dried, and evaporated to give products **10**, which were recrystallized from acetonitrile.

Registry No. **1c**, 17965-42-3; **1d**, 17313-50-7; **1e**, 14895-21-7; **2a**, 54107-17-4; **2b**, 87100-57-0; **2c**, 87100-58-1; **2d**, 87100-59-2; **2e**, 87100-60-5; **6aA**, 87100-61-6; **6aB**, 87100-62-7; **6aC**, 87100-63-8; **6aD** (isomer 1), 87114-10-1; **6aD** (isomer 2), 87114-11-2; **6aE**, 87100-64-9; **6bA**, 87100-65-0; **6bB**, 87100-66-1; **6bC**, 87100-67-2; **6bD** (isomer 1), 87100-68-3; **6bD** (isomer 2), 87100-69-4; **6bE**, 87100-70-7; **6cA**, 87100-71-8; **6cB**, 87100-72-9; **6cC**, 87100-73-0; **6cD** (isomer 1), 87100-74-1; **6cD** (isomer 2), 87100-75-2; **6cE**, 87100-76-3; **6dA**, 87100-77-4; **6dB**, 87100-78-5; **6dC**, 87100-79-6; **6dD** (isomer 1), 87100-80-9; **6dD** (isomer 2), 87100-81-0; **6dE**, 87100-82-1; **6eA**, 87100-83-2; **6eB**, 87100-84-3; **6eC**, 87114-12-3; **6eD** (isomer 1), 87100-85-4; **6eD** (isomer 2), 87100-86-5; **6eE**, 87100-87-6; **7a**, 64360-24-3; **7b**, 87100-88-7; **7c**, 87100-89-8; **7d**, 64360-25-4; **7e**, 87100-90-1; **8a**, 87100-91-2; **8b**, 87100-92-3; **8c**, 87100-93-4; **8d**, 87114-13-4; **8e**, 87100-94-5; **9a**, 87100-95-6; **9b**, 87100-96-7; **9c**, 87100-97-8; **9d**, 87114-14-5; **9e**, 87100-98-9; **10a**, 87100-99-0; **10b**, 87101-00-6; **10c**, 87101-01-7; **10d**, 87101-02-8; **10e**, 87101-03-9; phenylhydrazine, 100-63-0.

Supplementary Material Available: Microanalytical and ^{1}H NMR data for all the compounds **2**, **6**, **7**, **8** and **10** (2 pages). Ordering information is given on any current masthead page.

Eliminative Ring Fission of 4-Acyl-2,3-dihydro-4*H*-1,4-benzothiazines

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The behavior of 4-acyl-2,3-dihydro-1,4-benzothiazines **1–11** upon treatment with lithium diisopropylamide (LDA) in THF at −78 °C has been examined. Very marked differences have been observed. Whereas unsubstituted and monosubstituted derivatives (**1–4**) readily undergo "eliminative ring fission", providing 2-(alkylthio)phenyl enamides **12**, 2-aminophenyl vinyl sulfides **16**, and 3-acylbenzothiazolines **13**, 2,3-disubstituted derivatives (**5–7**) do not react at all. The relationship between structural features of the above-mentioned dihydrobenzothiazines and their reactivity is considered. Lithium ion plays a fundamental role in providing activation for the ring-opening reaction.

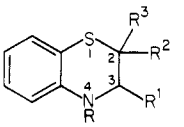
A number of reactions of dihydrobenzo-1,4-thiazines, compounds of considerable pharmacological interest,[1] which lead to heterocyclic ring cleavage have been described. Ring opening of the thiazino moiety may involve S–C_2 or C_3–N bond cleavage. The S–C_2 bond breaking has been reported for dihydro-1,4-thiazinones by reaction with sodium in liquid ammonia[2] and with Raney nickel.[3] The C_3–N bond of dihydrobenzothiazinones can be reductively cleaved[4] under certain circumstances, such as where aromatic stabilization is gained by the ring-opened product.

"Eliminative ring fission" reactions of dihydrothiazines and dihydrobenzothiazines are quite rare. The only known example of eliminative ring fission is that reported by Stoodley[5] for a few dihydrothiazines bearing an acidic hydrogen atom at the 3-position.

The present paper deals with a new dipole-stabilized-carbanion promoted "eliminative ring fission" reaction of some 2,3-dihydro-4*H*-1,4-benzothiazines. Attention will be focused upon the relationship between structure and reactivity in this type of reaction.

Results and Discussion

Following our studies[6] directed toward the synthesis of new dihydrobenzothiazine derivatives by metalation of simpler available precursors, we reasoned that 4-acyl-2,3-dihydro-4*H*-1,4-benzothiazines **1–10** bearing hydrogens on



1, R = COPh; R^1 = R^2 = R^3 = H
2, R = COPh; R^1 = Me; R^2 = R^3 = H
3, R = COPh; R^1 = R^3 = H; R^2 = Me
4, R = COPh; R^1 = R^3 = H; R^2 = Ph
5, R = COPh; R^1 = Me; R^2 = Ph; R^3 = H
6, R = COPh; R^1,R^2 = $(CH_2)_3$; R^3 = H
7, R = COPh; R^1,R^2 = $(CH_2)_5$; R^3 = H
8, R = COPh; R^1 = H; R^2 = R^3 = Cl
9, R = $COCF_3$; R^1 = R^2 = R^3 = H
10, R = CHO; R^1 = R^2 = R^3 = H
11, R = Me; R^1 = R^2 = R^3 = H

the carbon close to the nitrogen might be metalated at that position and that the resulting "dipole-stabilized carbanions" would undergo either alkylation or an "eliminative ring fission" reaction due to the presence of the sulfur, a good leaving group, in the 1-position of the heterocyclic ring. It has been established that base-promoted alkene-forming elimination can be greatly accelerated by insertion, β to the leaving group, of groups capable of stabilizing a carbanion.[7] Such a stabilization may also be provided in the form of a "dipole stabilization" by a heteroatom bonded to a carbonyl function.[8,9]

Treatment of 4-benzoyl-2,3-dihydro-1,4-benzothiazine (**1**) with lithium diisopropylamide (LDA) at −78 °C in tetrahydrofuran (THF) or *sec*-BuLi in hexane/THF and

(1) Kaiser, C.; Setler, P. E. In "Burger's Medicinal Chemistry", 4th ed.; Wolff, M. E., Ed.; Wiley: New York; 1980; Part III, p 890. Krapcho, J.; Turk, C. F. *J. Med. Chem.* **1972**, *16*, 776. Prasad R. N. *Ibid.* **1969**, *12*, 290.
(2) Hoff, S.; Blok, A. P.; Zwanemburg, E. *Tetrahedron Lett.* **1972**, 5199. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 879.
(3) Brown, R. F. C.; Rae, I. D. *Aust. J. Chem.* **1966**, *18*, 1071.
(4) Neelacantan, P.; Rao, N.; Bhalerao, U. T.; Thyagarajan, G. *Indian J. Chem.* **1973**, *11*, 1051; *Chem. Abstr.* **1974**, *80*, 82872z.
(5) Baxter, A. G. W.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 584.
(6) Babudri, F.; DiNunno, L.; Florio, S. *Synthesis* **1982**, 488; **1983**, 230; *Tetrahedron* **1982**, *38*, 3059.
(7) Marshall, D. R.; Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1898.
(8) Meyers, A. I.; Hellring, S.; Ten Hoeve, W. *Tetrahedron Lett.* **1981**, *22*, 5115. Meyers, A. I.; Hellring, S. *Ibid.* **1981**, *22*, 5119.
(9) Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 275 and references therein.

0022-3263/83/1948-4082$01.50/0

Table I. Reaction of 4-Acyl-2,3-dihydro-4*H*-1,4-benzothiazines 1-10 with Bases and Electrophiles at −78 °C in THF

compd	base	electrophile	reaction products (% yield)[a]
1	LDA	MeI	12a (87)
1	*sec*-BuLi	MeI	12a (71)
1	LDA	EtBr	12b (82)
1	LDA	NH_4Cl	13a (60)[b]
1	LDA/12-crown-4 ether	MeI	no reaction
1	*t*-BuOK	MeI	no reaction
1	KDA	MeI	
2	LDA	MeI	12c (64), 16a (31)
2	LDA	NH_4Cl	13b (57), 16b (12)
3	LDA	MeI	12d (82)
4	LDA	MeI	12e (53), 16c (39)
4	LDA	NH_4Cl	12f (18), 16d (43)
5	LDA	MeI	no reaction
6	LDA	MeI	
7	LDA	MeI	
8	LDA	MeI	18 (81)
9	LDA	MeI	16e (6), 12g (18), 19 (45)
10	LDA	MeI	11 (13), 19 (40)

[a] Yields determined from isolated and purified compounds. [b] Yield based on the starting dihydrobenzothiazine 1 reacted.

subsequent addition of alkyl halides such as MeI and EtBr led to the ring-opened products **12a** and **12b**, respectively, in good yields (see Chart I and Table I). The structure of such compounds was established by their spectral and analytical properties.

Repetition of the reaction of 1 with LDA followed by acidification with aqueous ammonium chloride provided the starting compound 1 and the benzothiazoline **13a**.

Under similar conditions methyldihydrobenzothiazine **11** did not undergo any reaction with LDA or with *n*-BuLi.

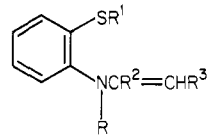
When the reaction of 1 and LDA was carried out in the presence of 12-crown-4 ether and MeI added, the formation of the enamide **12a** could not be observed. Again no reaction occurred when compound 1 was treated with *n*-BuLi and TMEDA. Such a inhibitory effect of 12-crown-4 ether and TMEDA can plausibly be ascribed to their binding of lithium so that this cation is not available for complexation with the amide **1**, a process which apparently provides activation for the ring-opening reaction. No ring opening of 1 was observed in the reaction with potassium *tert*-butoxide in DMF at room temperature nor with potassium diisopropylamide (KDA) in THF at −78 °C. The difference in the reactivity of **1** toward LDA and KDA is striking. The apparent lithium dependence may be explained in terms of complexation between lithium diisopropylamide and amide **1**;[10] lithium, as is well-known, exhibits a much better complexing ability than potassium.[10,11]

It seems probable that the foregoing reaction of 1 with LDA or *sec*-BuLi may involve the intermediacy of the

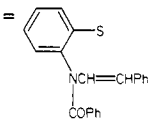
(10) For the role that lithium could play in providing activation for deprotonation see: Babudri, F.; Ciminale, F.; DiNunno, L.; Florio, S. *Tetrahedron* **1982**, *38*, 557 and ref 6 and 13.

(11) "Stability of Metal-Ion Complexes"; The Chemical Society: London, 1964.

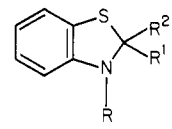
Chart I



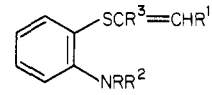
12a, R = COPh; R^1 = Me; R^2 = R^3 = H
b, R = COPh; R^1 = Et; R^2 = R^3 = H
c, R = COPh; R^1 = R^2 = Me; R^3 = H
d, R = COPh; R^1 = R^3 = Me; R^2 = H
e, R = COPh; R^1 = Me; R^2 = H; R^3 = Ph
f, R = COPh; R^2 = H; R^3 = Ph; R^1 =



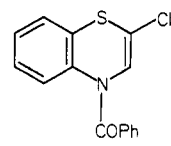
g, R = $COCF_3$; R^1 = Me; R^2 = R^3 = H



13a, R = COPh; R^1 = H; R^2 = Me
b, R = COPh; R^1 = R^2 = Me



16a, R = COPh; R^1 = R^2 = Me; R^3 = H
b, R = COPh; R^1 = Me; R^2 = R^3 = H
c, R = COPh; R^1 = H; R^2 = Me; R^3 = Ph
d, R = COPh; R^1 = R^2 = H; R^3 = Ph
e, R = $COCF_3$; R^1 = R^2 = R^3 = H



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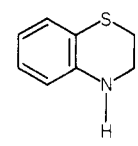

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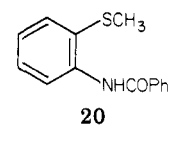

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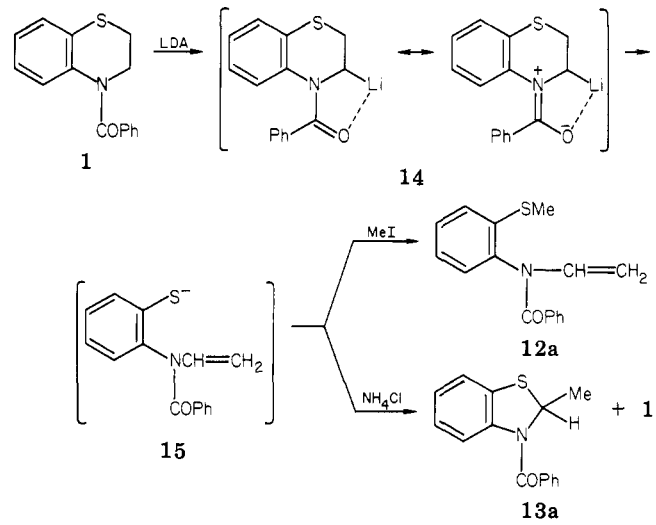
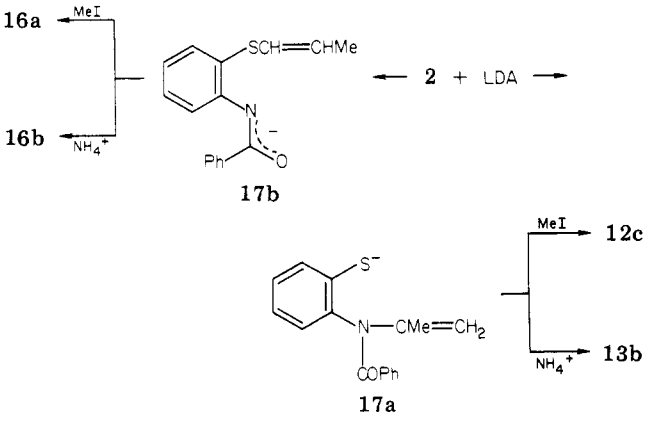
Scheme I



The enamidothiolate **15** that would form from the α-nitrogen dipole-stabilized carbanion **14**, generated by removal of the 3-hydrogen, by a β-elimination process (see Scheme I). Then **15** would react with MeI or EtBr to give compound **12a** (or **12b**) and with NH_4Cl to furnish 1 and **13a**. The generation of the α-nitrogen carbanion such as **14** is well precedented.[8] However, attempted trapping of **14** by immediate quenching of the reaction mixture with either MeI and MeOD failed. Evidently, **14** undergoes β elimination faster than alkylation. The failure of deuteration of **14** may

Scheme II



be ascribed to the fact that an irreversible E1cB or E2–E1cB-like mechanism is operating.

In order to evaluate the structural demand of the "eliminative ring fission" reaction of the thiazino moiety, we have prepared some 2- and 3-substituted 4-benzoyl-2,3-dihydro-4*H*-1,4-benzothiazines, and their reactions with LDA have been investigated.

The reaction of 4-benzoyl-3-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (**2**) with LDA in THF at −78 °C followed by addition of MeI led to the expected product **12c** and to the ring-opened compound **16a** (Scheme II). When NH_4Cl was used as the quencher for the reaction between **2** and LDA, compounds **13b** and **16b** were obtained. The formation of **12c** and **13b** can be accounted for by assuming, as in the case of **12a** and **13a**, the intermediacy of the enamidothiolate **17a**, while lithiation α to sulfur followed by β elimination involving C_3–N bond rupture to give **17b** would afford **16a** and **16b** upon addition of MeI and NH_4Cl, respectively. Metalation α to sulfur has been reported for sulfides.[12] Moreover, that the carbamoyl is a better leaving group than the amino group may explain the fact that **2** undergoes also β elimination involving C_3–N bond cleavage, whereas compound **11**, as mentioned above, does not.

The foregoing findings might be rationalized by assuming that the inductive effect of the methyl group in the 3-position disfavors the α-nitrogen carbanion formation such that metalation α to the sulfur becomes competitive. However, in the reaction of **2** with LDA/MeI the major product of the eliminative ring opening (see Table I) is **12c** that is that involving the S–C_2 bond breaking, probably because the sulfur leaving group is better than the amido leaving group.

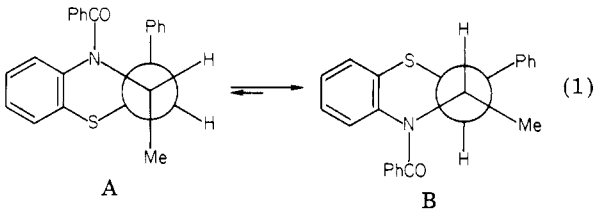
Accordingly, with the foregoing results the reaction of the 2-methyldihydrobenzothiazine **3** with LDA and MeI produced only compound **12d** and no ring-opened product involving C_3–N bond cleavage, while the reaction of **4** gave rise to the formation of both **12e** and **16c**. The rather high yield of **16c** (see Table I) is in agreement with the acidifying effect of the phenyl group on the hydrogen in the 2-position. ^1H NMR coupling constants between vinylic protons (J = 14 Hz) clearly indicate that compounds **12d** and **12e** have trans geometry. These results seem to further support the idea that the "eliminative ring fission" occurs via an E1cB or an E2–E1cB-like mechanism and that the intermediate α-nitrogen carbanion is an sp^3 configurationally stable one, as reported for other organolithiums.[13]

Accordingly, with the increased acidity of the hydrogen in the 2-position of **4** due to the presence of the phenyl group in this position, the reaction of **4** with LDA followed by the addition of NH_4Cl provides both the ring-opened products **12f** and **16d**.

It is worth noting that the presence of a good leaving group such as chlorine in the 2-position of the dihydrobenzothiazine derivative **8** brings about, upon treatment with LDA, a different β elimination, providing 4-benzoyl-1,4-benzothiazine (**18**). A likely explanation for this is that Cl^- is a better nucleofuge than S^-.

Structural limitation of the ring-opening reactions has also been checked by examining the behavior of the 2,3-disubstituted dihydrobenzothiazines **5**–**7** toward LDA under the same conditions described for the monosubstituted derivatives **1**–**4**. We have found that **5**–**7** give no "eliminative ring fission" even under relatively more severe conditions (longer reaction time) and are recovered practically unchanged.[14]

In accordance with the suggestions we made above for the reactivity of compounds **1**–**4**, the inertness of compounds **5**–**7** toward LDA can tentatively be explained in terms of both electronic and steric effects that would disfavor the anion formation α to both sulfur and nitrogen. As far as compound **5** is concerned, the presence of the methyl group in the 3-position would of course disfavor the α-nitrogen carbanion formation, but the phenyl group in the 2-position is expected to favor the α-sulfur anion formation as observed in the case of compound **4**. The fact that **5** does not undergo a ring-opening reaction might be accounted for by considering that, on the basis of the ^1H NMR coupling constants between 2-H and 3-H indicating a trans geometry,[15] **5** would exist largely as conformer B (eq 1), in view of the high steric compression which arises



(1)

in conformer A. As can be noted, in the more abundant conformer B the syn coplanarity between the α-nitrogen hydrogen atom and the carbonyl, that, as stressed by Beak,[13] is the prerequisite for the generation of the α-nitrogen carbanion, cannot be achieved. Moreover, steric factors can also intervene to inhibit the approach of the base for the deprotonation of A either in the 2- or in the 3-position.

Such conformational and steric considerations drawn for compound **5** can reasonably be extended to derivatives **6** and **7**. Therefore, it is not unreasonable to suppose that carbanion formation does not occur in the case of dihydrobenzothiazines **5**–**7** so that ring opening does not take place.

Activation of the α-nitrogen proton removal is provided by the acyl group, the benzoyl moiety being the most practical. No ortho metalation[16] was observed in the re-

(12) Beak, P.; Farney, R.; Helnick, L.; Reitz, D. *J. Am. Chem. Soc.* **1978**, *100*, 5424. Peterson, D. J. *J. Org. Chem.* **1967**, *32*, 1717. Beak, P.; Becker, P. D. *Ibid.* **1982**, *47*, 3855.

(13) Beak, P.; Chandrasekhar, J.; Houk, K. N.; Rondan, N. G.; Schleyer, P. v. R.; Zajdel, W. J. *J. Org. Chem.* **1981**, *46*, 4108. Beak, P.; Brubaker, G. R.; Farney, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 3621.

(14) A very low percentage of deuterium incorporation in the 3-position of compound **6** was detected by ^1H NMR.

(15) The coupling constant $J_{H_2-H_3}$ is not high, but lower values have been reported for dihydrothiazine derivatives having 2-H and 3-H in a cis arrangement: Dunn, A. R.; McMillan, I.; Stoodley, R. J. *Tetrahedron* **1968**, *24*, 2985. Dunn, A. R.; Stoodley, R. J. *Tetrahedron Lett.* **1969**, 2979; *Tetrahedron* **1972**, *28*, 3315.

Table II. Benzoylation of Amines 19 and 23-28 to Compounds 1-7

amine	method	product[a]	mp °C (solvent)[b]	yield, %	^{1}H NMR ($CDCl_3$),[c] δ
19	A	1	88-89 (C)	79	3.1-3.3 (m, 2 H), 3.9-4.1 (m, 2 H)
23	A	2	89-90 (C)	85	1.2 (d, J = 7 Hz, 3 H), 2.6-2.9 (dd, J = 5 Hz, 1 H), 3.3-3.7 (dd, J = 7 Hz, 1 H), 5.1-5.6 (m, 1 H)
24	A	3	140-141 (D)	90	1.4 (d, 3 H), 3.3-3.8 (m, 2 H), 4.3-4.6 (m, 1 H)
25	B	4	143-145 (E)	76	3.4-3.7 (m, 1 H), 4.7-5.1 (m, 2 H)
26	B	5	95-96 (D)	55	0.95 (d, J = 7 Hz, 3 H), 5.1 (d, J = 5 Hz, 1 H), 5.5 (m, J = 7, 5 Hz, 1 H)
27	B	6	170-172 (F)	50	1.2-2.4 (m, 6 H), 3.7-4.2 (m, 1 H), 5.4-5.8 (m, 1 H)
28	A	7	160-161 (D)	80	1.2 (m, 10 H), 4.2 (m, 1 H), 5.3 (m, 1 H)

[a] Compounds 1-7 showed the C=O stretching in the range 1640-1680 cm^{-1}. [b] Crystallization solvents: C, ether-petroleum ether; D, ethanol; E, petroleum ether-isopropanol; F, isopropanol. [c] Selected data.

action of compounds 1–8 with LDA nor the debenzoylation. We have also attempted activation with trifluoroacetyl and formyl groups, but we found that compounds **9** and **10** undergo substantial deacylation when treated with LDA. Thus, treatment of **9** with LDA and subsequent addition of methyl iodide afforded small amounts of the ring-opened products **12g** (18%) and **16e** (5%) and the free amine **19**, while reaction of **10** gave compounds **19** (29%) and **11** (13%) together with an unidentified compound (15%) and no ring-opened products. The lack of eliminative ring opening in these systems (**9**, **10**) compared to the benzoyl system may reasonably be ascribed to their tendency, for steric and electronic reasons, to suffer nucleophilic attack.

In conclusion, the present study demonstrates that 4*H*-2,3-dihydro-1,4-benzothiazines can undergo facile "eliminative ring fission" simply on acylation and treatment with LDA or an organolithium. The acyl group provides activation for the proton removal to generate the carbanion α to the nitrogen atom, and lithium ion plays an important role in favoring the ring-opening reaction. The syn coplanarity between the C_3–H bond and the carbonyl seems to be necessary for the successful ring-opening reaction. This new ring cleavage of 4*H*-2,3-dihydro-1,4-benzothiazines represents a useful route to benzo enamides, which are otherwise rather difficult to prepare.[17] The presence of substituents in the 2- and 3-position of the thiazino moiety markedly affects the direction of the ring-opening reaction.

Experimental Section

Melting points were determined on a Electrothermal apparatus and are uncorrected. Infrared (IR) spectra were taken on Perkin-Elmer 681 spectrometer. Nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 60 MHz on a Varian EM 360A instrument or at 200 MHz on a Varian XL-200 spectrometer. Chemical shifts are reported as δ units downfield from internal tetramethylsilane. Satisfactory analytical data (±0.3 for C, H, and N) were reported for compounds **1–10**, **12a–g**, **13a,b**, **16a–e**, **18**, and **20**. Thin-layer chromatography (TLC) was performed on silica gel sheets with fluorescent indicator (Stratocrom SIF 254, Carlo Erba); preparative TLC employed Merck 20 cm × 20 cm (2 mm) plates. Column chromatography was conducted by using 70–230-mesh silica gel from Merck.

Reactions requiring anhydrous conditions were performed in oven-dried glassware under a nitrogen atmosphere. Tetrahydrofuran and diethyl ether from commercial sources (Carlo Erba) were purified by distillation (twice) from sodium (wire) and stored under nitrogen. Commercial *n*-BuLi and *sec*-BuLi (Fluka) were standardized by titration. *t*-BuOK and 12-crown-4 ether were commercial grade (Aldrich, Fluka). TMEDA and diisopropylamine (Fluka) were purified by distillation prior to use. KDA was made according to the reported procedure.[18] Petroleum ether was the 40–70 °C boiling fraction.

Compounds 1–7 were prepared by benzoylation of the related amines **19** and **23–28** according to the procedures described for 1 and 4 (Table II). **4-Methyl-2,3-dihydro-4*H*-1,4-benzothiazine (11)**,[19] **2,3-dihydro-4*H*-1,4-benzothiazine (19)**,[20] **3-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (23)**,[21] **2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine (25)**,[22] **2-phenyl-3-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (26)**,[23] **1,2,3,3a,9,9a-hexahydrobenzo[*b*]cyclopenta[*e*][1,4]thiazine (27)**,[24] and **5a,6,7,9,9a,10,10a,11-octahydrobenzo[*b*]cyclohepta[*e*][1,4]-thiazine (28)**[23] were prepared by following the reported procedures.

2-Methyl-2,3-dihydro-4*H*-1,4-benzothiazine (24). A solution of NaOH (32.8 g, 820 mmol) in 200 mL of H_2O was treated portionwise with 2-aminobenzenethiol (100 g, 800 mmol) while the temperature was maintained below 30 °C. The resulting solution was then treated with a solution of α-chloropropionic acid (91.8 g, 850 mmol) in 120 mL of H_2O. The reaction mixture was refluxed for 4 h and allowed to stand overnight at room temperature. A yellow solid precipitated and was filtered off, washed with cold water, and dried in a oven: 110 g; mp 125–126 °C; IR (CH_2Cl_2) 3400 (NH), 1680 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.5 (d, 3 H, J = 7.5 Hz), 3.6 (q, 1 H, J = 7.5 Hz), 6.8–7.4 (m, 4 H), 9.0 (br s, 1 H). These data and elemental analysis are consistent with **2-methyl-3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine (22)**. A 10-g (55.8 mmol) sample of this compound in 100 mL of THF was added to a stirred solution of $LiAlH_4$ (2.6 g, 63 mmol) in 100 mL of THF. The reaction mixture was refluxed for 1 h. After the mixture cooled, water was carefully added to destroy the excess $LiAlH_4$. The organic layer was then separated and dried over Na_2SO_4, and the solvent was removed under reduced pressure to give an oil which was purified by column chromatography (ether–petroleum ether (1:1) as eluent): 4.55 g (49% yield); IR (neat) 3400 (NH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.3 (d, 3 H), 2.9–3.5 (cm, 3 H), 3.9 (br s, 1 H), 6.3–7.0 (m, 4 H).

General Procedure for the Benzoylation of Amines 19 and 23–28. Method A. This was as described for the benzoylation of **1**. A solution of benzoyl chloride (14.1 g, 100 mmol) in 50 mL of ether was added dropwise to a stirred solution of **19** (15.1 g, 100 mmol) and pyridine (8.3 g, 105 mmol) in ether (250 mL) at −5 °C. The mixture was then allowed to warm to room temperature and kept there for 1 h. Water (200 mL) was added, and the organic layer was washed several times with 10% HCl and then with water and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave **1**.

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Method B. This was as described for the preparation of **4**. Benzoic anhydride (2.9 g, 13 mmol) was added to a stirred solution of **25** (2.9 g, 12 mmol) in 70 mL of dry toluene, and the reaction mixture was refluxed for 8 h. The toluene was removed under reduced pressure, and the residue was dissolved in 50 mL of $CHCl_3$ and washed with 10% aqueous $NaHCO_3$ and then with water. The $CHCl_3$ extract was dried over Na_2SO_4 and evaporated to give **4**.

4-Benzoyl-2,2-dichloro-2,3-dihydro-4*H*-1,4-benzothiazine (8). To a solution of **1** (1.5 g, 5.8 mmol) in 50 mL of CCl_4 at reflux was added a solution of SO_2Cl_2 (3.5 mL, 42 mmol) in 20 mL CCl_4 dropwise and with stirring. After 1.5 h the solvent was removed under reduced pressure, giving a residue which solidified on cooling: 1.8 g (94% yield); mp 94–95 °C (ethanol); white crystals; IR (CH_2Cl_2) 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.7 (s, 2 H), 6.5–7.4 (m, 9 H).

4-(Trifluoroacetyl)-2,3-dihydro-4*H*-1,4-benzothiazine (9). A 2-g (13 mmol) sample of **19** was treated with 35 mL of trifluoroacetic anhydride at room temperature for 1 h under N_2. Removal of the excess trifluoroacetic anhydride gave a residue that was dissolved in $CHCl_3$ (50 mL) and washed with 10% $NaHCO_3$. The organic layer was then washed with water and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure left an oil that was purified by column chromatography (petroleum ether–ethyl acetate (8:2) as the eluent): 2.7 g (82% yield); IR (neat) 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.20 (t, 2 H), 3.9 (t, 2 H), 6.70–7.50 (m, 4 H).

4-Formyl-2,3-dihydro-4*H*-1,4-benzothiazine (10). A 1.6-g (10.6 mmol) sample of **19** and 5 mL of formic acid were kept at room temperature for 24 h. The reaction mixture was then diluted with ether (50 mL), washed with Na_2CO_3 (saturated solution) and with water, and dried over Na_2SO_4. Removal of the solvent under reduced pressure left 1.8 g (95% yield) of a white solid: mp 63–64 °C (ether); ^1H NMR ($CDCl_3$) δ 3.1 (m, 2 H), 4.0 (m, 2 H), 6.9–7.3 (m, 4 H), 8.5 (s, 1 H).

Reaction of 4-Benzoyl-2,3-dihydro-4*H*-1,4-benzothiazine (1) with LDA. (A) Quenching with MeI. A solution of **1** (0.5 g, 1.96 mmol) in 10 mL of dry THF was added dropwise at −78 °C to stirred solution of LDA prepared in situ (at 0 °C) by adding 1.58 mL of 1.49 N *n*-BuLi (2.35 mmol) to a solution of diisopropylamine (0.24 g, 2.35 mmol) in 10 mL of THF under a nitrogen atmosphere. The reaction mixture was kept at −78 °C for 20 min, and then an excess of MeI (0.5 mL) was added. After 1 h the mixture was allowed to warm to room temperature and treated with NH_4Cl (saturated solution). Extraction with ether (150 mL), drying over Na_2SO_4, and removal of the solvent under reduced pressure left a residue (thick oil, 0.5 g). TLC (ether–petroleum ether, 7:3) showed the presence of essentially one product. Column chromatography gave 0.45 g of ***N*-benzoyl-*N*-[2-(methylthio)phenyl]ethenamine (12a)**: mp 98–99 °C (ethanol); IR (CH_2Cl_2) 1670 (C=O), 1615 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (s, 3 H), 3.95 (d, 1 H, J = 16 Hz), 4.40 (d, 1 H, J = 9 Hz), 7.1–7.6 (m, 10 H, 9 aromatic protons and 1 vinylic proton). Analogously prepared was ***N*-benzoyl-*N*-[2-(ethylthio)phenyl]ethenamine (12b)**: mp 55–56 °C (ether–petroleum ether); IR (CH_2Cl_2) 1660 (C=O), 1620 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (t, 3 H), 2.9 (q, 2 H), 3.9 (d, 1 H, J = 14 Hz), 4.4 (d, 1 H, J = 8 Hz), 7.0–7.6 (m, 10 H, 1 vinylic proton).

(B) Quenching with NH_4Cl. The dihydrobenzothiazine **1** (0.5 g, 1.96 mmol) was treated with LDA (2.1 mmol) as in method A. After 15 min at −78 °C NH_4Cl (saturated solution) was added and the mixture allowed to warm to room temperature. Extraction with ether (100 mL), drying over Na_2SO_4, and evaporation of the solvent yielded a residue (0.47 g). TLC showed the presence of two products which were separated by column chromatography with ether–petroleum ether (1:1) as the eluent. The first eluted material was **2-methyl-3-benzoylbenzothiazoline (13a)**: 0.3 g; mp 78–79 °C (ethanol); IR (CCl_4) 1660 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6 (d, 3 H, J = 7 Hz), 5.85 (q, 1 H, J = 7 Hz), 6.5–7.6 (m, 9 H). The second eluted product was the starting material **1**: 0.15 g; mp 88–89 °C (undepressed melting point).

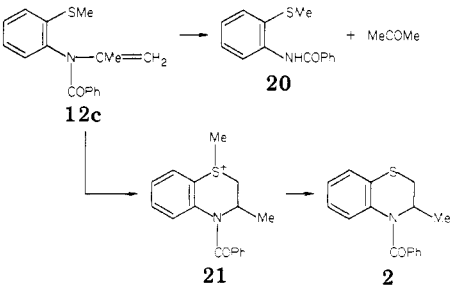
Reaction of 4-Benzoyl-3-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (2) with LDA. (A) Quenching with Methyl Iodide. Compound **2** (1.08 g, 4.02 mmol) in 10 mL of THF was added dropwise to a stirred solution of LDA (4.42 mmol) prepared as above at −78 °C. After 15 min an excess of methyl iodide (0.5 mL) was added and the mixture allowed to warm to room temperature. The usual workup gave a residue (1.10 g) that was a mixture (TLC) of two main products. Separation was accomplished by column chromatography by using ether–petroleum ether (1:1) as the eluent. The first-eluted product was ***N*-benzoyl-*N*-[2-(methylthio)phenyl]propen-2-ylamine (12c)**: 0.57 g; thick oil; IR (CH_2Cl_2) 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (s, 3 H), 2.4 (s, 3 H), 4.4 (s, 1 H), 4.7 (s, 1 H), 6.8–7.6 (cm, 9 H). Elemental analysis is roughly in agreement. Attempted purification of 0.25 g of this compound from ether led to a mixture of **2** (0.12 g) and **2-(benzoylamino)-1-(methylthio)benzene (20)**: 0.1 g; mp 97–98 °C; IR (CH_2Cl_2) 3375 (NH), 1675 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.3 (s, 3 H), 6.8–7.6 (cm, 6 H), 7.7–7.9 (m, 2 H), 8.3–8.5 (d, 1 H), 9.1 (br s, 1 H, exchange with D_2O). Compounds **2** and **20** were separated by column chromatography (ether–petroleum ether (2:8) as the eluent).[25] The second eluted product was **1-[[2-(benzoylmethylamino)phenyl]thio]prop-1-ene (16a)**: 0.35 g; thick oil; IR (CH_2Cl_2) 1650 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8 (d, 3 H), 3.35 (s, 3 H), 5.8–6.1 (m, 2 H), 6.8–7.4 (m, 9 H). However, ^1H NMR does not allow us to distinguish between cis and trans forms of this compound.

(B) Quenching with NH_4Cl. The dihydrobenzothiazine **2** (1 g, 3.7 mmol) was reacted with LDA as in procedure A. After 20 min NH_4Cl (saturated solution) was added and the mixture warmed to room temperature. Dilution with water, extraction with ether, drying over Na_2SO_4, and removal of the solvent under reduced pressure left a residue (1.1 g). TLC indicated the presence of two main products which were separated by column chromatography (ether–petroleum ether (8:2) as the eluent). The first product was **2,2-dimethyl-3-benzoylbenzothiazoline (13b)**: 0.46 g; mp 111–112 °C (ethanol); IR (CH_2Cl_2) 1665 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (s, 6 H), 5.8–7.5 (m, 9 H). The second eluted product seems to be a mixture of ***cis*-** and ***trans*-1-[[2-(benzoylamino)phenyl]thio]prop-1-ene (16b)**: 0.12 g; mp 70–75 °C; IR (CH_2Cl_2) 3390 (NH), 1680 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6–1.9 (2 d, 3 H), 5.8 (m, 1 H), 7.0–7.9 (cm, 9 H), 8.6 (d, 1 H), 8.9 (br s, 1 H, exchanges with D_2O).

Reaction of 4-Benzoyl-2-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (3) with LDA and Methyl Iodide. A solution of **3** (0.7 g, 2.6 mmol) in 40 mL of THF was added dropwise at −78 °C to a stirred solution of LDA (3.0 mmol) prepared as above. After 20 min methyl iodide (0.5 mL) was added and the reaction mixture allowed to warm to room temperature. Dilution with ether and the usual workup provided a residue (0.73 g). TLC showed the presence of a single product, which was purified by column chromatography (ether–petroleum ether (1:1) as the eluent). It was ***N*-benzoyl-*N*-[2-(methylthio)phenyl]-propen-1-ylamine (12d)**: 0.6 g; mp 114–115 °C (ethanol); IR (CH_2Cl_2) 1660 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6 (d, 3 H, J = 7 Hz), 2.4 (s, 3 H), 4.6 (sextet, 1 H, J = 7, 15 Hz), 7.0–7.7 (m, 10 H, 1 vinylic and 9 aromatic protons).

Reaction of 4-Benzoyl-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine (4) with LDA. (A) Quenching with MeI. A solution of **4** (0.7 g, 2.1 mmol) in 30 mL of THF was added to a stirred solution of LDA (2.5 mmol) in 15 mL of THF at −78 °C. After 45 min methyl iodide (0.5 mL) was added, and the reaction mixture was allowed to warm to ambient temperature. Dilution with ether (75 mL) and the usual workup gave a residue (0.72 g)

(25) A hydrolysis of **12c** might explain the formation of **20**, whereas the formation of **2** might be accounted for by assuming a nucleophilic attack of the sulfide group on the enamido function followed by demethylation as shown below. See: Lenz, G. R., ref 17. McKillop, A.; Sayer, T. S. B.; Bellinger, G. C. A. *J. Org. Chem.* **1976**, *41*, 1328.



that was a mixture of two main components that were separated by column chromatography (ether–petroleum ether (1:1) as the eluent). The first eluted component was ***trans*-1-*N*-benzoyl-*N*-[2-(methylthio)phenyl]-2-phenylethenamine (12e)**: 0.38 g; mp 148–149 °C (ethanol); IR (CH_2Cl_2) 1680 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.4 (d, J = 15 Hz, 1 H), 6.9–7.6 (m, 14 H), 8.0 (br d, J = 15 Hz, 1 H). The second eluted component was **1-phenyl-1-[[2-(benzoylmethylamino)phenyl]thio]ethene (16c)**: 0.28 g; oil; IR (CH_2Cl_2) 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.4 (s, 3 H), 5.4 (s, 1 H), 5.7 (s, 1 H), 6.5–7.7 (m, 14 H).

(B) Quenching with NH_4Cl. A solution of **4** (2 g, 6.04 mmol) in 40 mL of THF was treated with LDA (7.25 mmol) as above. After 45 min at −78 °C the reaction mixture was quenched with aqueous NH_4Cl and allowed to warm to room temperature. Dilution with ether and the usual workup gave a residue (2.1 g) that was a mixture of two main products which were separated by column chromatography (ether–petroleum ether (3:7) as the eluent). The first-eluted product was **1-phenyl-1-[[2-(benzoylamino)phenyl]thio]ethene (16d)**: 0.86 g; mp 66–68 °C (ether–petroleum ether); IR (CH_2Cl_2) 3385 (NH), 1680 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.7 (s, 1 H), 5.4 (s, 1 H), 7.0–7.9 (cm, 13 H), 8.7 (d, 1 H), 9.1 (br s, 1 H, slow exchange with D_2O). The second-eluted product was **bis(*N*-styryl-*N*-benzoylanilin-2-yl) disulfide (12f)**: 0.71 g; mp 183–185 °C (ethanol); IR (CH_2Cl_2) 1660 (C=O), 1600 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.5 (d, 1 H, J = 14 Hz), 6.9–7.6 (m, 14 H), 8.1 (br d, 1 H, J = 14 Hz); MS, m/e 330 ($M^+/2$).

Reaction of 4-Benzoyl-2,2-dichloro-2,3-dihydro-4*H*-1,4-benzothiazine (8) with LDA. A solution of **8** (0.35 g, 1.1 mmol) in 10 mL of THF was added dropwise at −60 °C to a stirred solution of LDA (2.2 mmol) in 15 mL of THF prepared as above. After 15 min the reaction mixture was warmed to room temperature and NH_4Cl added. Extraction with ether, drying over Na_2SO_4, and evaporation of the solvent left a residue (0.27 g). TLC (ether–petroleum ether (7:3) as the eluent) indicated the presence of one product, which was purified by column chromatography. Its structure is consistent with **4-benzoyl-2-chloro-4*H*-1,4-benzothiazine (18)**: 0.25 g; oil; IR (neat) 1665 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) does not allow to one distinguish between vinylic and aromatic protons. Elemental analysis is in agreement.

Reaction of 4-(Trifluoroacetyl)-2,3-dihydro-4*H*-1,4-benzothiazine (9) with LDA. A solution of **9** (1 g, 4 mmol) in 15 mmol of THF was added to a stirred solution of LDA (5.0 mmol) in 15 mL of THF at −78 °C. After 30 min 0.5 mL of MeI was added and the reaction mixture allowed to warm to room temperature. Dilution with ether (50 mL) and the usual workup left a residue (0.98 g). TLC showed the presence of three main products which were separated by column chromatography (ether–petroleum ether (1:9) as the eluent). The first eluted component was **[[2-[(trifluoroacetyl)amino]phenyl]thio]-ethene (16e)**: 0.06 g; oil; IR (CH_2Cl_2) 3400 (NH), 1660 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.85 (d, 1 H, J = 16 Hz), 5.2 (d, 1 H, 9 Hz), 6.0–6.4 (q, 1 H, J = 16, 9 Hz), 7.0–7.6 (m, 4 H), 8.3 (d, 1 H), 8.9 (br s, 1 H, exchanges slowly with D_2O). The second-eluted component was ***N*-(trifluoroacetyl)-*N*-[2-(methylthio)-phenyl]ethenamine (12g)**: 0.2 g; oil; IR (CH_2Cl_2) 1660 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (s, 3 H), 4.1 (d, 1 H, J = 15 Hz), 4.6 (d, 1 H, J = 9 Hz), 7.0–7.7 (cm, 5 H, 4 aromatic protons and 1 vinylic). The third eluted compound was **4*H*-2,3-dihydro-1,4-benzothiazine (19)**: 0.29 g; oil; IR and ^1H NMR consistent.

Reaction of 4-Formyl-2,3-dihydro-4*H*-1,4-benzothiazine (10) with LDA. A solution of **10** (1 g, 5.6 mmol) in 15 mL of THF was added dropwise to a stirred solution of LDA (7.0 mmol) at −78 °C. After 15 min 0.8 mL of MeI was added and the reaction mixture allowed to warm to room temperature. Dilution with ether and the usual workup afforded a residue (1.2 g) that was a mixture of three products. Separation was accomplished by column chromatography (ether–petroleum ether (1:1) as the eluent). The first-eluted product was **4-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (11)**: 0.12 g; oil; IR and ^1H NMR consistent. The second eluted product was **4*H*-2,3-dihydro-1,4-benzothiazine (19)**: 0.34 g; oil; IR and ^1H NMR consistent. The third eluted material (0.18 g; oil) was not identified.

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Registry No. 1, 6397-17-7; **2**, 87011-99-2; **3**, 87012-00-8; **4**, 87012-01-9; **5**, 87012-02-0; **6**, 87012-03-1; **7**, 87012-04-2; **8**, 87039-14-3; **9**, 87012-05-3; **10**, 76800-99-2; **11**, 6397-11-1; **12a**, 87012-06-4; **12b**, 87012-07-5; **12c**, 87012-08-6; **12d**, 87012-09-7; (*E*)-**12e**, 87012-10-0; **12f**, 87012-11-1; **12g**, 87012-12-2; **13a**, 72889-12-4; **13b**, 87012-13-3; **16a**, 87012-14-4; (*E*)-**16b**, 87012-21-3; (*Z*)-**16b**, 87012-15-5; **16c**, 87012-16-6; **16d**, 87012-17-7; **16e**, 87012-18-8; **18**, 87012-19-9; **19**, 3080-99-7; **22**, 7028-57-1; **23**, 87012-20-2; **24**, 58960-00-2; **25**, 83523-72-2; **26**, 25069-67-4; **27**, 66234-07-9; **28**, 25069-64-1; 2-aminobenzenethiol, 137-07-5; α-chloropropionic acid, 598-78-7.

Oxidative Decyanation of Secondary Nitriles to Ketones

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Procedures for the oxidative decyanation of secondary nitriles to ketones involve (1) iodination of *N*-(trialkylsilyl)ketenimines derived from secondary nitriles and subsequent hydrolysis of the α-iodo nitriles with silver oxide, (2) addition of nitrosobenzene to *N*-(trialkylsilyl)ketenimines, (3) conversion of secondary nitriles to α-(phenylthio) nitriles and subsequent hydrolysis with *N*-bromosuccinimide in aqueous acetonitrile, and (4) preparation of α-hydroperoxy nitriles by direct oxygenation of anions of secondary nitriles and subsequent reductive hydrolysis with stannous chloride followed by sodium hydroxide. The latter general procedure was applied to various secondary nitriles bearing dialkyl, aryl and alkyl, and diaryl substituents to provide ketones in good yield and was extended to the oxidative decyanation of α,β-unsaturated nitriles to furnish α,β-unsaturated ketones.

Kharasch and Sosnovsky[1] first demonstrated that secondary nitriles **1** would trap molecular oxygen in the presence of a base to provide ketones **2**. The selection of sodium methoxide in methanol limited the scope of this oxygenation procedure to the relatively acidic, aryl-substituted acetonitriles. For example, diphenylacetonitrile furnished benzophenone in 92% yield, but isobutyronitrile afforded only trace amounts of acetone. The authors suggested that the anion of diphenylacetonitrile trapped oxygen to form an α-hydroperoxy nitrile **3** which ultimately gave benzophenone. Subsequent reports on the aut-

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