(M^{+}) 307.0885. The IR and ^1H NMR spectra for **24** were in substantial agreement with literature data.[27]

(2*S*,5*R*,6*S*)-Benzyl 3,3-Dimethyl-7-oxo-6-[[(trifluoromethyl)sulfonyl]oxy]-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate. A solution of **24** (28 mg, 0.092 mmol) and Et_3N (20 mg, 0.18 mmol) in dry CH_2Cl_2 (3 mL) was cooled to 0 °C, and trifluoromethanesulfonyl chloride (24 mg, 0.14 mmol) was added dropwise under N_2. After 15 min, the solvent was evaporated under reduced pressure, and the residue was further dried under high vacuum for 1 h. The resultant oil was dissolved in CH_2Cl_2 and filtered through silica gel to afford the crude triflate (40 mg): IR (film) 2976, 2939, 2873, 1797, 1745, 1646, 1617, 1425, 1382, 1216, 1141, 1054, 957, 843, 812, 733, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (m, 5 H), 5.51 (br s, 2 H), 5.21 (m, 2 H), 4.58 (s, 1 H), 1.57 (s, 3 H), 1.40 (s, 3 H). The triflate was used directly in the next step.

(2*S*,5*R*,6*R*)-Benzyl 6-Azido-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (25). The foregoing triflate (40 mg, 0.092 mmol) was dissolved in dry DMF (1 mL), and LiN_3 (24 mg, 0.46 mmol) was added under N_2. After the reaction mixture was stirred at room temperature for 18 h, the DMF was evaporated under high vacuum at room temperature to leave a residue. This was extracted with $CHCl_3$ (3 × 10 mL), filtered, and concentrated. Purification by PLC (1:1 Et_2O–pentane) gave **25** (28 mg, 90%) as a clear, colorless oil: R_f 0.47 (1:1 Et_2O–pentane); $[\alpha]^{23}_D$ +125.7° (*c* 1.2, $CHCl_3$); IR (film) 3010, 2970, 2150, 1805, 1760, 1625, 1470, 1390, 1310, 1280, 1215, 1195, 1170, 1140, 1040, 980, 815, 760, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (m, 5 H), 5.48 (d, 1 H, J = 4 Hz), 5.19 (s, 2 H), 4.92 (d, 1 H, J = 4 Hz), 4.51 (s, 1 H), 1.65 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.9, 167.4, 134.6, 128.8, 128.76, 128.74, 70.3, 67.9, 67.6, 66.7, 64.7, 31.8, 26.7; MS (EI) *m/e* 304 (M^{+} – N_2, 4), 114 (35), 91 (100); high-resolution mass ion measurement calcd for $C_{15}H_{16}N_4O_3S$ (M^{+} – N_2) 304.0882, found (M^{+} – N_2) 304.0877.

(2*S*,5*R*,6*R*)-6-Amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic Acid (26). The azide **25** (21 mg, 0.063 mmol) in dry EtOAc (1.5 mL) was hydrogenolyzed over hydrogen-pretreated 10% Pd/C (Engelhard Industries) (50 mg) at room temperature until TLC (1:1 Et_2O–pentane) showed the reaction was completed (3 h). The reaction mixture was centrifuged, and the supernatant was decanted. The residue was extracted with 10% $NaHCO_3$ solution (3 × 0.5 mL), and the combined $NaHCO_3$ solutions were neutralized with 10% HCl at 0 °C to pH 7. PhMe (18 mL) was added, and the solvent was evaporated under reduced pressure at 30 °C to give a white crystalline solid. Recrystallization from a small volume of 10% aqueous $NaHCO_3$ solution by adding 10% aqueous HCl to pH 4 at 0 °C gave **26** (8 mg, 59%) as pure white crystals: mp 208–210 °C (lit.[31] mp 208–209 °C dec), mixed mp 208–209 °C; $[\alpha]^{23}_D$ +272.8° (*c* 0.50, 0.1 M HCl) (lit.[31] $[\alpha]^{31}_D$ + 273° (*c* 1.2, 0.1 M HCl)); IR (KBr) 3300–2300, 1795, 1650, 1550, 1440, 1360, 1280, 1235, 1140, 1120, 1045, 1020, 990, 930, 915, 885, 835, 780, 760, 710, 680, 600 cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.40 (d, 1 H, J = 4 Hz), 4.55 (d, 1 H, J = 4 Hz), 4.14 (s, 1 H), 1.56 (s, 3 H), 1.47 (s, 3 H); MS (EI) *m/e* 216 (M^{+}; 11), 160 (67), 114 (19), 75 (50); high-resolution mass ion measurement calcd for $C_8H_{12}N_2O_3S$: (M^{+}) 216.0569, found (M^{+}) 216.0577. The synthetic material was identical with authentic **26** by IR and ^1H NMR data.

Acknowledgment. We thank Drs. Sven J. Taylor, Minn-Chang Cheng, and Christopher D. Spilling for preliminary studies on the preparation of (benzyloxy)nitromethane and the aldehyde **7**. We thank the National Institutes of Health (AI-22034) for generous support of our program and for funds to purchase a 400-MHz NMR spectrometer (RR-01672) and a high-resolution mass spectrometer (RR-03245) used in these studies.

(31) Batchelor, F. R.; Doyle, F. P.; Nayler, J. H. C.; Robinson, G. N. *Nature* **1959**, *183*, 257.

A Novel Base-Catalyzed Carbon–Nitrogen Bond Fission in Some Heterocycles

Bansi Lal,* Ramesh M. Gidwani, and Noel J. de Souza

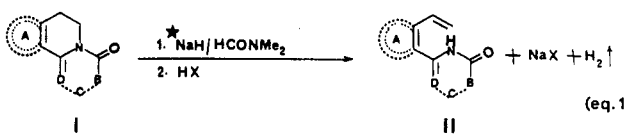
Department of Chemistry, Hoechst Centre for Basic Research, Hoechst India Limited, Mulund, Bombay 400 080, India

Received January 10, 1990

Nitrogen heterocycles bearing a nonbasic nitrogen atom and other defined structural features as exemplified by 9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (**1**), 8-oxypseudopalmatine (**22**), 8-oxypseudoberberine (**25**), rutaecarpine (**39**), and related systems, on heating with excess sodium hydride in polar aprotic solvents, undergo a facile carbon–nitrogen bond cleavage reaction to give new nitrogen heterocycles with an arylvinyl group as one of the substituents. The nature, scope, postulated mechanism, and limitations of this novel carbon–nitrogen cleavage reaction are described.

Introduction

We describe here a novel method for cleavage of a carbon–nitrogen bond in cyclic compounds of the general formula I incorporating a nonbasic nitrogen atom and other structural features as depicted and subsequently defined. Such structural moieties are present for instance in certain alkaloids of the classes of berberines and rutaecarpines. The novel reaction comprises treatment of a compound represented by the formula I with excess sodium hydride in dimethylformamide, resulting in the formation of the olefin II as a cleavage product according to eq 1.



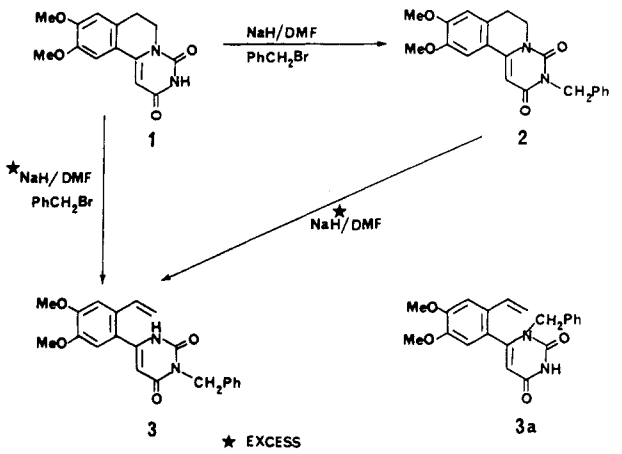
I II (eq. 1)

Although different methods such as the Hofmann,[1] Emde,[2] and Von Braun[3] degradation reactions are well known for cleavage of carbon–nitrogen bonds in which the nitrogen atom has a distinctly basic character, there is only one reported example[4] of a molecule corresponding to formula I, which has been found to cleave to a product of formula II. In this example, the olefin obtained was unexpected and an uncommon side product of the main objective of the study. No investigation or attempt was made to explain the mode of its formation. A few other

(1) (a) Hofmann, A. W. *Chem. Ber.* **1881**, *14*, 659. (b) Cope, A. C.; Trumbull, E. R. *Org. React.* **1960**, *11*, 320.
(2) (a) Emde, H. *Chem. Ber.* **1909**, *42*, 2590. (b) Emde, H.; Kull, H. *Arch. Pharm.* **1934**, 272, 469.
(3) Hageman, H. A. *Org. React.* **1953**, *7*, 198.
(4) (a) Kametani, T.; Honda, T.; Sugai, T.; Fukumoto, K. *Heterocycles* **1976**, *4*, 927. (b) Kametani, T.; Sugai, T.; Shoji, Y.; Honda, T.; Satoh, F.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1151.

0022-3263/90/1955-5117$02.50/0

Scheme I



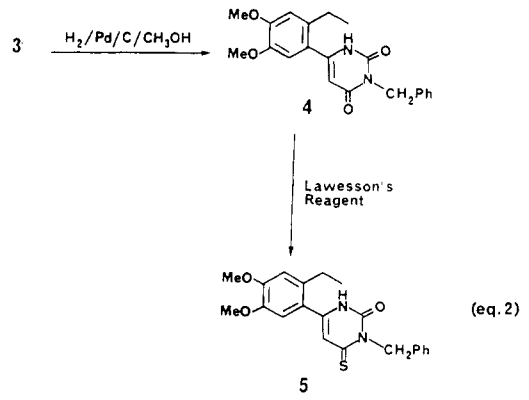
examples[5-9] of carbon–nitrogen bond fission reactions in nonbasic nitrogen compounds are reported, which to an extent bear relevance to this study.

In this paper we describe the nature, scope, advantages, and limitations of this novel reaction.

The finding of the reaction arose from the follow up of an unusual observation during the bulk preparation of a required intermediate[10] **2** (Scheme I) by treatment of **1** with benzyl bromide and sodium hydride. The products of the reaction could be varied depending on the amounts used of sodium hydride.

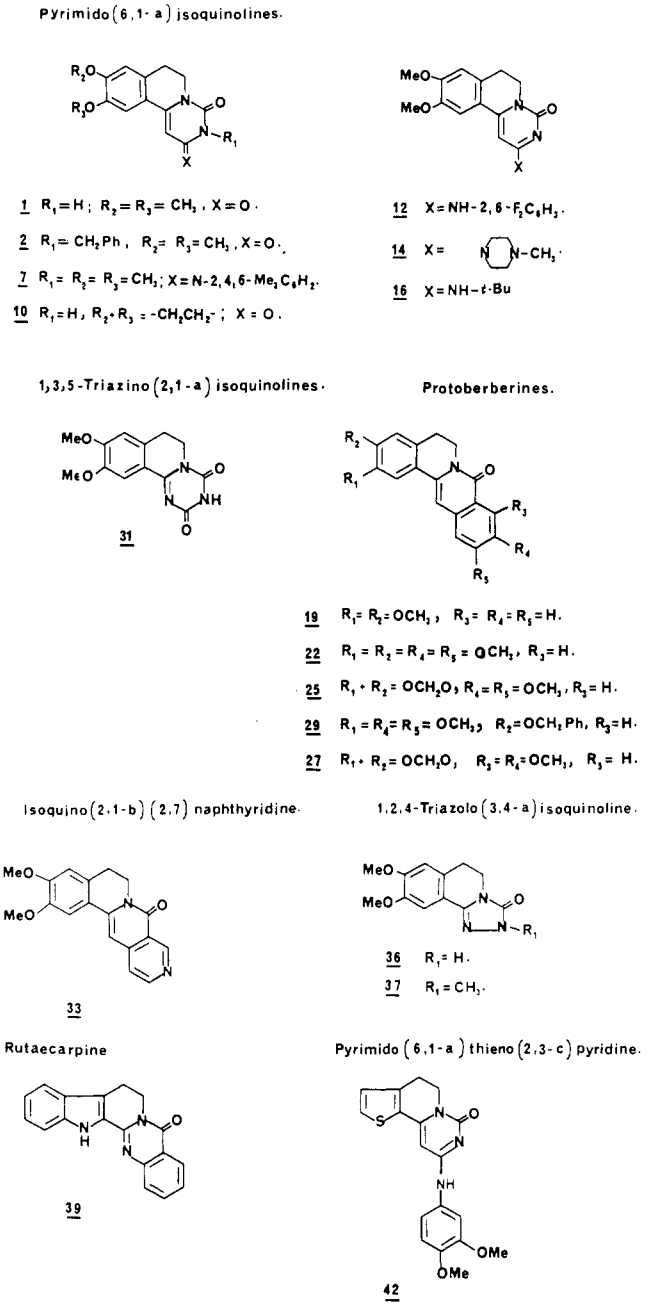
Results and Discussion

Treatment of **1** with an equimolar amount of sodium hydride followed by excess of benzyl bromide gave the desired intermediate **2** in 86% yield. In a scale-up preparation, in which more than equimolar amounts of sodium hydride were used, compound **2** was formed as a minor component of a mixture of products as indicated by TLC. The major component of this mixture was identified as the cleaved compound **3** (Scheme I) in clear distinction from a potentially possible isomer **3a**. Structural assignment was based on spectral data. The ^1H NMR spectrum of the major component lacked triplets due to H-6 and H-7 methylene protons. Instead, an ABX pattern typical for a vinyl group was observed. Catalytic hydrogenation of the above product gave the corresponding ethyl derivative **4** (eq 2). The location of the benzyl group was detemined



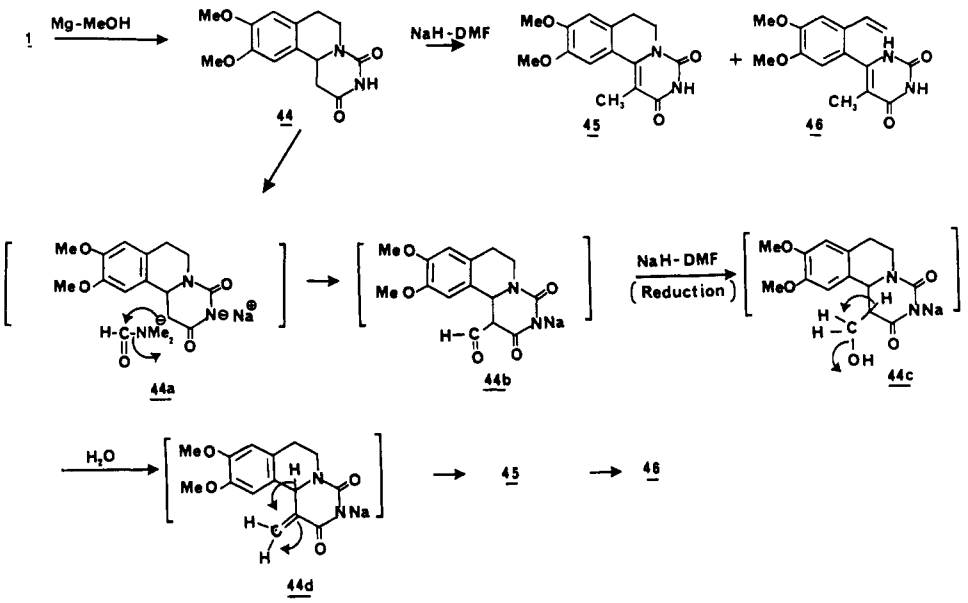
through thionation of compound **4** using Lawesson reagent[11] to provide compound **5** (eq 2). The ^1H NMR data for **5** showed downfield shifts for N-CH_2Ph and the olefinic proton of δ 0.66 and 1.0, respectively, as compared to **4**. The magnitude of this shift was explained by placing the C=S group in the sequence =CHCSNCH$_2$Ph as in **5**.

Chart I



(5) Cook, J. W.; Graham, W.; Cohen, A.; Lapsley, R. W.; Lawrence, C. A. *J. Chem. Soc.* **1944**, 322.
(6) Baumgarten, R. J. *J. Org. Chem.* **1968**, *33*, 234.
(7) Shamma, M.; Toke, L. *Tetrahedron* **1975**, *31*, 1991.
(8) Danieli, B.; Palmisano, G. *J. Heterocycl. Chem.* **1977**, *14*, 839.
(9) Yamada, S.; Murato, K.; Shioiri, T. *Tetrahedron Lett.* **1976**, 1605.
(10) Lal, B.; Dohadwalla, A. N.; Dadkar, N. K.; D'Sa, A.; de Souza, N. J. *J. Med. Chem.* **1984**, *27*, 1470.
(11) Pederson, B. S.; Scheibye, S.; Clausen, K.; Lawesson, S. O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223, 293.
(12) Lal, B., unpublished results.
(13) D'Sa, A. S.; Deodhar, K. D. *Ind. J. Chem.* **1980**, *19B*, 999.
(14) Patra, A.; Montgomery, C. T.; Freyer, A. J.; Guinaudeau, H.; Shamma, M.; Tantisewie, B.; Pharadai, K. *Phytochemistry* **1987**, *26*, 547.
(15) Haworth, R. D.; Perkin, W. H., Jr.; Pink, H. S. *J. Chem. Soc.* **1925**, *127*, 1709.
(16) **29** was prepared from [3-(benzyloxy)-4-methoxyphenyl]ethylamine and 3,4-dimethoxy homophthalic anhydride to give 2-carboxy-*N*-[2-[3-(benzyloxy)-4-methoxyphenyl]ethyl]-4,5-dimethoxyphenylacetamide, which was converted into methyl ester using $SOCl_2/CH_3OH$. The methyl ester was treated with $POCl_3$ to give **29**.
(17) Lal, B.; D'Sa, A. S.; de Souza, N. J. *Ind. J. Chem.* **1984**, *23B*, 1268.
(18) Naito, T.; Ninomiya, I. *Heterocycles* **1980**, *14*, 959.
(19) Bergman, J.; Bergman, S., *J. Org. Chem.* **1985**, *50*, 1246. (We thank the authors for providing us prepublication manuscript).
(20) Lal, B.; Krishnan, L.; de Souza, N. J. *Heterocycles* **1986**, *24*, 1977.

Scheme II



Unambiguous proof for structure **3** was provided by the reaction of 3-benzyl-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (**2**) with excess sodium hydride in DMF which resulted in N5–C6 bond cleavage to a product in 71% yield, identical in all respects with compound **3**. The formation of **3** and not **3a** is a clear indication that benzyl bromide does not play a role in quaternizing the ring junction nitrogen, and that the carbon–nitrogen bond fission is not a consequence of a Hofmann degradation reaction.

This conclusion was supported by treating compound **1** with excess NaH–DMF in the absence of benzyl bromide when it was readily cleaved to the olefin **6** (Table I).

The key to the success of this C–N bond cleavage reaction lies in the use of an excess of sodium hydride. The generality of the reaction was determined by applying it to different compounds in which variations of the moieties A, B, C and D in formula I were to be found. The classes of compounds which were successfully cleaved to products according to eq 1 are depicted in Chart I (cf. also Table I).

The compounds cleaved are representative of (a) natural products such as protoberberines (**22** and **25**) and rutaecarpine (**39**) and (b) synthetic compounds such as the variety of heterocyclic isoquinolines, which were readily available to us. The yield of the cleaved vinyl group bearing product was in the range of 45–86% in 11 out of 17 cases (cf. Table I). In five cases, namely the cleaved products of trequinsin (**7**), protoberberines (**19** and **22**), isoquino[2,1-*b*][2,7]naphthyridine (**33**), and rutaecarpine (**39**), the structure was further confirmed by subjecting the product to catalytic reduction, when the corresponding ethyl derivative was formed as in the case of conversion of **3** to **4**. Although the one exception found to the reaction was the triazolo[3,4-*a*]isoquinoline (**36**), its failure to cleave may be attributed to the proton on the nitrogen atom which is available for enolization, and the consequent overall stabilization of the molecule, thereby preventing the C–N cleavage reaction.

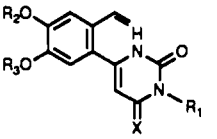
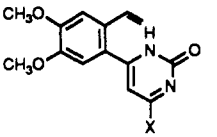
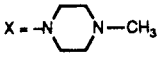
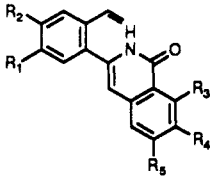
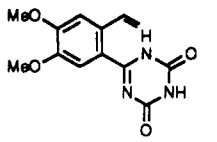
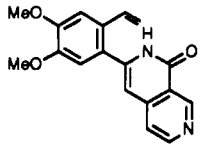
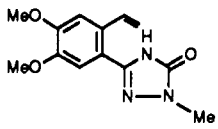
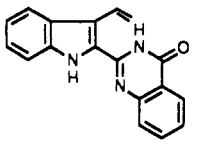
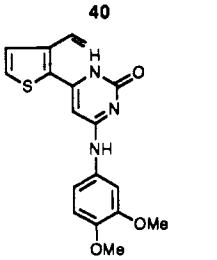
The consolidated data presented above permit a generalized definition of the moieties A, B, C, and D in formula I. A stands for an aromatic ring such as benzene, thiophene or indole. B and C are such that (a) when taken together, they stand for an aromatic ring such as benzene or pyridine; (b) when C stands for C=O or C=N, then B stands preferably for a tertiary nitrogen, but also for secondary nitrogen; (c) when C is omitted, then B in the D–B linkage is preferably tertiary nitrogen. D stands for CH or N.

The importance of the double bond linked to D in the general formula I is illustrated in the following example. Compound **44**, obtained by reduction of **1** with Mg–CH_3OH,[21] on treatment with NaH–DMF gave surprisingly and consistently in several repeated experiments two products **45** and **46** (Scheme II). Both the structures were confirmed by their mass spectra, which show M^+ at 288. The ^1H NMR spectrum of **45** has both H-6 and H-7 triplets intact at δ 3.75 and 2.84, respectively, and an extra methyl group at δ 2.12. Placing the new methyl at position 1 and introducing a double bond between positions 1 and 11b explained the proposed structure. Compound **45** fits the general formula I and therefore cleaves easily to furnish **46** under the NaH–DMF conditions. The ^1H NMR spectrum of **46** showed an ABX pattern for the vinyl group along with an extra singlet for the methyl group at δ 1.46. It is premature to discuss with confidence the mechanism of this reaction; however, a speculative mechanism is proposed (Scheme II). Following the analogy[22] that 4-(ethoxymethyl)pyridine reacts with NaH–DMF to give 4-(1-ethoxyvinyl)pyridine, similarly the reaction of compound **44** with NaH–DMF can give the exocyclic methylene compound **44d**. Alternatively, the NaH–DMF combination may formylate compound **44** at position 1, followed by reduction of the formyl group to an alcohol through single-electron transfer[23] and subsequent elimination of water to provide compound **44d**. Inward movement of the exocyclic double bond under basic conditions[24] will give compound **45**, which has the potential to undergo carbon–nitrogen bond fission in the presence of NaH–DMF to furnish compound **46**.

Compounds which do not conform to the prescribed definition of the general formula I such as compounds **47**,[25] **48**,[10] **49**,[26] and **50**[27] did not give the cleaved compounds on

(21) (a) Profitt, J. A.; Watt, D. S.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 127. (b) Brettle, R.; Shibib, S. M. *Tetrahedron Lett.* **1980**, *21*, 2915.
(22) Yamanaka, H.; Konno, S. *Heterocycles* **1976**, *4*, 1897.
(23) Caubere, P. *Top. Curr. Chem.* **1978**, *73*, 50.
(24) Mcelvain, S. M.; Robert, E. L., Jr. *J. Am. Chem. Soc.* **1950**, *72*, 384.
(25) Elliott, I. W., Jr. *J. Heterocycl. Chem.* **1967**, 639.

Table I. Experimental Details for Cleavage Reaction

entry	substrate and ref	mol[a] equiv of NaH	temp,[a] °C	time,[a] h	product	yield, %	mp, °C
							
1	**1**[10]	5.6	120–125	3.5	**6**: R_1 = H; R_2 = R_3 = CH_3; X = O	50	222–224
2	**2**[10]	6.0	110	0.5	**3**: R_1 = CH_2Ph; R_2 = R_3 = CH_3; X = 0	71	203–205
3	**7**[10]	5.0	80	0.75	**8**: R_1 = R_2 = R_3 = CH_3; X = *N*-2,4,6-$Me_3C_6H_2$	84	265–267
4	**10**[12]		125–130	1.75	**11**: R_1 = H; R_2 + R_3 = $-CH_2CH_2-$; X = 0	15	271–272
							
5	**12**[10]	9.5	120	4.25	**13**: X = HN-2,6-$F_2C_6H_3$	33	233–235
6	**14**[10]	9.0	105	2	**15**: 	45	242
7	**16**[36]	9.0	115–130	4	**17**: X = HN-$C(CH_3)_3$	33	270–271
							
8	**19**[13]	7.0	95–105	3	**20**: R_1 = R_2 = OCH_3; R_3 = R_4 = R_5 = H	78	220–222
9	**22**[14]	7.0	100–110	2.2	**23**: R_1 = R_2 = R_4 = R_5 = OCH_3; R_3 = H	86	255–256
10	**25**[15]	7.0	100–110	3.0	**26**: R_1 + R_2 = OCH_2O; R_4 = R_5 = OCH_3; R_3 = H	70	276–277 dec
11	**27**[37]	7.0	80–90	4.5	**28**: R_1 + R_2 = OCH_2O; R_3 = R_4 = OCH_3; R_5 = H	32	254–255 dec
12	**29**[16]	7.0	100–110	2.5	**30**: R_1 = R_4 = R_5 = OCH_3; R_2 = CH_2Ph; R_3 = H	54	253–254 dec
13	**31**[17]	8.4	120	0.75		12	275–276 dec
					32		
14	**33**[18]	9.0	100–110	3.0		53	219–220
					34		
15	**37**[12]	6.0	125	0.5		78	242–244
					38		
16	**39**[19]	10.0	100–105	22.0		68	274–275 dec
					40		
17	**42**[20]	8.0	100–110	4.0		49	227–229
					43		

[a] Optimization of mol equiv of NaH, temperature, and time has not been done in each case.

Scheme III

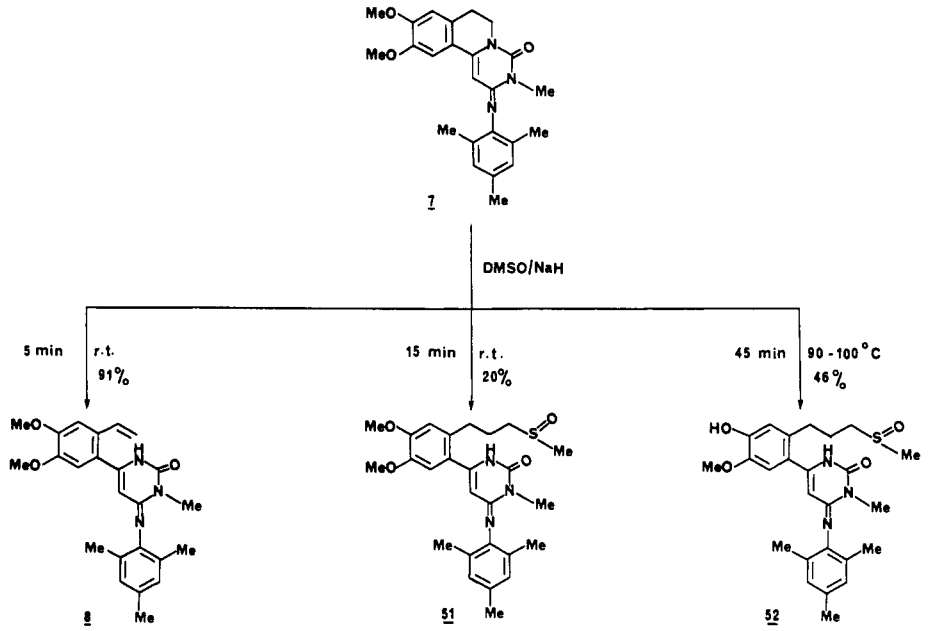
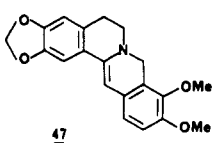


Table II. Reaction of Trequinsin with Different Bases

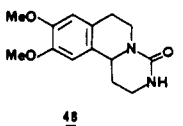
entry	base	solvent	temp, °C	time, min	products (% yield)
1	KOH	none	flame	15	demethylated products
2	$NaOC_2H_5$	C_2H_5OH	80	180	no reaction
3	NaH	$C_6H_5CH_3$	110	210	no reaction
4	KF/18-C-6	DMF	155	210	no reaction
5	NaH	HMPA	90	60	8 (13.6)
6	NaH	DMSO	27	5	8[a] (91)
7	NaH	DMSO	27	15	8[b] (33) + 51 (20)
8	NaH	DMSO	90–100	45	51[c] (4.5) + 52 (46)
9	NaH	DMF	80	45	8 (84)

[a] Reaction of trequinsin with NaH in DMSO or preformed dimsyl anion[28] at 27 °C for 5 min gave the expected cleavage product 8. [b] However, when reaction was continued for 15 min at 27 °C, compound 51 was formed in addition to compound 8. Compound 51 was formed by the addition[29] of dimsyl anion to the vinyl group of 8. [c] On application of heat, to the same reaction, it went beyond 51 to provide the demethylated compound 52. The evidence that compounds 51 and 52 were formed from 8 and not directly from 7 was provided by reaction of 8 with NaH–DMSO to furnish compounds 51 and 52 in 9% and 57% yields, respectively. The position of the hydroxyl group in compound 52 was further confirmed by an unambiguous synthesis which was achieved by the reaction of 9-OH derivative of trequinsin[12] with dimsyl anion.

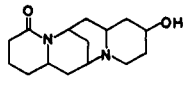
treatment with excess NaH–DMF. In compound 47 no polarization of charge is possible in contrast to compound 27, indicating the importance of the carbonyl group adjacent to the bridgehead nitrogen. Compounds 48, 49, and 50 illustrate the necessity of the cited structural elements in addition to those of a tertiary nitrogen atom attached to a carbonyl group.



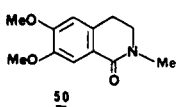
47



48



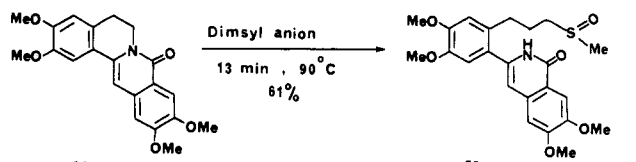
49



50

To determine whether the reaction would also proceed if sodium hydride was replaced by other bases, and dimethylformamide by other solvents, a representative compound of the general formula I, namely trequinsin (7), was subjected to various changes as indicated in Table II.

8-Oxypseudopalmatine (22) on treatment with dimsyl anion at 90 °C for 13 min also gave the dimsyl addition product 53 in 61% yield (eq 3).



22 53

(eq. 3)

Conclusion

The method describes the cleavage of a carbon–nitrogen bond, wherein the nitrogen atom is nonbasic, in nitrogen heterocyclic compounds. The specific environment around the ring junction nitrogen for cleavage to take place is defined. Cleavage is effected through use of excess of a base such as sodium hydride. The reaction is carried out in an aprotic polar solvent such as dimethylformamide. Other bases and aprotic polar solvents may also be used. Dimsyl anion as a base enhances the cleavage reaction rate, but may also produce side reactions of addition of the dimsyl ion and demethylation. The reaction is likely to

(26) Galinovsky, F.; Pohm, M.; Riedl, K. *Monatsh.* **1950**, *81*, 77.
(27) Sugasawa, S.; Sugimoto, N. *Chem. Ber.* **1939**, *72B*, 980.
(28) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1345.
(29) Walling, C.; Bollyky, L. *J. Org. Chem.* **1964**, *29*, 2699.

be applicable to a number of natural products such as Oxogambirtannine,[30] Angustidine,[31] Hortiacine,[32] Evodiamine,[33] Parvine,[34] and other molecules which fit the general formula I.

Experimental Section

Instruments. ^{1}H NMR spectra were recorded on Varian T-60 and JEOL FX-90Q spectrometers. ^{13}C NMR spectra were recorded on JEOL FX-90Q spectrophotometer. Mass spectra were obtained on a Kratos MS 80 RFA instrument. IR spectra were recorded on Perkin-Elmer 157 and Perkin-Elmer 782 spectrometers. Melting points were determined on Kofler hot stage melting point apparatus and are uncorrected.

Materials. Sodium hydride dispersion (55–60% in oil) was used and washed with dry benzene. DMF and DMSO were distilled from calcium hydride and kept over 4A molecular sieves. Methanol was distilled from magnesium methoxide. Substrates were prepared according to literature (references are indicated in Table I).

3-Benzyl-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (2). A mixture of sodium hydride (0.17 g, 4.25 mmol), dry DMF (20 mL), and 9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (1, 1.0 g, 3.65 mmol) was maintained at 70 °C for 30 min. After the mixture was cooled in ice bath, benzyl bromide (1 mL, 8.4 mmol) was added, and the temperature was maintained at 100–110 °C for 2 h. The solution was cooled, water was cautiously added, and the mixture was extracted with chloroform (50 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), and concentrated in vacuo. The residue was flash chromatographed on silica gel ($CH_3CN/CHCl_3$, 7:93) and further crystallized from EtOH–CH_2Cl_2 to give **2** (1.14 g; 86%): mp 220–221 °C (lit.[10] mp 220–221 °C); ^{1}H NMR ($CDCl_3$) δ 2.92 (t, J = 7 Hz, 2 H, C-7H), 3.92 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.12 (t, J = 7 Hz, 2 H, C-6H), 5.20 (s, 2 H, $NCH_2C_6H_5$), 6.15 (s, 1 H, C-1H), 6.73 (s, 1 H, C-8H), 7.13 (s, 1 H, C-11H), 7.21–7.68 (m, 5 H, ArH).

3-Benzyl-6-(4,5-dimethoxy-2-vinylphenyl)-2,4(1*H*,3*H*)-pyrimidinedione (3). A mixture of sodium hydride (0.87 g, 21.9 mmol), dry DMF (20 mL), and 1 (1.0 g, 3.65 mmol) was maintained at 70 °C for 30 min. After the mixture was cooled in ice bath, benzyl bromide (0.55 mL, 4.62 mmol) was added, and the temperature was maintained at 120–130 °C for 20 h. Excess sodium hydride was cautiously decomposed with methanol, the solvent was removed under reduced pressure, and the residue was neutralized with dilute CH_3COOH and extracted with chloroform (50 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), concentrated, and flash chromatographed on silica gel ($MeOH/CHCl_3$, 0.5:99.5) to give pure product **3** (0.51 g, 39%). Compound **3** was also prepared in 71% yield by treating **2** with sodium hydride and DMF: mp 203–205 °C; IR (KBr) 3105, 1724, 1653, 1613, 990, 903 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.97 (s, 2 H, $CH_2C_6H_5$), 5.23 (d, J = 11 Hz, 1 H, =C*H*H, trans to Ar), 5.57 (d, J = 18 Hz, 1 H, =CH*H*, cis to Ar) 5.70 (s, 1 H, C-5H), 6.73 (dd, J = 18, 11 Hz, 1 H, C*H*=CH_2), 6.83 (s, 1 H, ArH), 7.05 (s, 1 H, ArH), 7.20 (s, 5 H, ArH), 10.33 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.61; H, 5.93; N, 8.18.

General Procedure for the Cleavage Reaction. A mixture of sodium hydride, 5–10 molar equiv, dry DMF, and substrate was heated at 80–130 °C for 0.5–22 h. After the mixture was cooled, excess sodium hydride was decomposed with methanol, and the solvent was removed under reduced pressure, neutralized with dilute CH_3COOH, and extracted with chloroform. The organic layer was washed with water, dried (Na_2SO_4), and concentrated, and residue was flash chromatographed on silica gel ($MeOH/CHCl_3$) to yield pure cleaved products. The cleaved compounds prepared through the above method are **6**, **8**, **11**, **13**, **15**, **17**, **20**, **23**, **26**, **28**, **30**, **32**, **34**, **38**, **40**, and **43** (see Table I).

6-(4,5-Dimethoxy-2-vinylphenyl)-2,4(1*H*,3*H*)-pyrimidinedione (6): IR (KBr) 3125, 3030, 2899, 1678, 1639, 990 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.83 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.25 (dd, J = 10, 2 Hz, 1 H, =C*H*H, trans to Ar), 5.30 (s, 1 H, C-5H), 5.74 (dd, J = 17, 2 Hz, 1 H, =CH*H*, cis to Ar), 6.73 (dd, J = 17, 10 Hz, 1 H, C*H*=CH_2), 6.97 (s, 1 H, ArH), 7.17 (s, 1 H, ArH), 10.90 (br s, 2 H, NH, exchanges with D_2O). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 61.30; H, 5.14; N, 10.22. Found: C, 61.07; H, 5.07; N, 10.37.

6-(4,5-Dimethoxy-2-vinylphenyl)-3,4-dihydro-4-(mesitylimino)-3-methyl-2(1*H*)-pyrimidinone (8): IR (KBr) 3175, 3077, 1667, 1623, 991, 913 cm^{-1}; ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 1.97 (s, 6 H, 2 $ArCH_3$), 2.11 (s, 3 H, $ArCH_3$), 3.46 (s, 3 H, NCH_3), 3.77 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 5.03 (s, 1 H, C-5H), 5.05 (d, J = 10.8 Hz, 1 H, =C*H*H, trans to Ar), 5.39 (d, J = 18 Hz, 1 H, =CH*H*, cis to Ar), 6.54 (dd, J = 18, 10.8 Hz, 1 H, C*H*=CH_2), 6.63 (s, 1 H, ArH), 6.71 (s, 2 H, ArH), 6.87 (s, 1 H, ArH). Anal. Calcd for $C_{24}H_{27}N_3O_3$: C, 71.08; H, 6.71; N, 10.36. Found: C, 70.96; H, 6.46; N, 9.93.

7-(1,3-Dihydro-2,4-dioxo-6-pyrimidyl)-6-vinyl-2,3-dihydro-1,4-benzodioxin (11): IR (KBr) 3140, 3020, 1720, 980, 925 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 4.23 (s, 4 H, C-2,3H), 5.20 (dd, J = 11, 1 Hz, 1 H, =C*H*H, trans to Ar), 5.33 (s, 1 H, C-5H), 5.68 (dd, J = 16, 1 Hz, 1 H, =CH*H*, cis to Ar), 6.68 (dd, J = 16, 11 Hz, 1 H, C*H*=CH_2), 6.90 (s, 1 H, ArH), 7.20 (s, 1 H, ArH), 11.01 (br s, 2 H, 2 NH, exchanges with D_2O). Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44. Found: 61.98; H, 4.39.

4-(2,6-Difluoroanilino)-6-(4,5-dimethoxy-2-vinylphenyl)-2(1*H*)-pyrimidinone (13): IR (KBr) 2941, 1639, 1605 cm^{-1}; ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 3.93 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 5.27 (d, J = 10.3 Hz, 1 H, =C*H*H, trans to Ar), 5.58 (d, J = 18 Hz, 1 H, =C*H*H, cis to Ar), 5.58 (br s, 1 H, C-5H), 6.77 (dd, J = 18, 10.3 Hz, C*H*=CH_2), 6.88–7.41 (6 H, ArH); MS m/e (%) 386 (M^+ + 1, 100), 366 (9), 257 (13). Anal. Calcd for $C_{20}H_{17}F_2N_3O_2$: C, 62.33; H, 4.45; N, 10.90. Found: C, 62.56; H, 4.84; N, 10.40.

6-(4,5-Dimethoxy-2-vinylphenyl)-4-(*N*-methylpiperazino)-2(1*H*)-pyrimidinone (15): IR (KBr) 2899, 2788, 1645, 1607, 990, 791 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3 H, NCH_3), 2.43 (br s, 4 H, $(CH_2)_2NCH_3$), 3.72 (br s, 4 H, $(CH_2)_2N$), 3.97 (s, 6 H, 2 OCH_3), 5.21 (dd, J = 11, 2 Hz, 1 H, =C*H*H, trans to Ar), 5.57 (dd, J = 16, 2 Hz, 1 H, =CH*H*, cis to Ar), 5.73 (s, 1 H, C-5H), 6.78 (dd, J = 16, 11 Hz, 1 H, C*H*=CH_2), 6.92 (s, 1 H, ArH), 7.0 (s, 1 H, ArH). Anal. Calcd for $C_{19}H_{24}N_4O_3$: C, 64.02; H, 6.79; N, 15.72. Found: C, 63.69; H, 6.53; N, 15.91.

4-(*tert*-Butylamino)-6-(4,5-dimethoxy-2-vinylphenyl)-2-(1*H*)-pyrimidinone (17): IR (KBr) 3175, 2985, 1618, 1590, 995, 913 cm^{-1}; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 1.45 (s, 9 H, 3 CH_3), 3.91 (s, 6 H, 2 OCH_3), 5.19 (dd, J = 11, 2 Hz, 1 H, =C*H*H, trans to Ar) 5.55 (dd, J = 18, 2 Hz, 1 H, =CH*H*, cis to Ar), 5.57 (s, 1 H, C-5H), 6.18 (br s, 1 H, NH), 6.78 (dd, J = 18, 11 Hz, 1 H, C*H*=CH_2), 7.0 (s, 2 H, ArH), 10.66 (br s, 1 H, NH). Anal. Calcd for $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.60; N, 12.68. Found: C, 65.47; H, 7.74; N, 13.01.

3-(4,5-Dimethoxy-2-vinylphenyl)-1(2*H*)-isoquinolinone (20): IR (KBr) 2941, 1639, 1587, 982, 894 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.98 (s, 6 H, 2 OCH_3), 5.21 (dd, J = 10, 2 Hz, 1 H, =C*H*H, trans to Ar), 5.63 (dd, J = 17, 2 Hz, 1 H, =CH*H*, cis to Ar), 6.48 (s, 1 H, C-4H), 6.85 (dd, J = 17, 10 Hz, 1 H, C*H*=CH_2), 7.07 (s, 1 H, ArH), 7.10 (s, 1 H, ArH), 7.53–7.56 (3 H, ArH), 8.30 (d, J = 7 Hz, 1 H, C-8H), 10.30 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 73.93; H, 5.21; N, 4.17.

6,7-Dimethoxy-3-(4,5-dimethoxy-2-vinylphenyl)-1(2*H*)-isoquinolinone (23): IR (KBr) 3279, 3058, 1653, 1634, 1000, 926 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 6 H, 2 OCH_3), 4.0 (s, 6 H, 2 OCH_3), 5.20 (dd, J = 10, 1 Hz, 1 H, =C*H*H, trans to Ar), 5.59 (d, J = 17 Hz, 1 H, =CH*H*, cis to Ar), 6.37 (s, 1 H, C-4H), 6.81 (dd, J = 17, 10 Hz, 1 H, C*H*=CH_2), 6.88 (s, 1 H, ArH), 6.98 (s, 1 H, ArH), 7.08 (s, 1 H, ArH), 7.67 (s, 1 H, ArH), 9.95 (br s, 1 H, NH, exchanges with D_2O). The above NMR data is in agreement with literature[4] data. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.85; H, 5.37; N, 3.72.

6,7-Dimethoxy-3-[4,5-(methylenedioxy)-2-vinylphenyl]-1-(2*H*)-isoquinolinone (26): IR (KBr) 3160, 3020, 2980, 1650, 1625, 950, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 4.04 (s, 6 H, 2 OCH_3),

(30) Merlini, L.; Mondelli, R.; Nasini, G. *Tetrahedron* **1967**, *23*, 3129.
(31) Au, T. Y.; Cheung, H. T.; Sternhell, S. *J. Chem. Soc., Perkin Trans 1* **1973**, 13.
(32) Pachter, I. J.; Raffauf, R. F.; Ullyot, G. E.; Ribeiro, O. *J. Am. Chem. Soc.* **1960**, *82*, 5187.
(33) Asahina, Y.; Ohta, T. *Chem. Ber.* **1928**, *61*, 319.
(34) Sainsbury, M.; Webb, B. *Phytochemistry* **1975**, *14*, 2691.

5.2 (dd, J = 10.8, 1 Hz, 1 H, =C*H*H, trans to Ar), 5.61 (dd, J = 18, 1 Hz, 1 H, =CH*H*, cis to Ar), 6.02 (s, 2 H, OCH_2O), 6.45 (s, 1 H, NH, exchanges with D_2O), 6.67 (dd, J = 18, 10.8 Hz, 1 H, C*H*=CH_2), 6.85 (s, 1 H, C-4H), 6.97 (s, 1 H, ArH), 7.11 (s, 1 H, ArH), 7.43 (s, 1 H, ArH), 7.73 (s, 1 H, ArH). Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.98. Found: C, 68.04; H, 5.08; N, 3.59.

7,8-Dimethoxy-3-[4,5-(methylenedioxy)-2-vinylphenyl]-1-(2*H*)-isoquinolinone (28): IR (KBr) 3160, 1650, 1490, 980, 850 cm^{-1}; ^1H NMR ($CDCl_3$ + TFA) δ 4.0 (s, 3 H, OCH_3), 4.11 (s, 3 H, OCH_3), 5.21 (d, J = 10.8 Hz, 1 H, =C*H*H, trans to Ar), 5.60 (d, J = 18 Hz, 1 H, =CH*H*, cis to Ar), 6.04 (s, 2 H, OCH_2O), 6.61 (dd, J = 18, 10.8 Hz, 1 H, C*H*=CH_2), 6.76 (s, 1 H, C-4H), 6.80 (s, 1 H, C-3H), 7.04 (s, 1 H, C-6H), 7.42 (d, J = 7.2 Hz, 1 H, C-5H), 7.54 (d, J = 7.2 Hz, 1 H, C-6H); MS m/e (%) 351 (M^+, 100), 336 (83), 321 (57), 308 (23), 292 (44), 178 (29), 160 (27), 139 (17), 102 (23), 89 (53) 76 (41), 63 (60). Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.98. Found: C, 68.01; H, 4.50; N, 3.65.

3-[4-(Benzyloxy)-5-methoxy-2-vinylphenyl]-6,7-dimethoxy-1(2*H*)-isoquinolinone (30): IR (KBr) 3160, 2980, 1640, 1610, 1005, 920 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD) δ 3.97 (s, 3 H, OCH_3), 4.05 (s, 6 H, 2 OCH_3), 5.17 (d, J = 10.8 Hz, 1 H, =C*H*H, trans to Ar), 5.27 (s, 2 H, OCH_2), 5.51 (d, J = 16.7 Hz, 1 H, =CH*H*, cis to Ar), 6.48 (s, 1 H, C-4H), 6.68 (dd, J = 16.7, 10.8 Hz, 1 H, C*H*=CH_2), 6.94 (s, 1 H, ArH), 6.97 (s, 1 H, ArH), 7.17 (s, 1 H, ArH), 7.45 (br s, 5 H, ArH), 7.74 (s, 1 H, ArH); MS m/e (%) 443 (M^+, 62), 352 (40), 324 (64), 195 (9), 91 (100). Anal. Calcd for $C_{27}H_{25}NO_5$: C, 73.12; H, 5.68; N, 3.16. Found: C, 73.57; H, 5.88; N, 3.25.

6-(4,5-Dimethoxy-2-vinylphenyl)-1,3,5-triazine-2,4-(1*H*,3*H*)-dione (32): IR (KBr) 3125, 2985, 1730, 1675, 980, 901 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.83 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.18 (d, J = 10 Hz, 1 H, =C*H*H, trans to Ar), 5.73 (d, J = 17 Hz, 1 H, =CH*H*, cis to Ar), 6.97 (dd, J = 17, 10 Hz, 1 H, C*H*=CH_2), 7.05 (s, 1 H, ArH), 7.17 (s, 1 H, ArH), 11.20 (s, 1 H, NH, exchanges with D_2O), 12.0 (s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.43; H, 5.03; N, 14.93.

3-(4,5-Dimethoxy-2-vinylphenyl)-2,7-naphthyridin-1-(2*H*)-one (34): IR (KBr) 3226, 3077, 1667, 1626, 987, 921 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 5.24 (d, J = 10 Hz, 1 H, =C*H*H, trans to Ar) 5.64 (dd, J = 17, 1.5 Hz, 1 H, =CH*H*, cis to Ar), 6.45 (s, 1 H, C-4H), 6.78 (dd, J = 17, 10 Hz, 1 H, C*H*=CH_2), 7.05 (s, 1 H, ArH), 7.15 (s, 1 H, ArH), 7.35 (d, J = 5 Hz, 1 H, C-5H), 8.70 (d, J = 5 Hz, 1 H, C-6H), 9.47 (s, 1 H, C-8H), 10.93 (br s, 1 H, NH, exchanges with D_2O); MS m/e (%) 308 (M^+, 100), 265 (9), 169 (12), 119 (12), 95 (15), 69 (24). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09. Found: C, 70.18; H, 5.52; N, 8.85.

5-(4,5-Dimethoxy-2-vinylphenyl)-2-methyl-2,4-dihydro-3*H*-1,2,4-triazol-3-one (38): IR (KBr) 1710, 1625, 1590, 950, 920 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.37 (s, 3 H, NCH_3), 3.83 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 5.24 (dd, J = 10.3, 1 Hz, 1 H, =C*H*H, trans to Ar), 5.70 (dd, J = 18, 1 Hz, 1 H, =CH*H*, cis to Ar), 7.05 (s, 1 H, ArH), 7.24 (s, 1 H, ArH), 7.27 (dd, J = 18, 10.3 Hz, 1 H, C*H*=CH_2). Anal. Calcd for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.36; H, 6.01; N, 15.85.

2-[2-(3-Vinylindolyl)]-4(3*H*)-quinazolinone (40): IR (KBr) 3400, 1667, 1600, 957, 893 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD) δ 5.64 (dd, J = 11.5, 1.5 Hz, 1 H, =C*H*H trans to Ar), 5.91 (dd, J = 18, 1.5 Hz, 1 H, =CH*H* cis to Ar), 7.59 (dd, J = 18, 11.5 Hz, 1 H, C*H*=CH_2), 7.08–7.91 (7 H, ArH), 8.24 (d, J = 7.7 Hz, 1 H, ArH); MS m/e (%) 287 (M^+, 59). Anal. Calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63. Found: C, 75.07; H, 4.78; N, 14.35.

4-(3,4-Dimethoxyanilino)-6-[2-(3-vinylthienyl)]-2(1*H*)-pyrimidinone (43): IR (KBr) 3125, 2959, 1639, 1613, 1034, 917 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD) δ 3.88 (s, 6 H, 2 OCH_3), 5.38 (dd, J = 10.3, 1 Hz, 1 H, =C*H*H, trans to Ar), 5.67 (dd, J = 18, 1 Hz, 1 H, =CH*H*, cis to Ar), 5.94 (s, 1 H, C-5H), 6.76 (dd, J = 18, 10.3 Hz, 1 H, C*H*=CH_2), 6.88 (s, 3 H, ArH), 7.24 (d, J = 5.1 Hz, 1 H, ArH), 7.43 (d, J = 5.1 Hz, 1 H, ArH). Anal. Calcd for $C_{18}H_{17}N_3OS$: C, 60.83; H, 4.82; N, 11.82; S, 9.02. Found: C, 60.54; H, 4.94; N, 11.52; S, 9.36.

General Procedure for the Reduction of Arylvinyl Compounds. The substrate was dissolved either in methanol or in a mixture of DMF–methanol. To this was added 10% palladium on carbon (10–20% by weight of substrate) and hydrogenated at 45–50 psi for 1–7 h using a Parr hydrogenator. The catalyst was filtered, and the product was isolated. The reduced compounds prepared through the above method are **4**, **9**, **18**, **21**, **24**, **35**, and **41**.

3-Benzyl-6-(4,5-dimethoxy-2-ethylphenyl)-2,4(1*H*,3*H*)-pyrimidinedione (4): mp 191–192 °C; IR (KBr) 1727, 1667 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (t, J = 6 Hz, 3 H, CH_3), 2.58 (q, J = 6 Hz, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 4.95 (s, 2 H, $CH_2C_6H_5$), 5.66 (s, 1 H, C-5H), 6.70 (s, 1 H, ArH), 6.76 (s, 1 H, ArH), 7.20 (s, 5 H, ArH), 10.62 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{21}H_{22}N_2O_4$: C, 68.83; H, 6.05; N, 7.64. Found: 68.84; H, 5.88; N, 7.75.

6-(4,5-Dimethoxy-2-ethylphenyl)-3,4-dihydro-4-(mesitylimino)-3-methyl-2-(1*H*)-pyrimidinone (9): mp 227–229 °C; IR (KBr) 3012, 1724, 1678, 1626 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (t, J = 8 Hz, 3 H, CH_3), 2.0 (s, 6 H, 2 $ArCH_3$), 2.18 (s, 3 H, $ArCH_3$), 2.53 (q, J = 8 Hz, 2 H, CH_2), 3.45 (s, 3 H, NCH_3), 3.85 (s, 6 H, 2 OCH_3), 5.11 (s, 1 H, C-5H), 6.63 (s, 1 H, ArH), 6.66 (s, 1 H, ArH), 6.76 (s, 2 H, ArH). Anal. Calcd for $C_{24}H_{29}N_3O_3$: C, 70.73; H, 7.17; N, 10.31. Found: C, 71.08; H, 7.40; N, 10.44.

4-(*tert*-Butylamino)-6-(4,5-dimethoxy-2-ethylphenyl)-2-(1*H*)-pyrimidinone (18): mp 305–307 °C; IR (KBr) 3175, 3030, 2959, 1618, 1595 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 1.16 (t, J = 8 Hz, 3 H, CH_3), 1.46 (s, 9 H, 3 CH_3), 2.63 (q, J = 8 Hz, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 5.58 (s, 1 H, C-5H), 6.42 (br s, 1 H, NH, exchanges with D_2O), 6.70 (s, 1 H, ArH), 6.73 (s, 1 H, ArH). Anal. Calcd for $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.60; N, 12.68. Found: C, 65.47; H, 7.74; N, 13.01.

3-(4,5-Dimethoxy-2-ethylphenyl)-1(2*H*)-isoquinolinone (21): mp 203–204 °C; IR (KBr) 3226, 3003, 1639, 1608 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (t, J = 7 Hz, 3 H, CH_3), 2.68 (q, J = 7 Hz, 2 H, CH_2), 3.82 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 6.33 (s, 1 H, C-4H), 6.70 (s, 1 H, ArH), 6.80 (s, 1 H, ArH), 7.12–7.48 (3 H, ArH), 8.13 (br d, J = 7.5 Hz, 1 H, ArH), 10.35 (s, 1 H, NH exchanges with D_2O). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.52. Found: C, 73.47; H, 6.43; N, 4.72.

6,7-Dimethoxy-3-(4,5-dimethoxy-2-ethylphenyl)-1(2*H*)-isoquinolinone (24): mp 199–200 °C; IR (KBr) 3175, 2967, 1631, 1608 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (t, J = 8 Hz, 3 H, CH_3), 2.68 (q, J = 8 Hz, 2 H, CH_2), 3.87 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 4.0 (s, 6 H, 2 OCH_3), 6.35 (s, 1 H, C-4H), 6.77 (s, 1 H, ArH), 6.85 (s, 2 H, ArH), 7.65 (s, 1 H, ArH), 9.7 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.36; H, 6.38; N, 3.57.

3-(4,5-Dimethoxy-2-ethylphenyl)-2,7-naphthyridin-1-(2*H*)-one (35): mp 225–228 °C; IR (KBr) 2985, 2857, 1667, 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (t, J = 7 Hz, 3 H, CH_3), 2.69 (q, J = 7 Hz, 2 H, CH_2), 3.87 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 6.35 (s, 1 H, C-4H), 6.78 (s, 1 H, ArH), 6.83 (s, 1 H, ArH), 7.27 (d, J = 6 Hz, 1 H, C-5H), 8.58 (d, J = 6 Hz, 1 H, C-6H), 9.30 (s, 1 H, C-8H), 10.60 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.02. Found: C, 69.29; H, 5.96; N, 8.84.

2-[2-(3-Ethylindolyl)]-4(3*H*)-quinazolinone (41): mp 314–315 °C dec; IR (KBr) 3030–2941, 1667, 1600 cm^{-1}; ^1H NMR ($CDCl_3$ + a drop of TFA-d) δ 1.42 (t, J = 7 Hz, 3 H, CH_3), 3.20 (q, J = 7 Hz, 2 H, CH_2), 7.2–7.93 (7 H, ArH), 8.3 (d, J = 8 Hz, 1 H, ArH). Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.52; H, 5.41; N, 14.42.

3-Benzyl-6-(4,5-dimethoxy-2-ethylphenyl)-3,4-dihydro-4-thioxo-2(1*H*)-pyrimidinone (5). To a solution of **4** (2.0 g, 5.46 mmol) in dioxan (80 mL) was added Lawesson's reagent[11] (2.07 g, 5.12 mmol), and the temperature was maintained at 105–115 °C for 3 h. The mixture was concentrated under reduced pressure, and the residue was chromatographed on silica gel (CH_2Cl_2) to give **5** (1.89 g, 90%), which was crystallized from CH_2Cl_2–petroleum ether: mp 183–184 °C; IR (KBr) 2967, 1703, 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (t, J = 7 Hz, 3 H, CH_3), 2.64 (q, J = 7 Hz, 2 H, CH_2), 3.80 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 5.61 (s, 2 H, $CH_2C_6H_5$) 6.66 (s, 1 H, C-5 H), 6.75 (s, 1 H, ArH), 6.78 (s, 1 H, ArH), 7.23 (s, 5 H, ArH), 10.39 (br s, 1 H, NH, exchanges with D_2O). Anal. Calcd for $C_{21}H_{22}N_2O_3S$: C, 65.94; H, 5.80; N, 7.33; S, 8.38. Found: C, 66.36; H, 5.70; N, 7.25; S, 8.16.

9,10-Dimethoxy-1,2,3,4,6,7-hexahydro-11b*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (44). To dry methanol (50 mL) was

added magnesium turnings (1.3 g) and **1** (1.0 g, 3.65 mmol), and the mixture was stirred at room temperature for 2 h. It was concentrated, residue diluted with water, acidified with dilute HCl, and extracted with chloroform (50 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), and concentrated to give **44** (0.92 g, 91%), crystallized from CH_2Cl_2–EtOAc: mp 260–261 °C (lit.[35] mp 248 °C); ^1H NMR ($CDCl_3$) δ 2.65–3.21 (m, 5 H, 2 C-1H, C-6H, 2 C-7H), 3.88 (s, 6 H, 2 OCH_3), 4.51–4.97 (m, 2 H, C-6H, C-11bH), 6.57 (s, 1 H, ArH), 6.68 (s, 1 H, ArH), 7.91 (br s, 1 H, NH, exchanges with D_2O).

9,10-Dimethoxy-1-methyl-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinoline-2,4-dione (45) and 6-(4,5-Dimethoxy-2-vinylphenyl)-5-methyl-2,4(1*H*,3*H*)-pyrimidinedione (46). A mixture of sodium hydride (0.75 g, 18.75 mmol), dry DMF (18 mL), and **44** (0.55 g, 1.99 mmol) was maintained at 110 °C for 1.25 h. After cooling, excess sodium hydride was decomposed with methanol, and the solvent was removed under reduced pressure. The residue was treated with water, acidified with dilute HCl, and extracted with chloroform (70 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), concentrated, and flash chromatographed on silica gel (MeOH/$CHCl_3$, 2/98). Initial fractions gave compound **45** (0.197 g, 34%), which was crystallized from DMF: mp 310–312 °C; IR (KBr) 3175, 3021, 1653, 1587 cm^{-1}; ^1H NMR (TFA-*d*) δ 2.41 (s, 3 H, C_1-CH_3), 3.04 (t, *J* = 6 Hz, 2 H, C-7H), 4.01, (s, 3 H, OCH_3), 4.05 (s, 3 H, OCH_3), 4.19 (t, *J* = 6 Hz, 2 H, C-6H), 7.01 (s, 1 H, C-8H), 7.43 (s, 1 H, C-10H); MS[38] *m/e* (%) 288 (M^+, 100), 273 (100), 256 (37.5), 230 (100), 202 (85). Anal. Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.49; H, 5.83; N, 9.25.

Later fractions gave 6-(4,5-dimethoxy-2-vinylphenyl)-5-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**46**, 0.131 g, 23%), crystallized from $CHCl_3$–CH_3OH: mp 282–284 °C; IR (KBr) 3311, 3175, 3030, 1695, 1653, 993, 907 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.46 (s, 3 H, C-5CH_3), 3.75 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 5.21 (d, *J* = 11.9 Hz, 1 H, =C*H*H, trans to Ar), 5.82 (d, *J* = 15.9 Hz, 1 H, =CH*H*, cis to Ar), 6.47 (dd, *J* = 15.9, 11.9 Hz, 1 H, C*H*=CH_2), 6.86 (s, 1 H, ArH), 7.28 (s, 1 H, ArH), 10.88 (s, 1 H, NH, exchanges with D_2O), 11.28 (s, 1 H, NH, exchanges with D_2O); MS[38] *m/e* (%) 288 (M^+, 100), 273 (44), 257 (94), 245 (44), 230 (41), 216 (29), 202 (50). Anal. Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.56; H, 5.27; N, 9.55.

Reaction of Trequinsin with Dimsyl Ion. Dimsyl ion[29] was prepared from sodium hydride (0.175 g, 4.37 mmol) and dry dimethyl sulfoxide (4 mL), and to this was added trequinsin (**7**, 0.81 g, 1.99 mmol). The reaction mixture was stirred at room temperature for 5 min, diluted with brine, and extracted with chloroform (70 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), concentrated, and flash chromatographed on silica gel (MeOH/$CHCl_3$, 2:98) to give **8** (0.737 g, 91%).

Variation A. When the above reaction was continued for 15 min at room temperature, after usual workup and purification two products were obtained. The initial fractions gave compound **8** (0.268 g, 33%). The later fractions gave 6-[4,5-dimethoxy-2-[3-(methylsulfinyl)prop-1-yl]phenyl]-3,4-dihydro-4-(mesitylimino)-3-methyl-2(1*H*)-pyrimidinone (**51**, 0.199 g, 20%). It was crystallized from acetone–petroleum ether: mp 205–206 °C; IR (KBr) 3333, 3226, 3030, 1704, 1667, 1618, 1063 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84–2.10 (m, 2 H, $CH_2CH_2CH_2$), 2.0 (s, 6 H, 2 $ArCH_3$), 2.20 (s, 3 H, $ArCH_3$), 2.4–2.8 (m, 4 H, Ar-CH_2 and SCH_2), 2.50 (s, 3 H, SCH_3), 3.48 (s, 3 H, NCH_3), 3.86 (s, 6 H, 2 OCH_3), 5.01 (s, 1 H, C-5H), 6.64 (s, 1 H, ArH), 6.68 (s, 1 H, ArH), 6.76 (s, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 152.51, 150.51, 149.80, 147.69, 144.87, 144.06, 131.55, 131.38, 128.67 (2 C), 128.02 (2 C), 124.66, 112.74, 111.88, 94.92, 56.13 (2 C), 53.53, 38.52, 31.37, 28.49, 24.16, 20.69 (2 C), 18.09; MS *m/e* (%) 483 (M^+, 93), 466 (26), 459 (11), 451 (20), 419 (20), 404 (26), 392 (13), 332 (7), 161 (26), 150 (17), 138 (17), 123 (37), 118 (48), 107 (22), 83 (100). Anal. Calcd for $C_{26}H_{33}N_3O_4S$: C, 64.57; H, 6.68; N, 8.69; S, 6.63. Found: C, 64.54; H, 6.69; N, 8.39; S, 6.77.

Variation B. The above reaction was done at 90–100 °C for 45 min. Solvent was evaporated under reduced pressure. The residue was diluted with water, acidified with dilute HCl, and extracted with chloroform (70 mL × 3). The organic layer was washed with water, dried (Na_2SO_4), concentrated, and chromatographed on silica gel (CH_3OH/$CHCl_3$, 1.5/98.5 → 5/95). The initial fractions gave **51** (0.44 g, 4.56%). The later fractions gave 6-[4-hydroxy-5-methoxy-2-[3-(methylsulfinyl)prop-1-yl]phenyl]-3,4-dihydro-4-(mesitylimino)-3-methyl-2(1*H*)-pyrimidinone (**52**, 0.431 g, 46%). It was crystallized from CH_2Cl_2–EtOAc–petroleum ether: mp 259–260 °C; IR (KBr) 3257, 3125, 2985, 1692, 1642, 1058, 1053 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 1.74–2.11 (m, 2 H, $CH_2CH_2CH_2$), 2.03 (s, 6 H, 2 $ArCH_3$), 2.20 (s, 3 H, $ArCH_3$), 2.27–2.80 (m, 4 H, $ArCH_2$, CH_2S), 2.48 (s, 3 H, SCH_3), 3.54 (s, 3 H, NCH_3), 3.83 (s, 3 H, OCH_3), 5.03 (s, 1 H, C-5H), 6.69 (s, 1 H, ArH), 6.74 (s, 1 H, ArH), 6.80 (s, 1 H, ArH), 7.31 (s, 1 H, ArH), 7.68 (s, 1 H, OH, exchanges with D_2O), 9.40 (br s, 1 H, NH, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 151.27, 149.91, 147.80, 145.63, 144.49, 131.44, 130.19, 128.30, 127.43, 123.26, 116.43, 112.91, 93.24, 55.75, 52.60, 38.68, 27.80, 23.62, 20.31, 17.71; MS *m/e* (%) 469 (M^+, 57), 451 (30), 436 (20), 428 (13), 419 (46), 405 (78), 390 (80), 279 (11), 149 (20), 132 (43), 119 (28), 105 (22), 91 (33), 83 (100), 77 (50), 73 (70), 64 (33). Anal. Calcd for $C_{25}H_{31}N_3O_4S$: C, 63.93; H, 6.66; N, 8.94; S, 6.83. Found: C, 63.55; H, 6.78; N, 8.69; S, 6.85.

Reaction of 8-Oxypseudopalmatine (22) with Dimsyl Ion. **22** was treated with dimsyl ion at 90 °C for 13 min, after usual workup and purification, 6,7-dimethoxy-3-[4,5-dimethoxy-2-[3-(methylsulfinyl)prop-1-yl]phenyl]-1(2*H*)-isoquinolinone (**53**) was obtained in 61% yield: mp 151–153 °C; IR (KBr) 2924, 1626, 1600, 1087, 1052 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.78–2.41 (m, 2 H, $CH_2CH_2CH_2$), 2.42 (s, 3 H, SCH_3), 2.54–3.38 (m, 4 H, $ArCH_2$, CH_2S), 3.85 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.98 (s, 6 H, 2 OCH_3), 6.35 (s, 1 H, C-4H), 6.75 (s, 1 H, ArH), 6.83 (s, 1 H, ArH), 6.88 (s, 1 H, ArH), 7.60 (s, 1 H, ArH), 10.22 (br s, 1 H, NH, exchanges with D_2O).

Acknowledgment. We gratefully acknowledge Drs. J. Reden and R. H. Rupp for their encouragement, Dr. P. K. Inamdar and his group for analytical data, and Amanda Nogueira for typing the manuscript.

Registry No. **1**, 68619-18-1; **2**, 91209-62-0; **3**, 127819-54-9; **4**, 127819-55-0; **5**, 127819-56-1; **6**, 127819-57-2; **7**, 79855-88-2; **8**, 127819-58-3; **9**, 127819-59-4; **10**, 127819-60-7; **11**, 127819-61-8; **12**, 91210-08-1; **13**, 127819-62-9; **14**, 91209-93-7; **15**, 127819-63-0; **16**, 76536-74-8; **17**, 127819-64-1; **18**, 127819-65-2; **19**, 32255-47-3; **20**, 127819-66-3; **21**, 127819-67-4; **22**, 10211-78-6; **23**, 60315-12-0; **24**, 127819-68-5; **25**, 19716-54-2; **26**, 127819-69-6; **27**, 549-21-3; **28**, 127819-70-9; **29**, 127819-71-0; **30**, 127819-72-1; **31**, 85686-51-7; **32**, 127819-73-2; **33**, 70474-52-1; **34**, 127819-74-3; **35**, 127819-75-4; **37**, 127819-76-5; **38**, 127819-77-6; **39**, 84-26-4; **40**, 127819-78-7; **41**, 127819-79-8; **42**, 127819-80-1; **43**, 127819-81-2; **44**, 127819-82-3; **45**, 127819-83-4; **46**, 127819-84-5; **51**, 127819-85-6; **52**, 127819-86-7; **53**, 127819-87-8.

(35) Yamazaki, T. *Yakugaku Zasshi* **1959**, *79*, 1008; *Chem. Abstr.* **1960**, *54*, 5679 d.

(36) Lal, B.; Dornauer, H.; Bhattacharya, B. K.; Dohadwalla, A. N.; de Souza, N. J. U.S. Patent 4,482,556, 1984.

(37) Elango, V.; Shamma, M. *J. Org. Chem.* **1983**, *48*, 4879.

(38) We are thankful to Dr. H. W. Fehlhaber for providing us with mass spectra.