Reactions of Benzocyclic β-Keto Esters with Tosyl and 4-Nitrophenyl Azide. Structural Influence of Dicarbonyl Substrate and Azide Reagent on Distribution of Diazo, Azide and Ring-Contraction Products†

Luisa Benati,*[,‡] Gianluca Calestani,[§] Daniele Nanni,[‡] and Piero Spagnolo[‡]

Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy, and Dipartimento di Chimica Generale ed Inorganica, Analitica e Chimica Fisica, Viale delle Scienze 78, I-43100 Parma, Italy

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The reactions of β-keto esters derived from 1- and 2-indanone, 1- and 2-tetralone, and benzosuberone with toluene-4-sulfonyl- (tosyl) and 4-nitrobenzenesulfonyl azide (PNBSA) in the presence of Et_3N have been investigated in order to evaluate the influence of both dicarbonyl substrate and azide reagent on the product distribution. With tosyl azide the keto esters derived from both 2-benzocycloalkanones exhibit deacylating diazo transfer, but those derived from the 1-benzocycloalkanones undergo additional azido transfer to a significant or even exclusive extent. The finding is mainly explained in terms of the lesser reactivity of the conjugate aryl ketone than alkyl ketone moiety. This would discourage cyclization of the initial sulfonyltriazenyl anion—the presumable azide precursor—to the triazoline adduct, in turn envisaged as the diazo progenitor. With PNBSA both indanones smoothly undergo diazo transfer, whereas their higher homologues lead to ring-contraction products ascribable to corresponding triazolines that curiously prefer to suffer Favorskii-type ring fragmentation. Evidence has been obtained that tosyl azide acts as a azide-transfer reagent superior to PNBSA. A possible explanation of this fact is discussed. An X-ray crystal structure analysis of the phthalazine compound **18** (Ar = 4-Me-C_6H_4) has been performed.

Introduction

Diazo-group transfer from a sulfonyl azide to the active methylene of a β-dicarbonyl compound is a valuable method for the production of α-diazocarbonyl compounds.[1] With simple ketones or esters the diazo transfer can be normally accomplished through prior acylation and subsequent elimination of the activating acyl group in the course of the actual diazo transfer.[1] In previous work[2] we have observed that toluene-4-sulfonyl (tosyl) azide can smoothly transform 2-substituted indan-1,3-diones into ring-opened *o*-*N*-tosylcarbamoyl-substituted α-diazoacetophenones, thus providing the first instances of deacylating diazo transfer with cyclic β-diones. We have next examined a similar process upon several monocyclic β-keto esters.[3] The five- to seven-membered-ring compounds cleanly led to diazo amido esters, whereas other derivatives exhibited significant or even preferential occurrence of the azidation product. It has been therefore inferred that structural features of the cyclic substrate may discourage a deacylating diazo-transfer process in favor of an alternative azido transfer, which is only encountered in special cases with resonance-stabilized enolates.[4] To gain a further insight into the effect of cyclic keto ester structure, we were led to study the behavior of the available benzocyclic keto esters **1a**−**c** and **2a**,**b**, derived from 1- and 2-benzocycloalkanones, respectively (Figure 1). Since we were also interested in ascertaining the effect of sulfonyl azide reagent, the reactivity of the above compounds **1a**−**c** and **2a**,**b** toward more electrophilic 4-nitrobenzenesulfonyl azide (PNBSA) was additionally examined. Very recently,[5] PNBSA has found an advantageous use in promoting deacylating diazo transfer to acyclic benzoyl-activated esters and ketones, though PNBSA was originally reported to be inferior to tosyl azide as a diazo-transfer reagent.[6] Herein, we report the results obtained from the present work.

Results and Discussion

Following a procedure analogous to that previously reported for the monocyclic examples,[3] 2-ethoxycarbonyl-1-indanone **1a** was reacted with tosyl azide and triethylamine at room temperature in anhydrous tetrahydrofuran for ca. 6 days. Column chromatography of the

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‡ Università di Bologna.

§ Università di Parma e Centro di Studio per la Strutturistica Diffrattometrica del CNR.

(1) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. Regitz, M.; Maas, G. *Diazo Compounds: Properties and Synthesis*; Academic Press: New York, 1986, ch. 13. Scriven, E. F. V.; Turnbull, K *Chem. Rev.* **1988**, *88*, 298.

(2) (a) Benati, L.; Montevecchi, P. C.; Spagnolo, P.; Foresti, E. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2845. (b) Benati, L.; Calestani, G.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2637. (c) Benati, L.; Calestani, G.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1381.

(3) Benati, L.; Nanni, D.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 457.

(4) Mataka, S.; Koga, G.; Anselme, J.-P.; Weininger, S. J.; Kohen, S. *J. Org. Chem.* **1974**, *39*, 1591. Wasserman, H. H.; Hlasta, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 6780. Hakimelahi, G. H.; Just, G. *Synth. Commun.* **1980**, *10*, 429.

(5) Taber, D. F.; You, K.; Song, Y. *J. Org. Chem.* **1995**, *60*, 1093. Taber, D. F.; Gleave, D. M.; Herr, R. J.; Moody, K.; Hennessy, M. J. *J. Org. Chem.* **1995**, *60*, 2283.

(6) Hendrickson, J. B.; Wolf, W. A. *J. Org. Chem.* **1968**, *33*, 3610.

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Table 1. Yields (%)[a] of Diazo-Transfer, Azido-Transfer, and Ring-Contraction Products from the Reactions of Benzocyclic Keto Esters 1a−c, 2a,b with Tosyl Azide and PNBSA[b]

entry	keto ester	azide	time	diazo-transfer product(s) (% yield)	azido-transfer product (% yield)	ring-contraction product (% yield)
1	**1a**	TsN_3	6 d	**3a** (55), **6** (25)	**5a** (16)	
2	**1b**	TsN_3	4 d	**3b** (traces)	**5b** (75)	
3	**1c**	TsN_3	5 d	**3c** (51), **8** (15)	**5c** (31)	
4	**2a**	TsN_3	12 h	**17a**/**b** (84)[c]		
5	**2b**	TsN_3	12 h	**9b** (51)[d]		
6	**1a**	PNBSA	2 h	**7** (94)[e]		
7	**2a**	PNBSA	1 h	**13** (45), **17a**/**b** (10)[f]		
8	**1b**	PNBSA	20 h		**5b** (21)	**14a** (R = Et) (47)
9	**2b**	PNBSA	1 h	**16** (8)		**14a** (R = Me) (37)[g]
10	**1c**	PNBSA	4 h			**14b** (R = Et) (75)

[a] Yields isolated by column chromatography. [b] Reactions were normally carried out in THF at rt in the presence of Et_3N. [c] **17a** or **17b** (Ar = 4-Me-C_6H_4). [d] 30 min at 0 °C, then 12 h at rt; the aminated tetralone **11** was also produced in 20% yield. [e] 30 min at 0 °C, then 2 h at rt; the triethylammonium salt of **4a** was obtained in 94% yield. By chromatography, **4a** furnished **7**. [f] 10 min at 0 °C, then 1 h at rt; **17a** or **17b** (Ar = 4-NO_2-C_6H_4). [g] The aminated tetralone **12** was also produced in 28% yield.

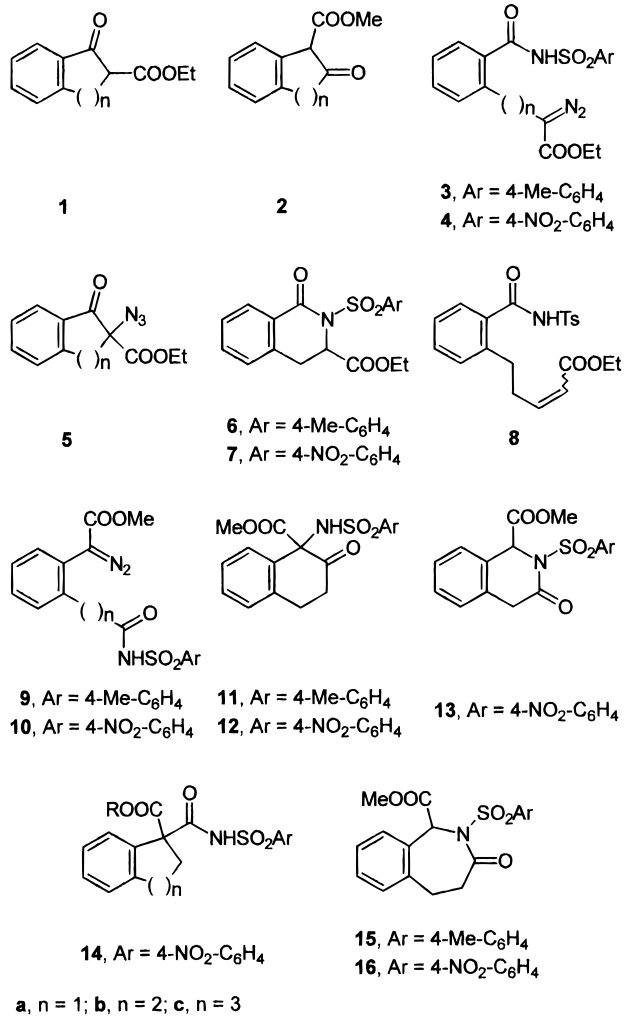


Figure 1.

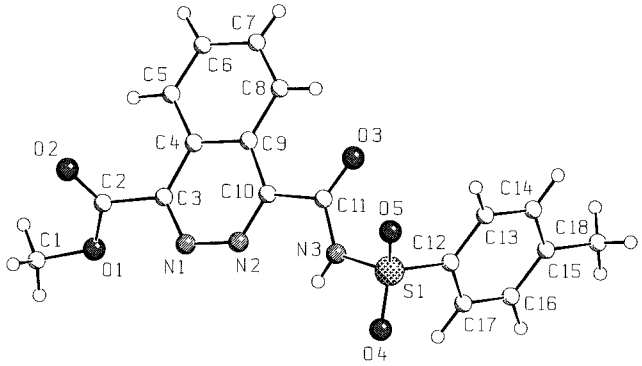


Figure 2. The X-ray molecular structure of methyl 4-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-1-phthalazinecarboxylate **18** (Ar = 4-Me-C_6H_4) showing the atom-numbering scheme.

crude mixture separated the rather unstable diazo propanoate **3a** and the formal carbene decomposition product—the cyclized isoquinolinone **6** (see the Experimental Section)—in 80% overall yield, together with minor amounts of the azidation product **5a** (Table 1, entry 1).

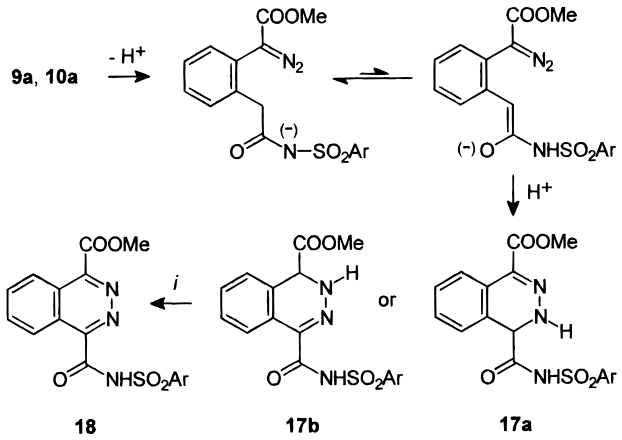
A somewhat comparable finding was provided by 2-ethoxycarbonyl-1-benzosuberone **1c**, but in such case the proportion of the corresponding azide **5c** to the overall diazo-transfer products—the diazo pentanoate **3c** and the β-hydride-elimination carbene product **8**[3]—was significantly enhanced (Table 1, entry 3). Moreover, 2-ethoxycarbonyl-1-tetralone **1b** surprisingly furnished a fairly high yield of azide **5b** and only trace amounts of the expected diazo butanoate **3b** (Table 1, entry 2).

Differently from the above keto esters **1a**−**c**, their more acidic congeners **2a**,**b** reacted fairly rapidly with tosyl azide and, additionally, failed to afford any azidation product. 1-Methoxycarbonyl-2-indanone **2a**, in fact, interestingly furnished a high yield of a single compound whose spectral data strongly suggested that it had a dihydrophthalazine (**17a**, Ar = 4-Me-C_6H_4) structure or was its tautomer (**17b**, Ar = 4-Me-C_6H_4). Upon treatment with *o*-chloranil in refluxing benzene this compound was rapidly converted to the aromatic phthalazine **18** (Ar = 4-Me-C_6H_4), whose structure was fully established by X-ray crystallographic analysis (Figure 2).[7]

The observed production of a dihydrophthalazine compound, **17a** or **17b** (Ar = 4-Me-C_6H_4), clearly points to the primary intervention of the intermediate diazo acetate **9a** that, under the basic reaction conditions, would readily undergo intramolecular cyclization onto the adjacent carbamoyl enolate (Table 1, entry 4 and Scheme 1). 1-Methoxycarbonyl-2-tetralone **2b** gave instead the isolable diazo acetate **9b**, but in moderate yield, together with the tosylamino-substituted tetralone **11** to a minor extent (Table 1, entry 5).

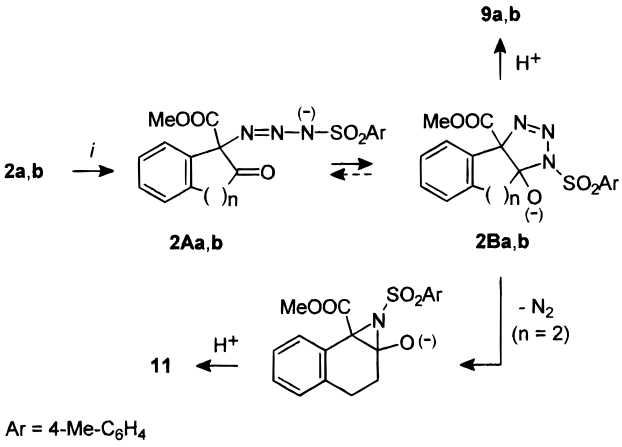
(7) Listings of atomic coordinates, thermal parameters, bond lengths, and bond angles have been deposited at the Cambridge Crystallographic Data Centre. The data can be obtained, on request, from the Director, the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2, 1EZ, UK.

Scheme 1[a]



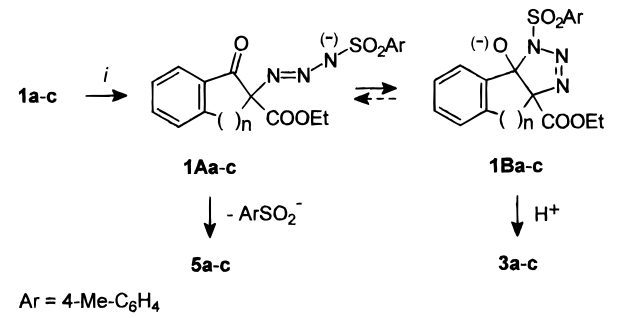
[a] Reagents: (i) *o*-chloranil, benzene, 80 °C.

Scheme 2[a]



[a] Reagents: (i) TsN_3, Et_3N, 20 °C.

Scheme 3[a]



[a] Reagents: (i) TsN_3, Et_3N, 20 °C.

The present findings therefore revealed that the keto esters **2a**,**b** are fairly prone to undergo diazo transfer from tosyl azide, in contrast with the analogues **1a**−**c**, which show a marked tendency to exhibit azido transfer. This fact can be explained on the basis of the likely mechanism outlined in Schemes 2 and 3 for compounds **2a**,**b** and **1a**−**c**, respectively. This would involve the initial intervention of a triazenyl anion **A** and thence a cyclized triazoline **B**.[2,3] The keto esters **2a**,**b**, like the monocyclic counterparts,[3] smoothly lead to intermediate triazolines **2Ba**,**b**, whose usual fragmentations subsequently furnish the corresponding diazo esters **9a**,**b**. Triazoline **2Bb** additionally furnishes the amino-substituted tetralone **11** through a minor decomposition mode probably entailing ring-cleavage isomerization of a transient aziridine (Scheme 2).[2a]

Instead, in the case of keto esters **1a**−**c**, the ensuing triazenyl adducts **1Aa**−**c** are evidently encouraged to fragment into toluene-4-sulfinate and azides **5a**−**c** at the expense of the competing cyclization to the diazo precursors **1Ba**−**c** (Scheme 3).

Consequently, the different behavior of **1a**−**c** and **2a**,**b** is primarily ascribable to the lesser reactivity of the conjugated aryl ketone moiety versus the alkyl one. However, it is likely that unfavorable conformational restraints also play a significant role, at least in limiting diazo transfer to **1b**.

Our subsequent study of the reactions of the benzocyclic keto esters **1a**−**c** and **2a**,**b** with PNBSA proved that the use of this azide reagent, while generally resulting in sizable reaction-rate enhancement as well as essential azido transfer suppression, was of limited advantage for diazo transfer production. In fact, both indanones **1a** and **2a** were rapidly consumed by PNBSA to afford the respective diazo amide esters **4a** and **10a**. The diazo compound **4a** was obtained in high yield as its triethylammonium salt, but on attempted chromatographic purification, it was totally converted into the cyclized isoquinolin-1-one **7** (Table 1, entry 6). The isomeric diazo ester **10a** was decomposed under the reaction conditions to give predominantly the isoquinolin-3-one **13** and only modest amounts of dihydrophthalazine compound **17a** or **17b** (Ar = 4-NO_2-C_6H_4), in contrast to the diazo analogue **9a** (Table 1, entry 7). The poor capability of the diazo compound **10a** to cyclize to phthalazine presumably resulted from higher acidity of its carbamoyl nitrogen, which largely prevented possible production of the adjacent enolate (Scheme 1). Instead, the higher tetralone homologues **1b** and **2b** underwent no virtual diazo-transfer reaction with PNBSA. Compound **1b** gave the indan derivative **14a** (R = Et) in addition to minor amounts of azide **5b** (Table 1, entry 8). Compound **2b** preferentially led to the analogous indan **14a** (R = Me). This product was accompanied by the aminated tetralone **12** and, to a little extent, the benzazepine **16**, which probably arose from spontaneous cyclization of some produced diazo ester **10b** (Table 1, entry 9). Similarly, no evidence for any occurrence of diazo (or azido) transfer from provided by the benzosuberone **1c**, which only led to a corresponding tetralin derivative **14b** (R = Et) in fairly good yield (Table 1, entry 10). The ring-contracted compounds **14a** (R = Et, Me) and **14b** (R = Et) were most likely due to Favorskii-type rearrangements of the respective triazoline adducts **1Bb**, **2Bb**, and **1Bc** (Ar = 4-NO_2-C_6H_4), which possibly proceeded through transient diazonium betaines (Scheme 4). However, the underlying reasons why these triazolines would prefer to exhibit the Favorskii-type rearrangement rather than the expected fragmentation to diazo compounds are not clear at present. It is worth noting that such a rearrangement has never been encountered in the reported examples of diazo transfer from PNBSA to benzoylated esters and ketones.[5]

Our present observation that PNBSA is less prone than tosyl azide to promote azido transfer substantiates recent, unexplained evidence furnished by related reactions of both sulfonyl azides with (acyclic) imide and ester eno-

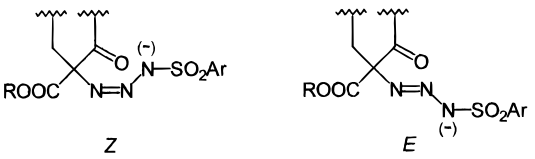
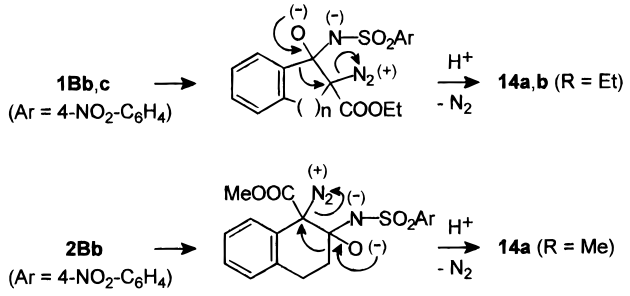


Figure 3.

Scheme 4



lates.[8] For unknown stereoelectronic reasons the nitro substituent might strongly encourage the initial occurrence of *Z*- rather than *E*-triazenyl anions, thus favoring the subsequent cyclization to triazoline (Figure 3). Alternatively, more reactive PNBSA would normally react with our keto ester enolates to give directly triazoline adducts via a 1,3-dipolar cycloaddition process.

Conclusions

Our present and previous findings have proved that the reactions of enolates derived from carbocyclic β-keto esters with tosyl azide and PNBSA are strongly sensitive to both the dicarbonyl substrate and the azide reagent structures. With the five-, six- and seven-membered mono- and benzocyclic keto esters, the tosyl azide reaction normally results in successful deacylating diazo transfer, but with those benzocyclic compounds bearing a conjugated aryl ketone moiety, competing azido transfer can represent a serious drawback. Replacement of tosyl azide with PNBSA normally results in suppression of the azidation process. The diazo transfer may be however accompanied or even prevented by the preferential occurrence of novel ring-contraction rearrangements. Finally, we wish to conclude that our deacylating diazo transfer with cyclic keto esters (and diones) is an appealing process, owing to the availability of the starting substrates and the synthetic potential of the ensuing carbamoyl-substituted diazocarbonyl compounds.[2,3] In the present work, the usefulness of our diazocarbonyl compounds has been further documented by the ready cyclization of the diazo esters **3a**, **4a**, and **10a** to the isoquinolinones **6**, **7**, and **13** and of the higher homologues **9b** and **10b** to the benzazepinones **15** and **16** (see the Experimental Section), as well as by the novel entry to the phthalazine ring system provided by the diazo acetate **9a**.

Experimental Section

General Procedures. The starting keto esters **1a**,[9] **1b**,[10] **1c**,[11] **2a**,[12] **2b**,[13] as well as tosyl[14] and 4-nitrobenzenesulfonyl[15] azide, were prepared following known procedures. [**CAUTION**: like all sulfonyl azide derivatives, PNBSA and especially tosyl azide are potentially explosive; these compounds have been recently subjected to risk evaluation.[16]] All solvents were distilled before use. THF was distilled from sodium-benzophenone and dichloromethane from calcium hydride. All melting points (Kofler melting point apparatus) are uncorrected. ^{1}H and ^{13}C NMR spectra were normally recorded in $CDCl_3$ solutions, using tetramethylsilane as internal standard, unless otherwise stated. Mass spectra were determined by the electron impact method (70 eV). IR spectra were recorded in chloroform solutions. Column chromatography was performed on ICN silica gel (63−200, 60 Å) by gradual elution with light petroleum (bp = 40−70 °C)/diethyl ether and final elution with ethyl acetate and dichloromethane.

Reaction of Arylsulfonyl Azide with Keto Esters 1a−c and 2a,b: General Procedure. A solution of arylsulfonyl azide (8 mmol) and the appropriate keto ester **1a−c** or **2a**,**b** (8 mmol) in THF (10 mL) was treated with freshly distilled triethylamine (8 mmol). The resulting mixture was stirred at rt until disappearance of the starting reagents (monitored by TLC or IR) and quenched by addition of water (30 mL) to pH ∼7. The solution was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo, and the residue (crude 1) was chromatographed. The aqueous solution was acidified with concentrated HCl (pH ∼2) and extracted three times with diethyl ether, and the combined extracts were dried over sodium sulfate and concentrated in vacuo (crude 2). Approximate reaction times and isolated product yields are given in Table 1.

Reaction of Tosyl Azide with Ethyl 1-Oxo-2-indancarboxylate (1a). Column chromatography of crude 1 gave ethyl 2-azido-1-oxo-2-indancarboxylate **5a** [mp = 53−55 °C; ^{1}H NMR (200 MHz) δ 1.28 (3H, t), 3.22 (1H, d, J = 17 Hz), 3.72 (1H, d, J = 17 Hz), 4.32 (2H, q), 7.47−7.94 (4H, m); ^{13}C NMR (50 MHz) 14.49, 38.98, 63.43, 70.61 (q), 126.08, 126.91, 128.88, 136.92, 135.50 (q), 152.60 (q), 168.95 (q), 198.00 (q). Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.14. Found: C, 58.65; H, 4.50; N, 17.17.] and ethyl 2-[(4-methylphenyl)sulfonyl]-1-oxo-1,2,3,4-tetrahydro-3-isoquinolinecarboxylate **6** [mp = 134−135 °C; ^{1}H NMR (300 MHz) δ 1.00 (3H, t, J = 6.7 Hz), 2.43 (3H, s), 3.45 (1H, dd, J_1 = 3.0 Hz, J_2 = 16.8 Hz), 3.56 (1H, dd, J_1 = 7.5 Hz, J_2 = 16.8 Hz), 4.02 (2H, m, becoming an AB system, J = 10.5 Hz, upon irradiation at δ = 1.0), 5.59 (1H, dd, J_1 = 3.0 Hz, J_2 = 7.5 Hz), 7.16−7.99 (4H, m), 7.36 (2H, d, J = 8.1 Hz), 8.06 (2H, d, J = 8.1 Hz); ^{13}C NMR (50 MHz) 14.30, 22.18, 32.54, 57.29, 62.62, 128.04, 128.34, 128.55 (q), 128.81 (q), 129.39, 129.57, 130.08, 134.12, 136.21 (q), 145.42 (q), 163.09 (q), 170.08 (q). Anal. Calcd for $C_{19}H_{19}NO_5S$: C, 61.11; H, 5.13; N, 3.75; S, 8.59. Found: C, 61.20; H, 5.12; N, 3.76; S, 8.62.].

Crude 2 gave ethyl 2-diazo-3-[2-({[(4-methylphenyl)-sulfonyl]amino}carbonyl)phenyl]propanoate **3a** as an oil; ^{1}H NMR (200 MHz) δ 1.22 (3H, t), 2.44 (3H, s), 3.67 (2H, s), 4.22 (2H, q), 7.25−8.11 (8H, m). Compound **3a** furnished quantitatively isoquinolinone **6** after 8 days at rt in chloroform solution; the decomposition of **3a** to **6** was virtually immediate in the presence of silica gel.

Reaction of Tosyl Azide with Ethyl 1-Oxo-1,2,3,4-tetrahydro-2-naphthalenecarboxylate (1b). Without aqueous workup, column chromatography of the crude product obtained by evaporation of the solvent gave ethyl 2-azido-1-oxo-1,2,3,4-tetrahydro-2-naphthalenecarboxylate **5b** [mp = 31−33 °C; ^{1}H NMR (200 MHz) δ 1.28 (3H, t, J = 6.9 Hz), 2.08−2.25 (1H, m), 2.51−2.70 (1H, m), 2.83−3.23 (2H, m), 4.29 (2H, q, J = 6.9 Hz), 7.21−8.08 (4H, m); ^{13}C NMR (50 MHz) 14.07, 24.81, 31.40, 62.71, 70.89 (q), 127.27, 128.50, 129.91, 129.96

(8) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 4011.
(9) Sartori, G.; Bigi, F.; Maggi, R.; Bernardi, G. L. *Tetrahedron Lett.* **1993**, *34*, 7339.
(10) Bachmann, W. E.; Wendler, N. L. *J. Am. Chem. Soc.* **1946**, *68*, 2580.
(11) Anderson, A. G., Jr.; Greef, H. F. *J. Am. Chem. Soc.* **1952**, *74*, 5203.
(12) Harmata, M.; Murray, T. *J. Org. Chem.* **1989**, *54*, 3761.
(13) Oommen, P. K. *Aust. J. Chem.* **1976**, *29*, 1393.
(14) Regitz, M.; Hocker, J.; Liedhegeum, A. *Org. Synth.* **1968**, *48*, 36.
(15) Reagan, M. T.; Nickon, A. *J. Am. Chem. Soc.* **1968**, *90*, 4102.
(16) Bollinger, F. W.; Tuma, L. D. *Synlett.* **1996**, 407.

(q), 134.70, 143.57 (q), 168.58 (q), 189.51 (q). Anal. Calcd for $C_{13}H_{13}N_3O_3$: C, 60.23; H, 5.05; N, 16.21. Found: C, 60.32; H, 5.07; N, 16.17.] and trace amounts of ethyl 2-diazo-4-[2-({[(4-methylphenyl)sulfonyl]amino}carbonyl)phenyl]butanoate **3b** as a yellow oil.

Reaction of Tosyl Azide with Ethyl 5-Oxo-6,7,8,9-tetrahydro-5*H*-benzo[*a*]cycloheptene-6-carboxylate (1c). Column chromatography of crude 1 gave ethyl 6-azido-5-oxo-6,7,8,9-tetrahydro-5*H*-benzo[*a*]cycloheptene-6-carboxylate **5c** as an oil [^{1}H NMR (200 MHz) δ 1.22 (3H, t, J = 6.9 Hz), 1.71−2.37 (4H, m), 2.73−3.10 (2H, m), 4.24 (2H, m), 7.14−7.57 (4H, m); ^{13}C NMR (50 MHz) 14.40, 21.90, 31.25, 32.35, 63.05, 74.14 (q), 127.42, 129.25, 129.61, 133.06, 138.42 (q), 139.15 (q), 169.30 (q), 202.20 (q). Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.65; H, 5.50; N, 15.42.] and a 3:2 *E*/*Z* mixture of ethyl 5-[2-({[(4-methylphenyl)-sulfonyl]-amino}carbonyl)phenyl]-2-pentenoate **8** [*E*-isomer: ^{1}H NMR (200 MHz) δ 1.30 (3H, t, J = 6.9 Hz), 2.17−2.41 (2H, m), 2.48 (3H, s), 2.78 (2H, bt, J = 8 Hz), 4.26 (2H, q, J = 6.9 Hz), 5.74 (1H, d, J = 16 Hz), 6.89 (1H, dt, J_d = 16 Hz, J_t = 6.8 Hz), 7.17−8.17 (8H, m); *Z*-isomer: ^{1}H NMR (200 MHz) δ 1.22 (3H, t, J = 6.9 Hz), 2.48 (3H, s), 2.87−3.09 (2H, m), 3.37−3.61 (2H, m), 4.13 (2H, q, J = 6.9 Hz), 5.78 (1H, d, J = 12 Hz), 6.17 (1H, dt, J_d = 12 Hz, J_t = 7.6 Hz), 7.17−8.08 (8H, m)].

The crude 2 gave ethyl 2-diazo-5-[2-({[(4-methylphenyl)-sulfonyl]amino}carbonyl)phenyl]pentanoate **3c** as a yellow oil. Compound **3c** gave quantitatively alkene **8** (*E*/*Z* mixture) after 10 days in chloroform solution.

Reaction of Tosyl Azide with Methyl 2-Oxo-1-indancarboxylate (2a). Without aqueous workup, flash column chromatography (ethyl acetate/ethanol) of the crude material obtained by evaporation of the solvent gave a product that was suspended in water and acidified with concentrated HCl. Extraction with diethyl ether afforded methyl 4-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-3,4-dihydro-1-phthalazinecarboxylate **17a** (Ar = 4-Me-C_6H_4) or methyl 4-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-1,2-dihydro-1-phthalazinecarboxylate **17b** (Ar = 4-Me-C_6H_4); mp = 181−183 °C (from toluene); ^{1}H NMR (200 MHz, THF-d_8) δ 2.37 (3H, s), 3.72 (3H, s), 4.98 (1H, s), 7.00 (1H, m), 7.21−7.34 (4H, m), 7.82 (2H, d, J = 8.4 Hz), 8.17 (1H, m), 8.47 (1H, bs); ^{13}C NMR (50 MHz, DMSO-d_6) 21.20, 51.81, 57.15, 123.36 (q), 124.32, 125.98 (q), 126.76, 127.71, 129.32, 129.83, 130.60, 130.70 (q), 135.80 (q), 145.09 (q), 164.07 (q), 169.14 (q). Anal. Calcd for $C_{18}H_{17}N_3O_5S$: C, 55.81; H, 4.42; N, 10.85; S, 8.28. Found: C, 55.89; H, 4.40; N, 10.90; S, 8.32.]. The dihydrophthalazine slowly aromatized in solution into methyl 4-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-1-phthalazinecarboxylate **18** (Ar = 4-Me-C_6H_4); mp = 200−202 °C; ^{1}H NMR (300 MHz) δ 2.44 (3H, s), 4.18 (3H, s), 7.38 (2H, d, J = 8.2 Hz), 8.03−8.12 (2H, m), 8.15 (2H, d, J = 8.2 Hz), 8.60−8.70 (1H, m), 9.40−9.50 (1H, m), 10.80 (1H, bs); ^{13}C NMR (50 MHz) 22.17, 54.19, 126.12, 126.29 (q, 2C, probably C_{4a} and C_{8a}), 126.84, 129.10, 130.17, 134.86, 135.33, 135.93 (q), 145.88 (q), 147.55 (q), 153.23 (q), 161.86 (q), 164.85 (q). Anal. Calcd for $C_{18}H_{15}N_3O_5S$: C, 56.10; H, 3.92; N, 10.90; S, 8.32. Found: C, 56.17; H, 3.91; N, 10.94; S, 8.29. The structure of **18** (Ar = 4-Me-C_6H_4) was confirmed by X-ray diffraction (see below). The dihydrophthalazine was quantitatively converted into **18** by a 10-min reflux in benzene solution in the presence of *o*-chloranil.

Reaction of Tosyl Azide with Methyl 2-Oxo-1,2,3,4-tetrahydro-1-naphthalenecarboxylate (2b). This reaction was carried out at 0 °C for 30 min and then at rt for 12 h. Without aqueous workup, the solvent was evaporated and the residue chromatographed to give methyl 1-{[(4-methylphenyl-)sulfonyl]amino}-2-oxo-1,2,3,4-tetrahydro-1-naphthalenecarboxylate **11** [mp = 126−127 °C; ^{1}H NMR (200 MHz) δ 2.35 (3H, s), 2.90−3.52 (4H, m), 3.65 (3H, s), 6.44 (1H, bs), 6.76−6.90 (2H, m), 7.05 (2H, d, J = 8.1 Hz), 7.19−7.30 (4H, m); ^{13}C NMR (50 MHz) 21.32, 27.93, 38.29, 54.07, 69.00 (q), 127.13, 127.21, 128.86, 129.02, 129.13, 129.48, 132.40 (q), 137.50 (q), 138.50 (q), 142.90 (q), 168.05 (q), 204.00 (q). Anal. Calcd for $C_{19}H_{19}NO_5S$: C, 61.11; H, 5.13; N, 3.75; S, 8.59. Found: C, 61.16; H, 5.11; N, 3.74; S, 8.63.] and methyl 2-diazo-2-[2-(3-{[(4-methylphenyl)sulfonyl]amino}-3-oxopropyl)phenyl]acetate **9b** [yellow solid, mp = 56−58 °C (dec); ^{1}H NMR (200 MHz) δ 2.33−2.56 (2H, m), 2.44 (3H, s), 2.71−3.02 (2H, m), 3.87 (3H, s), 7.02−7.35 (6H, m), 7.83 (2H, d, J = 8.1 Hz)]. In benzene solution, compound **9b** was quantitatively converted (slowly at rt, in 10 min at 80 °C) into methyl 2-[(4-methylphenyl)sulfonyl]-3-oxo-2,3,4,5-tetrahydro-1*H*-2-benzazepine-1-carboxylate **15**: mp = 186−187 °C (from 2-propanol); ^{1}H NMR (200 MHz) δ 2.47 (3H, s), 2.55−2.94 (2H, m), 2.96−3.13 (2H, m), 3.81 (3H, s), 6.55 (1H, s), 7.23−7.61 (6H, m), 7.97 (2H, d, J = 8.4 Hz); ^{13}C NMR (50 MHz) 22.16, 28.56, 36.79, 54.16, 62.42, 127.47, 129.59 (b, 2C), 129.77, 130.77, 132.55 (q), 132.66, 136.22 (q), 137.48 (q), 145.29 (q), 170.95 (q), 172.66 (q). Anal. Calcd for $C_{19}H_{19}NO_5S$: C, 61.11; H, 5.13; N, 3.75; S, 8.59. Found: C, 61.15; H, 5.14; N, 3.75; S, 8.62.

Reaction of PNBSA with 1a. This reaction was carried out at 0 °C for 30 min and then at rt for 2 h. Without aqueous workup, the solvent was evaporated and the oily yellow residue was washed several times with diethyl ether. ^{1}H NMR analysis of this crude product (94% yield) was consistent with the triethylammonium salt of ethyl 2-diazo-3-[2-({[(4-nitrophenyl)sulfonyl]amino}carbonyl)phenyl]propanoate (**4a**): ^{1}H NMR (200 MHz) δ 1.27 (3H, t, J = 7.2 Hz), 1.31 (9H, t, J = 7.4 Hz), 3.18 (6H, q, J = 7.4 Hz), 3.91 (2H, s), 4.17 (2H, q, J = 7.2 Hz), 7.13−7.35 (3H, m), 7.77 (1H, bd), 8.17 (2H, d, J = 8.8 Hz), 8.26 (2H, d, J = 8.8 Hz). By column chromatography, the triethylammonium salt of **4a** quantitatively gave ethyl 2-[(4-nitrophenyl)sulfonyl]-1-oxo-1,2,3,4-tetrahydro-3-isoquinolinecarboxylate **7**: mp = 178−180 °C; ^{1}H NMR (200 MHz) δ 1.07 (3H, t), 3.42−3.71 (2H, m), 4.00−4.20 (2H, m), 5.56−5.64 (1H, m), 7.20−7.58 (3H, m), 7.96 (1H, bd), 8.40 (4H, bs); ^{13}C NMR (50 MHz) 14.43, 32.45, 57.47, 63.00, 123.99, 127.82 (q), 128.15, 128.66, 129.01, 131.79, 134.70, 136.24 (q), 144.57 (q), 151.09 (q), 163.13 (q), 169.94 (q). Anal. Calcd for $C_{18}H_{16}N_2O_7S$: C, 53.46; H, 3.99; N, 6.93; S, 7.93. Found: C, 53.50; H, 4.00; N, 6.95; S, 7.96.

Reaction of PNBSA with 1b. Column chromatography of crude 1 gave **5b**. Crude 2 was ethyl 1-({[(4-nitrophenyl)-sulfonyl]amino}carbonyl)-1-indancarboxylate **14a** (R = Et); mp = 130−132 °C (from chloroform); ^{1}H NMR (200 MHz) δ 1.19 (3H, t, J = 6.9 Hz), 2.60−2.88 (2H, m), 3.06 (2H, bt), 4.21 (2H, q, J = 6.9 Hz), 7.22−7.48 (4H, m), 8.28 (2H, d, J = 8.5 Hz), 8.42 (2H, d, J = 8.5 Hz), 9.92 (1H, bs); ^{13}C NMR (50 MHz) 14.27, 31.69, 33.52, 63.44, 66.93 (q), 124.42, 124.52, 126.16, 127.89, 130.11, 130.40, 138.94 (q), 144.10 (q), 145.14 (q), 151.23 (q), 168.48 (q), 171.90 (q). Anal. Calcd for $C_{19}H_{18}N_2O_7S$: C, 54.54; H, 4.34; N, 6.70; S, 7.66. Found: C, 54.60; H, 4.33; N, 6.72; S, 7.69.

Reaction of PNBSA with 1c. A vigorous evolution of nitrogen was observed. Direct acidification of the reaction mixture and extraction gave ethyl 1-({[(4-nitro-phenyl)-sulfonyl]amino}carbonyl)-1,2,3,4-tetrahydro-1-naphthalenecarboxylate **14b** (R = Et); mp = 155−157 °C; ^{1}H NMR (200 MHz) δ 1.17 (3H, t, J = 6.9 Hz), 1.59−1.98 (2H, m), 2.25−2.48 (2H, m), 2.83 (2H, bt), 4.18 (2H, q, J = 6.9 Hz), 7.07−7.34 (4H, m), 8.15 (2H, d, J = 8.5 Hz), 8.40 (2H, d, J = 8.5 Hz), 9.09 (1H, bs); ^{13}C NMR (50 MHz, acetone-d_6) 14.56, 20.63, 29.77, 31.41, 62.40 (q), 62.91, 125.42, 126.95, 129.25, 130.71, 131.04, 131.32, 132.44 (q), 138.89 (q), 145.71 (q), 152.15 (q), 172.22 (q), 172.03 (q). Anal. Calcd for $C_{20}H_{20}N_2O_7S$: C, 55.55; H, 4.66; N, 6.48; S, 7.42. Found: C, 55.60; H, 4.64; N, 6.51; S, 7.45.

Reaction of PNBSA with 2a. This reaction was carried out at 0 °C for 10 min and then at rt for 1 h. A vigorous evolution of nitrogen was observed. Direct acidification of the reaction mixture gave a crude 2 that was washed many times with diethyl ether, affording methyl 4-({[(4-nitrophenyl)-sulfonyl]amino}carbonyl)-3,4-dihydro-1-phthalazinecarboxylate **17a** (Ar = 4-NO_2-C_6H_4) or methyl 4-({[(4-nitrophenyl)-sulfonyl]amino}carbonyl)-1,2-dihydro-1-phthalazinecarboxylate **17b** (Ar = 4-NO_2-C_6H_4); mp = 193−195 °C (dec); ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.74 (3H, s), 5.15 (1H, s), 7.30−7.46 (3H, m), 7.90−8.00 (1H, m), 8.09 (2H, d, J = 8.8 Hz), 8.37 (2H, d, J = 8.8 Hz), 9.09 (1H, bs). Anal. Calcd for $C_{17}H_{14}N_4O_7S$: C, 48.80; H, 3.37; N, 13.39; S, 7.66. Found: C, 48.88; H, 3.37; N, 13.36; S, 7.69. Treatment of this dihydrophthalazine with *o*-chloranil in refluxing benzene for 10 min quantitatively

afforded methyl 4-({[(4-nitrophenyl)sulfonyl]amino}carbonyl)-1-phthalazinecarboxylate **18** (Ar = 4-NO_2-C_6H_4); mp = 237−238 °C (dec); ^{1}H NMR (200 MHz, DMSO-d_6) δ 4.11 (3H, s), 8.17−8.36 (4H, m), 8.41 (2H, d, J = 8.4 Hz), 8.54 (1H, bs), 8.60 (2H, d, J = 8.4 Hz); ^{13}C NMR (50 MHz, DMSO-d_6) 53.83, 124.04 (q), 124.22 (q), 124.81, 125.19, 125.67, 129.57, 134.96, 135.11, 145.47 (q), 150.50 (q), 152.25 (q), 153.24 (q), 164.69 (q), 164.72 (q). Anal. Calcd for $C_{17}H_{12}N_4O_7S$: C, 49.04; H, 2.91; N, 13.46; S, 7.70. Found: C, 49.11; H, 2.91; N, 13.42; S, 7.73. Column chromatography of the above ethereal washings **17a** or **17b** gave methyl 2-[(4-nitrophenyl)sulfonyl]-3-oxo-1,2,3,4-tetrahydro-1-isoquinolinecarboxylate **13**; mp = 159−161 °C; ^{1}H NMR (200 MHz) δ 3.73 (1H, d, J = 18 Hz), 3.76 (3H, s), 3.84 (1H, d, J = 18 Hz), 6.16 (1H, s), 7.07−7.16 (1H, m), 7.27−7.36 (2H, m), 7.43−7.53 (1H, m), 8.22 (2H, d, J = 8.5 Hz), 8.34 (2H, d, J = 8.5 Hz); ^{13}C NMR (50 MHz) 39.53, 54.04, 62.27, 124.11, 128.14, 128.23, 128.43, 129.13 (q), 130.15, 131.29 (q), 131.46, 144.04 (q), 151.26 (q), 169.02 (q), 169.39 (q). Anal. Calcd for $C_{17}H_{14}N_2O_7S$: C, 52.31; H, 3.61; N, 7.18; S, 8.21. Found: C, 52.38; H, 3.62; N, 7.14; S, 8.25.

Reaction of PNBSA with 2b. The IR spectrum of the reaction crude showed neither diazo nor azido absorption. The crude was then poured into water, acidified with concentrated HCl, and extracted with diethyl ether. The solvent was evaporated and the residue chromatographed to give methyl 2-[(4-nitrophenyl)sulfonyl]-3-oxo-2,3,4,5-tetrahydro-1*H*-2-benzazepine-1-carboxylate **16** [mp = 196−197 °C; ^{1}H NMR (200 MHz) δ 2.60−2.87 (2H, m), 2.95−3.10 (2H, m), 3.80 (3H, s), 6.40 (1H, s), 7.15−7.53 (4H, m), 8.20 (2H, d, J = 8.5 Hz), 8.35 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz) 27.98, 36.34, 54.04, 62.23, 123.69, 127.30, 129.69, 130.41, 130.56, 131.70 (q), 132.19, 136.95 (q), 144.45 (q), 150.57 (q), 170.41 (q), 172.40 (q). Anal. Calcd for $C_{18}H_{16}N_2O_7S$: C, 53.46; H, 3.99; N, 6.93; S, 7.93. Found: C, 53.52; H, 3.98; N, 6.95; S, 7.96.], methyl 1-{[(4-nitrophenyl)sulfonyl]amino}-2-oxo-1,2,3,4-tetrahydro-1-naphthalenecarboxylate **12** [mp = 173−174 °C; ^{1}H NMR (200 MHz) δ 2.93−3.27 (3H, m), 3.47−3.55 (1H, m), 3.70 (3H, s), 6.70 (1H, bs), 6.80−6.85 (2H, m), 7.17−7.30 (2H, m), 7.50 (2H, d, J = 8.5 Hz), 8.10 (2H, d, J = 8.5 Hz); ^{13}C NMR (50 MHz) 28.50, 39.10, 50.92, 69.65 (q), 124.11, 127.24, 128.44, 128.50, 129.28, 129.57, 132.92 (q), 138.38 (q), 147.44 (q), 149.99 (q), 168.19 (q), 203.67 (q). Anal. Calcd for $C_{18}H_{16}N_2O_7S$: C, 53.46; H, 3.99; N, 6.93; S, 7.93. Found: C, 53.53; H, 3.99; N, 6.91; S, 7.96.], and methyl 1-({[(4-nitrophenyl)sulfonyl]amino}carbonyl)-1-indancarboxylate **14a** (R = Me) [mp = 161−162 °C (by dissolving in dichloromethane and reprecipitating with diethyl ether); ^{1}H NMR (200 MHz) δ 2.55−2.86 (2H, m), 3.05 (2H, bt, J = 7.3 Hz), 3.73 (3H, s), 7.16−7.40 (4H, m), 8.20 (2H, d, J = 8.5 Hz), 8.35 (2H, d, J = 8.5 Hz), 9.80 (1H, bs); ^{13}C NMR (50 MHz) 31.88, 33.95, 54.40, 66.67 (q), 124.79, 125.10, 126.37, 128.15, 130.39, 130.64, 138.96 (q), 144.23 (q), 146.36 (q), 151.48 (q), 168.73 (q), 172.61 (q). Anal. Calcd for $C_{18}H_{16}N_2O_7S$: C, 53.46; H, 3.99; N, 6.93; S, 7.93. Found: C, 53.55; H, 4.01; N, 6.90; S, 7.97.].

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Supporting Information Available: IR and MS data for compounds **3a**−**c**, **4a**, **5a**−**c**, **6**, **7**, **9b**, **11**−**13**, **14a**,**b** (R = Et), **14a** (R = Me), **15**, **16**, **17a**/**b** (Ar = 4-Me-C_6H_4 and 4-NO_2-C_6H_4), **18** (Ar = 4-Me-C_6H_4), X-ray crystal structure analysis and selected bond lengths and angles for the phthalazine **18** (Ar = 4-Me-C_6H_4) (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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