*N'*-phenylurazole (**5**)

Scheme II



also produced benzaldehyde in high yield. In fact the first five entries in Table I afforded reasonable to excellent yields of the corresponding carbonyl compounds under these extremely mild conditions (method A). However, while similar treatment of the urazolyl diketone **11** occasionally afforded the triketone **12** in excellent yield, the yields of **12** were somewhat variable and usually significantly lower than that recorded in Table I. In addition, cyclohexane-1,2-dione (**13**) could be obtained only in low yield from **9** by this procedure, whereas Regitz and coworkers had obtained **13** in 75% yield via the aforementioned ylide trapping with ethanol followed by hydrolysis.[7a]

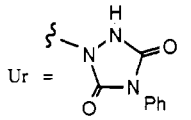
The urazole compounds in Table I are listed with those containing electron-donating substituents at the top and those with electron-withdrawing substituents at the bottom of the table. The relative ease with which these urazoles afford carbonyl products via this direct ylide hydrolysis procedure (method A) indicates that there may be fundamental differences in the mechanisms of ylide formation and/or hydrolysis upon going from urazoles with donor groups to urazoles with acceptor groups.

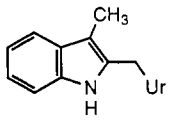
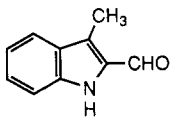
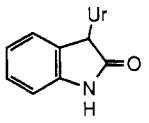
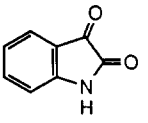
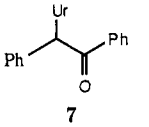
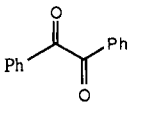
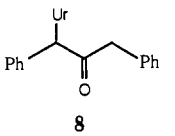
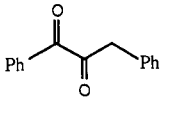
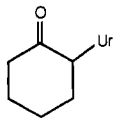
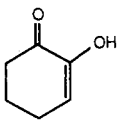
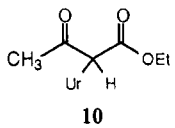
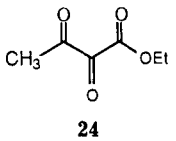
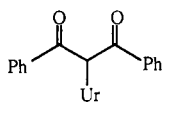
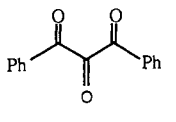
One possibility is that the structures of the intermediate ylides might be affected significantly by the electron-donating or -withdrawing properties of their substituents. For instance, the ylide derived from **3** might be regarded as having contributions from the two resonance forms **14** and **15** as shown in Scheme II. The highly electron-donating indole substituent plus the possibility of internal hydrogen bonding would be expected to strongly bias this particular ylide in favor of resonance contributor **14**. Thus, attack of a water molecule on this ylide would be expected to proceed with protonation on the ylide nitrogen to afford the intermediate **16**, which would in turn collapse to the

(3) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405.
(4) Gregoire, B.; Carre, M.-C.; Caubere, P. *J. Org. Chem.* **1986**, *51*, 1419.
(5) Rao, D. V.; Stuber, F. A.; Ulrich, H. *J. Org. Chem.* **1979**, *44*, 456.
(6) (a) Wieland, H.; Bloch, S. *Ber.* **1904**, *37*, 1524. (b) Dahn, H.; Hauth, H. *Helv. Chim. Acta* **1959**, *42*, 1214.
(7) (a) Theis, W.; Bethäuser, W.; Regitz, M. *Tetrahedron* **1985**, *41*, 1965. (b) Bethäuser, W.; Regitz, M.; Theis, W. *Tetrahedron Lett.* **1981**, *22*, 2535.
(8) (a) Wilson, R. M.; Hengge, A. C. *Tetrahedron Lett.* **1985**, *26*, 3673. (b) Wilson, R. M.; Hengge, A. C. *J. Org. Chem.* **1987**, *52*, 2699.
(9) Wilson, R. M.; Hengge, A. C.; Ataei, A.; Chantarasiri, N. *J. Org. Chem.*, previous paper in this issue.

Table I. Conversion of N-Substituted Urazoles to the Corresponding Carbonyl Compounds

Ur =



starting urazoles	products	reaction conditions	yield, %
 **3**	 **4**	A,[a] (1) *t*-BuOCl, THF; (2) Et_3N, H_2O, 90 min	99[b]
$PhCH_2Ur$ **5**	PhCHO	A,[a] (1) *t*-BuOCl, THF; (2) H_2O	>90[c]
 **6**	 isatin	A,[a] (1) *t*-BuOCl, DME; (2) Et_3N, H_2O, 30 min	75
 **7**		A,[a,d] (1) *t*-BuOCl, CH_3CN; (2) Et_3N, H_2O, 60 min	79
 **8**		A,[a,d] (1) *t*-BuOCl, CH_3CN; (2) Et_3N, H_2O, 15 min	56[e]
 **9**	 **13**	A,[a] (1) *t*-BuOCl, CH_3CN; (2) Et_3N, H_2O, 0 °C B,[f] (1) *t*-BuOCl, CH_3CN; (2) Na_2CO_3, DMSO; 50 °C, 10 min	22 62
 **10**	 **24**	B,[f] (1) *t*-BuOCl, CH_3CN; (2) Na_2CO_3, DMSO; 50 °C, 60 min	45
 **11**	 **12**	A,[a,d] (1) *t*-BuOCl, CH_3CN; (2) $NaHCO_3$, H_2O, 1 h B,[d,f] (1) *t*-BuOCl, CH_3CN; (2) Na_2CO_3, DMSO, 5 min	89[g] 92

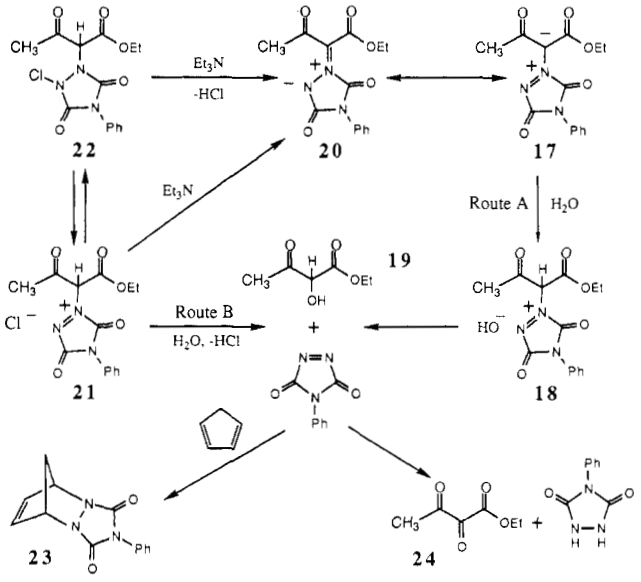
[a] Method A: hydrolytic quench. [b] Reference 8b. [c] Yield determined by NMR. [d] Experimental details provided in the supplementary material of ref 14. [e] Reference 17. [f] Method B: oxidative quench. [g] Variable yield.

aldehyde **4** with loss of 4-phenylurazole. Indeed this regiochemistry for the addition of alcohols to a number of triazolinedione ylides has been observed previously.[7-9] On the other hand, ylides with only electron-withdrawing, carbonyl, or dicarbonyl substituents (**9**–**11**) might be expected to have greater contributions from the alternative resonance structure related to **17** in Scheme III. Thus, by analogy to the well-known chemistry of α-diazoketones, these ylides might be expected to undergo hydrolysis via protonation on carbon to form **18** followed by loss of PTAD to form α-ketols such as **19** (route A in Scheme III). Subsequent oxidation of the α-ketol by the displaced PTAD[10] then might produce the 1,2-dicarbonyl compound and 4-phenylurazole.

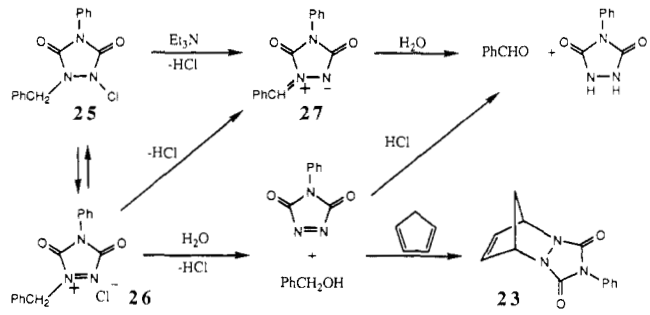
The uncatalyzed oxidation of alcohols with PTAD usually is not a rapid process and in many cases does not occur at all. For instance, treatment of benzoin with PTAD forms very little benzil after several days, and the oxidation of benzyl alcohol to benzaldehyde with PTAD requires 12 h at 40 °C to go to completion (63%). It was interesting to observe that the benzoin oxidation when conducted in the presence of catalytic amounts of HCl afforded a smooth oxidation of benzoin to benzil. However, even this acid-catalyzed reaction required several days to go to completion at room temperature and therefore cannot account for all of the benzil formation from urazole **7**, since ylide hydrolysis is complete within 1 h under similar conditions. Nevertheless, α-ketols of 1,3-dicarbonyl systems such as **19** in Scheme III would be expected to be much more reactive, since their enol tautomers should be highly reactive toward PTAD. Consequently, while the α-diazo

(10) Cookson, R. C.; Stevens, I. D. R.; Watts, C. T. *Chem. Commun.* **1966**, 744. Dao, L. H.; Mackay, D. *Can. J. Chem.* **1979**, *57*, 2727. Wilson, R. M.; Schnapp, K. A.; Merwin, R. K.; Ranganathan, R.; Moats, D. L.; Conrad, T. T. *J. Org. Chem.* **1986**, *51*, 4028.

Scheme III



Scheme IV



ketone analogy does not seem to be paralleled in the chemistry of simple acyltriazolinedione ylides, it may be active in the chemistry of the more specialized ylides derived from 1,3-dicarbonyl compounds.

To explore the effect of the substituent groups on the ylide structure, the ^{13}C NMR spectra of the stable ylides derived from urazoles **3** and **8** were acquired, and the ylide carbon atoms determined to afford signals at δ 141.2 and 187.5, respectively. These values are in accord with those observed by Regitz and co-workers for a series of stable triazolinedione ylides, δ 157.5–188.1, which includes the ylide derived from **8**, δ 188.0.[11] Unfortunately, the ylides with dicarbonyl substituents are not stable enough to permit the acquisition of their ^{13}C NMR spectra. However, all of the ylides derived from urazoles **3** and **5–11** undergo attack by carbanions at the ylide carbon atom,[12] and simple acyltriazolinedione ylides have been observed to undergo attack by ethanol at the ylide carbon atom.[7a] On this basis the resonance structures related to **14** in Scheme II and **20** and Scheme III would seem to be the major contributors to the ylides under consideration here.

Thus, even though urazolium salts such as **18** are probably not formed from ylide protonation at carbon (route A in Scheme III), closely related urazolium salts (**21**) might be formed from *N*-chlorourazoles such as **22** as shown in route B. If this is so, then displacement of PTAD by water from urazolium salts such as **21** should produce the same products as ylide protonation by water at carbon followed by displacement of PTAD. To test this possibility, a number of the *N*-chlorourazoles derived from the urazoles in Table I were treated directly with water in the *absence* of triethylamine. Under these conditions, the characteristic yellow or orange color of the ylide is not produced. Instead a cherry red color develops immediately upon the addition of the water. That this color is due to PTAD was easily demonstrated in several cases by conducting these reactions in the presence of cyclopentadiene and isolating the Diels–Alder adduct of cyclopentadiene and PTAD (**23**, Scheme III). When this procedure was applied to urazole **10**, even though the adduct **23** could be isolated, neither the expected ethyl 2-hydroxy-3-oxobutanoate (**19**) nor ethyl 2,3-dioxobutanoate (**24**) could be detected. In contrast, when the benzylurazole **5** was treated with *tert*-butyl hypochlorite followed by water in the presence of cyclopentadiene, all of the expected products (4-phenylurazole, the PTAD Diels–Alder adduct, benzaldehyde, and benzyl alcohol) could be detected as indicated in Scheme IV. However, since the ratio benzaldehyde:benzyl alcohol was 4.3:1, it would seem that substantial amounts of the ylide are being generated even in the absence of base.[13]

The observations described above have led us to the working hypothesis outlined for the *N*-benzylurazole system in Scheme IV. Apparently, *N*-chlorourazole **25** can easily release chloride ion to form urazolium salt **26**, and even in the presence of very weak bases such as water, this urazolium salt might be deprotonated to generate the corresponding ylide **27**. Thus, a rather complex relationship would seem to exist between these three species (**25**, **26**, and **27**), and the system can be driven completely to the ylide by the addition of base. In those systems that afford relatively stable ylides, the ylides will persist long enough to undergo hydrolysis upon the subsequent addition of water. However, ylide decomposition becomes an important competing process in those systems that afford less stable ylides (vide infra), and reduced yields of the ketonic hydrolysis products result. If base is not added to drive these equilibria to the ylide, then the urazolium salt becomes a significant intermediate and competes with the ylide for the water to form the undesired alcohol. This alcohol might in turn be oxidized to some extent by the PTAD to form the corresponding carbonyl compound and 4-phenylurazole.[10]

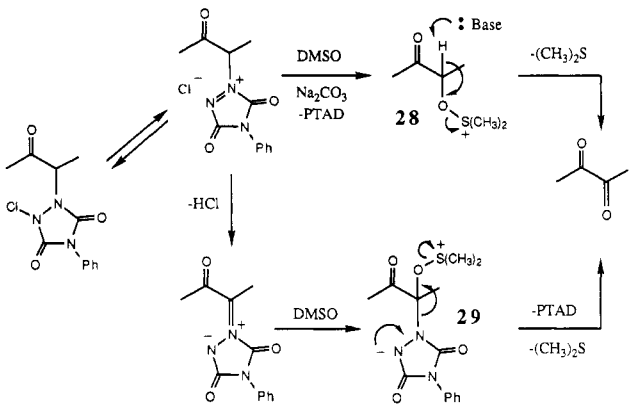
On the basis of this model (Scheme IV), a set of conditions has been developed with which both the triazolinedione ylide and the related urazolium salt can be converted to the desired carbonyl compound (method B in Table I). Under these modified conditions, the initial oxidation of the α-urazolylcarbonyl to the *N*-chlorourazole is immediately followed by the addition of a few drops of a Na_2CO_3 slurry in DMSO. As might be expected, the cherry red color of PTAD is formed immediately upon the addition of the DMSO slurry and slowly dissipates over the course of the next few minutes. This method affords substantial improvements in the yields of the di- and tricarbonyl compounds that either were formed in low yields or gave erratic results using the simple ylide hydrolysis procedure (method A in Table I).

The strategy underlying this method is based upon the mechanism for the Swern oxidation.[2] Accordingly, urazolium salts might react with DMSO to form sulfoxonium salts (**28**) as shown in Scheme V. Decomposition of these sulfoxonium salts should form the desired carbonyl prod-

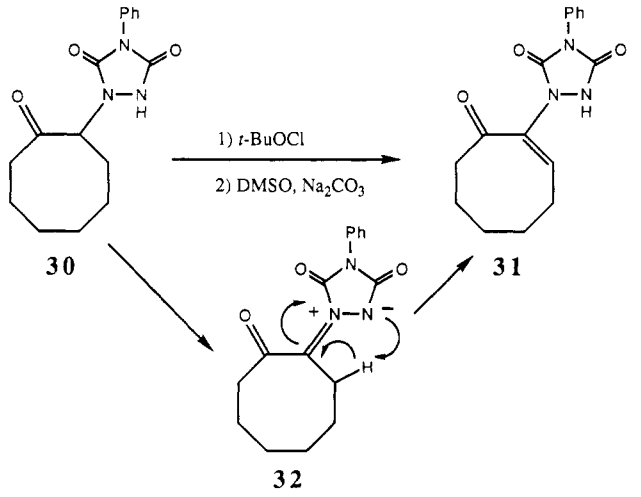
(11) Theis, W.; Bethäuser, W.; Regitz, M. *Chem. Ber.* **1985**, *118*, 28.
(12) Hengge, A. C. Ph.D. Thesis, University of Cincinnati, 1987.

(13) This observation is consistent with more recent results involving the formation of a stable ylide where the ylide color is formed immediately upon treatment of the urazole with *tert*-butyl hypochlorite but intensifies upon the addition of base; Wilson, R. M.; Chantarasiri, N., unpublished results.

Scheme V



Scheme VI



ucts. Alternatively, the triazolinedione ylides might be expected to add a molecule of DMSO to form adducts such as **29** in Scheme V. These betaine species should collapse spontaneously to the desired carbonyl constituents as well as PTAD and dimethyl sulfide. Since PTAD reacts very rapidly with sulfides, the dimethyl sulfide released in both of these pathways should scavenge the PTAD and prevent its further reaction with the carbonyl products.

Finally, it must be noted that this procedure also has some significant limitations. For example when 2-(4-phenylurazolyl)cyclooctanone (**30**) was examined by using either method A or B, no diketone could be detected. However, with method B a new product was isolated in 28% yield and shown to have structure **31** (Scheme VI). Apparently this material arises through annihilation of the ylide **32** via an intramolecular hydrogen abstraction as illustrated in Scheme VI. The analogous product is formed in 22% yield when 3-(4-phenylurazolyl)heptan-4-one is reacted under these conditions.[14] Although 2-(4-phenylurazolyl)cyclohexanone (**9**) might have given rise to the same type of enone product, no products other than **13** were observed with this system. Therefore, while this type of ylide annihilation may pose a serious limitation to the application of this methodology to molecules with appropriately situated β-protons, it also might provide novel starting materials for the synthesis of some most unusual triazolinedione ylides. Further research will be required to determine whether these difficulties can be circumvented or these opportunities exploited.

(14) For a detailed experimental procedure and spectroscopic data, see the paragraph about supplementary material at the end of this paper.

In summary, the oxidation of N-substituted urazoles to their corresponding ylides or urazolium salts followed by a hydrolytic or oxidative quenching step provides access to a variety of di- and tricarbonyl compounds. While these procedures have some distinct limitations, they also would seem to provide the methods of choice for the synthesis of carbonyl compounds that are very sensitive to further oxidation such as the aldehyde **4**, as well as for the synthesis of extremely sensitive tricarbonyl systems such as **12** and **24**. Furthermore, the methodology developed here provides a most useful probe for a variety of transient triazolinedione ylides, the chemistry of which is proving to be quite fascinating indeed and will be the subject of future reports.

Experimental Section

Melting points were determined with a Mettler FP2 melting point apparatus using a polarizing microscope and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with either an IBM NR 80-MHz or a Nicolet NT 300-MHz spectrometer. Spectra were recorded in $CDCl_3$ except where noted otherwise, and chemical shifts are reported in ppm downfield from tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer 599 infrared spectrometer and were calibrated with a polystyrene film. High-resolution mass spectra were obtained with a Kratos MS801-DS55 spectrometer. Preparative chromatographic separations were conducted by centrifugal chromatography with a Chromatotron using plates coated with E. Merck 60-PF254 silica gel. All urazole starting materials other than **3**[8] and **5**[8] were prepared by the methodology described in the previous paper.[9]

Conversion of 1-Benzyl-4-phenylurazole (5) to Benzaldehyde. A solution of **5** (35.1 mg, 0.131 mmol) in 1 mL of acetonitrile was treated with *tert*-butyl hypochlorite (15.7 μL, 0.137 mmol). After about 30 s, one drop of dilute aqueous $NaHCO_3$ was added, and a deep red color developed immediately. One drop of cyclopentadiene was added, and the red color was immediately bleached. The reaction mixture was dried over $MgSO_4$, the solvent evaporated under reduced pressure, and the residue analyzed by ^1H NMR (80 MHz, $CDCl_3$): $PhCHO:PhCH_2OH:23$ = 4.3:1.0:2.3, $PhCHO:PhCH_2OH$ = 81:19. The Diels–Alder adduct **23** has been isolated from this and several of the systems described below and compared with authentic material.[15] Treatment of the urazole **5** with *tert*-butyl hypochlorite followed by triethylamine and then with water led to nearly quantitative conversion to benzaldehyde as judged by NMR analysis.

Preparation of Isatin from 3-(4-Phenylurazolyl)-2-oxoindoline (6). Oxindole urazole **6** (31.5 mg, 0.102 mmol) was dissolved in 7.5 mL of DME and treated with *tert*-butyl hypochlorite (13.1 μL, 0.11 mmol). After about 1 min, excess water (0.5 mL) was added followed by triethylamine (15.2 μL, 0.11 mmol). The resulting mixture was allowed to stir for 30 min and then dried with $MgSO_4$, and the solvent removed under reduced pressure. The residue was passed through a 1.5 × 4.5 cm column of flash silica gel eluting with dichloromethane to afford 12.1 mg of isatin (0.76 mmol, 75%) as orange crystals, mp 195–197 °C (lit.[16] mp 196–197 °C): ^1H NMR (80 MHz, $CDCl_3$) δ 6.85–7.62 (m, 4 H), 9.75 (br s, 1 H); mass spectrum, *m/e* 147 (M^+), 119.

Preparation of 1,2-Cyclohexanedione (13) from 2-(4-Phenylurazolyl)cyclohexanone (9). The urazole **9** (72.9 mg, 0.267 mmol) was dissolved in 2.2 mL of acetonitrile and treated with *tert*-butyl hypochlorite (31.8 μL, 0.267 mmol). After 30 s, three drops of a saturated solution of Na_2CO_3 in DMSO was added. The reaction mixture was warmed to 50 °C for 10 min and, upon cooling, poured into water and extracted twice with ether. The combined ether extracts were washed with water and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Kugelrohr distillation under 1 mmHg of pressure at 70 °C afforded 14.5 mg (0.13 mmol) of pure **13** as colorless crystals,

(15) Cookson, R. C.; Gupte, S. S.; Stevens, I. D. R.; Watts, C. T. *Org. Synth.* **1971**, *51*, 121.
(16) Marvel, C. S.; Hiers, G. S. *Organic Syntheses*; Wiley: New York, 1932; Coll. Vol. 1, p 321.
(17) Kohler, E. P.; Barnes, R. P. *J. Am. Chem. Soc.* **1934**, *56*, 211.

mp 32.0–33.0 °C (lit.[16] mp 34 °C). Centrifugal chromatography of the distillation residue eluting with 10% ethyl acetate in dichloromethane resulted in recovery of 15.0 mg of **9**. Thus, the yield of **13** based upon recovered starting material was 62%: ^{1}H NMR[18] (80 MHz, $CDCl_3$) δ 1.91–2.14 (m, 2 H), 2.28–2.62 (m, 4 H), 5.95 (br s, 1 H), 6.14 (t, J = 4.6 Hz, 1 H).

In an alternative procedure, method A in Table I, a solution of **9** (40.3 mg, 0.148 mmol) in acetonitrile was treated with *tert*-butyl hypochlorite (19.3 μL, 0.162 mmol). After 2 min, this solution was cooled to 0 °C and treated with 0.5 mL of water and 34 μL (0.252 mmol) of triethylamine and stirred for 45 min at 0 °C. Isolation as described above afforded only 3.7 mg (0.033 mmol, 22%) of **13**.

Finally, when **9** is treated with cyclopentadiene following the addition of *tert*-butyl hypochlorite, the Diels–Alder adduct **23** can be isolated from the final reaction mixture.

Preparation of Ethyl 2,3-Dioxobutanoate (24) from Ethyl 2-(4-Phenylurazolyl)-3-oxobutanoate (10). The urazole **10** (212 mg, 0.695 mmol) was dissolved in 8 mL of acetonitrile and treated with *tert*-butyl hypochlorite (83.0 μL, 0.697 mmol). After about 30 s, four drops of a saturated solution of Na_2CO_3 in DMSO was added, and the solution warmed to 50 °C for 1 h. Upon cooling, the yellow solution was poured into water, and the aqueous mixture extracted twice with ether. The combined ether layers were washed with water, dried with $MgSO_4$, and evaporated to dryness. Kugelrohr distillation of the residue at 60 °C at 1 mmHg of pressure afforded the tricarbonyl product **24** as a bright yellow oil (45.3 mg, 0.315 mmol, 45%), bp 70 °C (12 mmHg) [lit.[6b] bp 68 °C (12 mmHg)]: IR ($CHCl_3$) 1745, 1728 cm^{-1} (lit.[6b] 1748, 1730 cm^{-1}); mass spectrum, m/e 144 (M^+), 116.

Treatment of urazole **10** (34.0 mg, 0.111 mmol) with *tert*-butyl hypochlorite (13.3 μL, 0.111 mmol) in 2.5 mL of acetonitrile followed by 30 μL of 0.1 M Na_2CO_3 afforded a pink–orange solution that contained no **24** as judged by TLC and NMR. Heating at 45 °C for 10 h afforded a red–pink solution. This color was discharged immediately by the addition of cyclopentadiene (5 μL). The only product that could be isolated from this reaction mixture (thick-layer chromatography eluting with CH_2Cl_2) was **23** (3.3 mg, 0.0137 mmol, 12%).

Preparation of 2-(4-Phenylurazolyl)-2-cycloocten-1-one (31). The urazole **30** (42.9 mg, 0.142 mmol) was dissolved in 1.5 mL of benzene at 45 °C and treated with *tert*-butyl hypochlorite (17.0 μL, 0.143 mmol). Three drops of distilled water was added, and the mixture stirred for 1 h. Upon cooling, the reaction mixture was dried over $MgSO_4$ and evaporated to dryness. Centrifugal chromatography of the residue eluting with 10% ethyl acetate in dichloromethane resulted in recovery of 15.1 mg of urazole starting material **30** and 7.6 mg (0.025 mmol, 28% based on recovered **30**) of the unsaturated urazole **31** as a colorless oil: ^{1}H NMR (80 MHz, $CDCl_3$) δ 1.55–1.90 (m, 6 H), 2.59–2.93 (m, 4 H), 6.85 (t, J = 7 Hz, 1 H), 7.45–7.56 (m, 5 H); mass spectrum, m/e 299 (M^+, base peak), 257, 177.

Acknowledgment. The financial support of the National Science Foundation (CHE-8312691) and the University of Cincinnati for the award of a fellowship to A.C.H. is gratefully acknowledged. In addition we thank the National Science Foundation for grants used to purchase the NMR (CHE-810274) and mass spectrometry (PCM-8219912) facilities used in this research.

Registry No. **3**, 103865-85-6; **4**, 5257-24-9; **5**, 107798-93-6; **6**, 123209-00-7; **7**, 123209-01-8; **8**, 123209-02-9; **9**, 98186-09-5; **10**, 72708-74-8; **11**, 72708-78-2; **12**, 643-75-4; **13**, 10316-66-2; **23**, 15971-63-8; **24**, 1723-25-7; **30**, 123209-06-3; **31**, 123209-07-4; PhCHO, 100-52-7; $PhCH_2OH$, 100-51-6; $Ph(CO)_2Ph$, 134-81-6; $Ph(CO)_2CH_2Ph$, 23464-17-7; cyclopentadiene, 542-92-7; isatin, 91-56-5; 3-(4-phenylurazolyl)-2-hepten-4-one, 123209-04-1; 2-(4-phenylurazolyl)cycloheptanone, 123209-05-2.

Supplementary Material Available: Experimental procedures and spectroscopic data for the ylide formation and conversion to carbonyl compounds from urazoles **7**, **8**, and **11**, as well as for the formation of 3-(4-phenylurazolyl)-2-hepten-4-one (4 pages). Ordering information is given on any current masthead page.

(18) *Aldrich Library of NMR Spectra*, 2nd ed.; Aldrich Chemical Co.: Milwaukee, WI, 1983; Vol. 1, p 390B.

Total Synthesis of (±)-Gnididione and (±)-Isognididione

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Received August 28, 1989

(±)-Gnididione (**1**) and (±)-isognididione (**2**) have been prepared in a totally stereospecific fashion beginning with the oxazole aldehyde **20**, which was efficiently elaborated to the tertiary alcohols **3Z-R** and **3E-R** by a chelation controlled addition of 1-propynylmagnesium bromide to the intermediate enones **24Z** and **24E**. Alcohol **3Z-R** was converted in a single step to **1** via a process involving sequential chemoselective oxy-Cope reaction to produce the acetylenic ketone **5**, intramolecular Diels–Alder reaction of **5** to afford gnididione ketal **7**, and acid hydrolysis. In identical fashion, **3E-R** was directly converted to **2** with 100% stereoselectivity.

Introduction

During the course of a search for plant-based tumor inhibitors, Kupchan et al. isolated the furanosesquiterpene gnididione (**1**) from ethanolic extracts of *Gnidia latifolia* and proposed the structure **1** for this material on the basis of chemical and spectroscopic evidence.[1] At the time, **1** was the only known example of a guaiane type sesquiterpene incorporating a furan ring.[2] As a part of these studies, **1** was equilibrated with HCl to afford an approximately 50:50 mixture of **1** and an isomeric material formulated as the C-1 epimer, isognididione (**2**, Figure 1). This assignment was based mainly on an upfield shift of the C-10 methyl group in the NMR spectrum of **2**, relative to **1**, due to its close proximity to the 6,7 double bond. The

(1) Kupchan, S. M.; Shizuri, Y.; Baxter, R. L.; Haynes, H. R. *J. Org. Chem.* **1977**, *42*, 348.

(2) One other example of a furanoguaiane has subsequently been reported: (a) Li, M. K. W.; Sheuer, P. J. *Tetrahedron Lett.* **1984**, *25*, 2109. (b) Imre, S.; Thomson, R. H.; Yalhi, B. *Experientia* **1981**, *37*, 442.

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