Substituted (Carbazol-9-yl)(benzotriazol-1-yl)methanes: Novel Acyl Anion Equivalents

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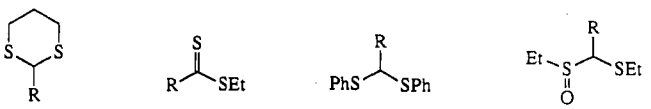
Alkyl(carbazol-9-yl)(benzotriazol-1-yl)methanes are deprotonated by BuLi to form anions which react with alkyl halides, aldehydes, and isocyanates to afford the expected products and which add 1,4 to α,β-unsaturated ketones. These products are hydrolyzed by dilute acid at ambient temperature to afford the corresponding ketones.

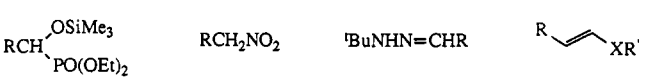
Introduction

Carbon atoms attached to two heteroatoms are versatile intermediates in synthetic organic chemistry. The greater electronegativity of these heteroatoms renders facile removal of the protons on the carbon atom allowing further functionalization and/or carbon–carbon bond formation. Hydrolytic removal of these heteroatoms forms carbonyl compounds. Thus compounds of type $XYHC^-$ are utilized as formyl anion equivalents, while $XYRC^-$ are potential acyl anion equivalents. In many cases, the parent precursor ($XYCH_2$) is the same for both these types of anion equivalents.

Acyl anion equivalents are of intense current interest: Sengupta and Snieckus[1] have summarized recent references and the subject has been comprehensively reviewed.[2,3] Among the more common acyl anion precursors where X = Y = S are the 2-substituted 1,3-dithianes **1**,[4-6] the thioester **2**,[7] diaryl dithioacetals **3**,[8,9] and also oxidized thioacetals **4**.[10,11] In most cases, these precursors are treated with a strong base to generate the acyl anion equivalent which is then reacted with an electrophile, followed by removal of the heteroatom moiety. These systems are limited by the conditions required for initial deprotonation, by the reactivity of the anion, and by the conditions needed for the final hydrolysis step. Whereas the anions of **1** and **4** react readily with electrophiles, conversion to the carbonyl compound requires complex formation with a heavy-metal cation (usually a mercury(II) salt[12,13]) or making one of the sulfur atoms more electrophilic (for **1** through oxidation).[14] Recently, electrolysis, involving anodic oxidation followed by nucleophilic attack with water,[15] has been employed in cases where chemical transformations were unsuccessful, but only examples with an α-carbonyl or an α-hydroxy group were discussed. Alkylations of dialkyl dithioacetals occur in low yields[16] unless alternative approaches involving initial addition of a Grignard reagent to the dithioester **2** followed by reaction with an electrophile are used.[17] Although the arylthio groups enhance the stabilization of the anion of **3**, compounds **3** have not found widespread applications due to the difficulty in alkylating the corresponding lithium derivatives. Thus, α,β-unsaturated ketones will react only after formation of the cuprates[18] and with aldehydes and ketones the reaction occurs only in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA).[8] Furthermore, alkylations of **3** are possible only via treatment with butyllithium in hexane at 0 °C in the presence of TMEDA.[9] In certain cases, organometallic reagents such as Grignard reagents, phenyllithium, or butyllithium have cleaved one of the phenylthio groups.[19]



1 **2** **3** **4**



5 **6** **7** **8** a X = O, b X = S, c X = Se

An example of an acyl anion precursor of type X ≠ Y ≠ S is the silyloxy phosphonate **5** which can be deprotonated and treated with electrophiles.[20-23] Deprotonation, reaction with the electrophile, and subsequent hydrolysis to the ketone all occur in high yield. However, most of the examples deal with cases where R = phenyl. When R = alkyl,[21] the electrophiles employed were alkyl and benzyl halides. Thus only simple ketones have been prepared by this route.

The ability of a nitro group to stabilize an α-carbanion has led to the use of primary nitroalkanes **6** for the syn-

(1) Sengupta, S; Snieckus, V. *J. Org. Chem.* **1990**, *55*, 5680.
(2) Ager, D. J. In *Umpoled Synthons: A Survey of Sources and Uses in Synthesis*; Hase, T. A., Ed.; Wiley: New York, 1987; p 19 and references within.
(3) (a) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239. (b) Martin, S. F. *Synthesis* **1979**, 633. (c) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1.
(4) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.
(5) Mori, M.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Tetrahedron Lett.* **1982**, *23*, 667.
(6) Williams, D. R.; Sit, S.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 2949.
(7) Meyers, A. I.; Tait, T. A.; Comins, D. L. *Tetrahedron Lett.* **1978**, 4657.
(8) Blatcher, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1074.
(9) Ager, D. J. *Tetrahedron Lett.* **1980**, 4763.
(10) Richman, J. E.; Herrmann, J. L.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 3267.
(11) Carey, F. A.; Dailey, O. D., Jr.; Hernandez, O.; Tucker, J. R. *J. Org. Chem.* **1976**, *41*, 3975.
(12) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431.
(13) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434.
(14) Abdallah, M. A.; Shah, J. N. *J. Chem. Soc., Perkin Trans. 1* **1975**, 888.
(15) Martre, A.-M.; Mousset, G.; Rhlid, R. B.; Veschambre, H. *Tetrahedron Lett.* **1990**, *31*, 2599.
(16) Froling, A.; Arens, J. F. *Recl. Trav. Chim. Pays-Bays* **1962**, *81*, 1009.
(17) Masson, S.; Saquet, M.; Thuillier, A. *Tetrahedron* **1977**, *33*, 2949.
(18) Mukaiyama, T.; Narasaka, K.; Furusato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641.
(19) Truce, W. E.; Roberts, F. E. *J. Org. Chem.* **1963**, *28*, 961.
(20) Hata, T.; Hashizume, A.; Nakajima, M.; Sekine, M. *Tetrahedron Lett.* **1978**, 363.
(21) Sekine, M.; Nakajima, M.; Kume A.; Hata, T. *Tetrahedron Lett.* **1979**, 4475.
(22) Koenigkramer, R. E.; Zimmer, H. *Tetrahedron Lett.* **1980**, 1017.
(23) Koenigkramer, R. E.; Zimmer, H. *J. Org. Chem.* **1980**, *45*, 3994.

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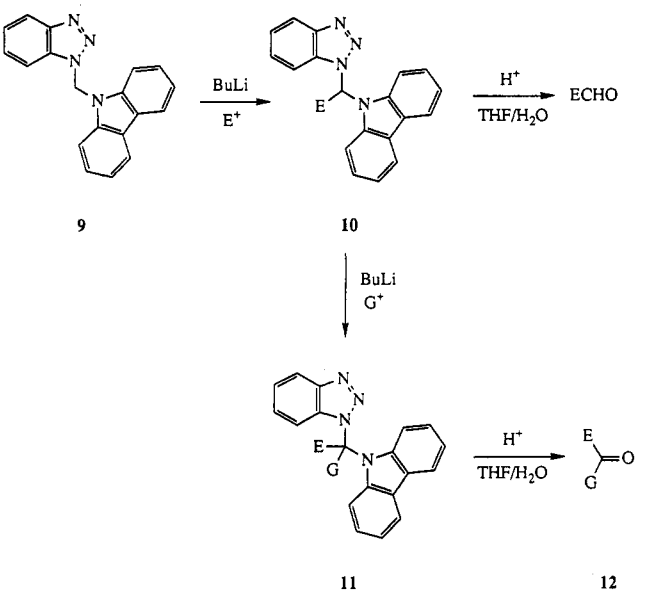
thesis of ketones;[24,25] this is an example of an acyl anion precursor containing only one heteroatom-linked group. Primary nitroalkanes, on base-catalyzed treatment with carbonyl compounds, afford the adducts in moderate yields.[24,25] If additional activating groups are present at the β-position, an α,β-dideprotonated species is obtained with subsequent electrophilic addition occurring at the β-position.[26] These nitro derivatives can then be converted to the ketones by electrolysis,[27] by the Nef reaction,[28] by chromium[29] or persulfate[30] oxidation, or by titanium(III) chloride.[25] However, difficulties associated with simple C-alkylation have hindered exploitation of nitroalkanes in synthetic schemes.

Other examples of this type are the *tert*-butylhydrazone[31] **7** (obtained by the reaction of an aldehyde and *tert*-butylhydrazine) and vinyl compounds such as vinyl ethers **8a**,[32,33] vinyl sulfides **8b**,[34,35] and vinyl selenides **8c**.[36-38] Recently, Yamamoto et al.[39] have developed a protected hydroxymalononitrile as an acyl anion equivalent which has been employed in the preparation of masked activated esters but not ketones. The reaction of alkyl halides with the anion of **7** is slow (1–2 days). The initially formed azo intermediate tautomerises in trifluoroacetic acid to yield the ketone hydrazone. With carbonyl compounds as the electrophiles, the intermediate azo alcohol is unstable and requires further in situ treatment with butyllithium followed by a water quench to generate the α-hydroxyhydrazones in fair yields. Hydrolysis of these intermediates is carried out in the presence of oxalic acid–water or with phosphoric acid.[31]

Vinyl ethers **8a** (R = H) furnish anions on treatment with *tert*-butyllithium which react with alkyl halides and carbonyl compounds in good yields. Acid hydrolysis then affords the methyl ketons.[33] For the vinyl sulfides **8b**, acyl anion equivalents where R ≠ H are also known. Thus organometals such as *sec*-butyllithium,[34] LDA in THF/HMPA,[40] or LDA in hexanes[41] form the corresponding anions which then react with various electrophiles in good to moderate yields. The selective choice for the base and the solvent system is to prevent addition of the alkyllithium across the double bond.[42] For the selenoethers **8c**, both types of vinyl precursors (R = H and R = alkyl) are known. As in the previous case, carefully controlled conditions are required for proton abstraction. Alkylation occurs with LDA, while with butyllithium in tetrahydrofuran, or in diethyl ether, cleavage of the C–Se bond or addition across the double bond occurs.[36] When R = alkyl, the strongly basic mixture of potassium diisopropylamide–lithium *tert*-butoxide (KDA) is required.[37] The selenium is then usually removed by mercury reagents.[38]

There has previously been little interest in acyl anion equivalents where the carbon atom is attached to two heterocyclic rings. We now describe such a system.

Scheme I



Results and Discussion

We have recently demonstrated[43] that 1-(carbazol-9-ylmethyl)benzotriazole (**9**) is a versatile formyl anion equivalent: its readily formed anion reacts with a variety of electrophiles to afford products **10** in good yields which on acid-catalyzed hydrolysis (tetrahydrofuran/0.85 M sulfuric acid at 20 °C) afford the corresponding aldehydes. We have now found that the intermediates of type **10** can themselves undergo deprotonation and that the resulting anions react with electrophiles to form the disubstituted derivatives **11**, which upon mild hydrolysis afford ketones **12**. Hence the compounds **10** are general acyl anion equivalents (Scheme I).

Phenacetyl Anion Equivalent 21: Reactions with Electrophiles. Our initial work was carried out with 1-(benzotriazol-1-yl)-1-(carbazol-9-yl)-2-phenylethane (**20**) readily prepared[43] from easily available 1-(carbazol-9-ylmethyl)benzotriazole. The benzyl derivative **20** underwent deprotonation with butyllithium at −78 °C, and anion **21** reacted with benzyl bromide, methyl iodide, and butyl iodide to give the corresponding alkylated products (**22a–c**) (78–88%) (Scheme II). Similar reactions of anion **21** with phenyl and *tert*-butyl isocyanates, with diphenyl disulfide, and with ethyl chloroformate proceeded smoothly and afforded the expected amides (**25a,b**), the phenylthio derivative (**16**), and the ester (**24**) (84–95%) (see Table I).

Anion **21** also reacted with aldehydes to afford the expected secondary alcohol products. These compounds showed some tendency to revert back to the starting materials. However, good yields (67–85%) could be obtained with benzaldehyde and trimethylacetaldehyde provided the intermediate alcohol anions (**17a,b**) were converted to

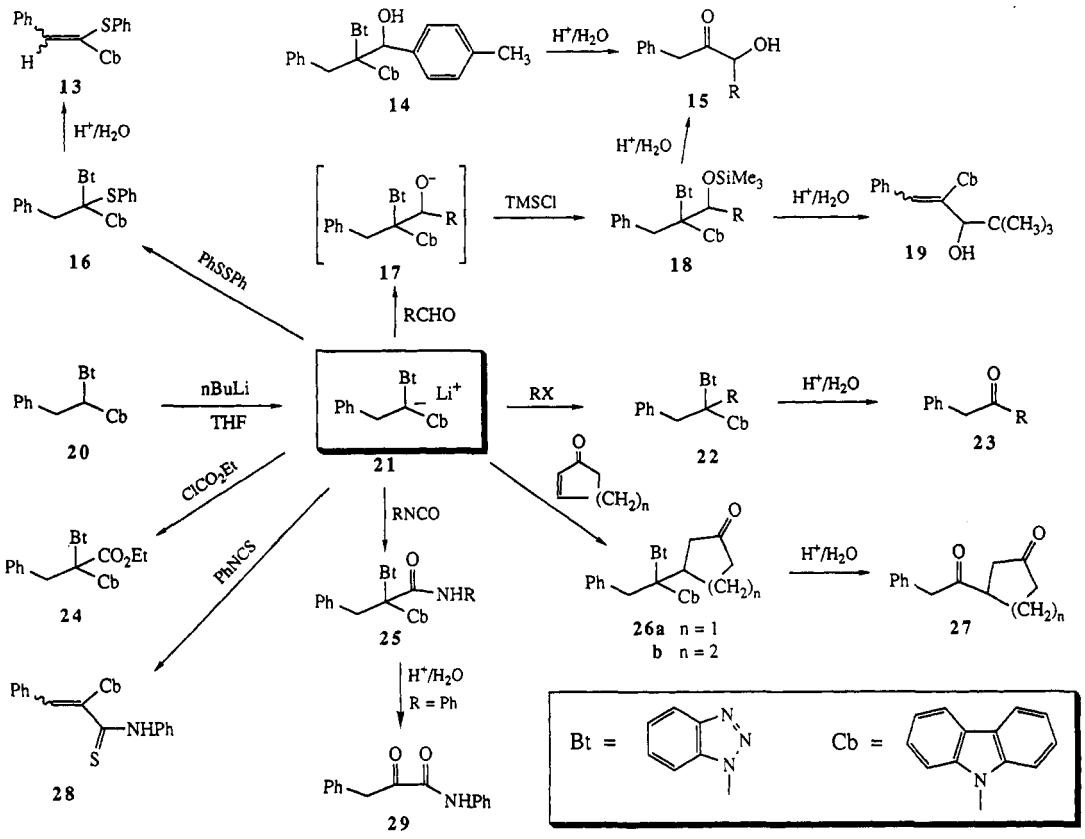
(24) Lehr, F.; Gonnermann, J.; Seebach, D. *Helv. Chim. Acta* **1979**, *62*, 2258.
(25) Hewson, A. T.; MacPherson, D. T. *Tetrahedron Lett.* **1983**, *24*, 647.
(26) Seebach, D.; Henning, R.; Lehr, F.; Gonnermann, J. *Tetrahedron Lett.* **1977**, 1161.
(27) Nokami, J.; Sonoda, T.; Wakabayashi, S. *Synthesis* **1983**, 763.
(28) Jacobson, R. M. *Tetrahedron Lett.* **1974**, 3215.
(29) Hanson, J. R.; Organ, T. D. *J. Chem. Soc. C* **1970**, 1182.
(30) Pagano, A. H.; Shechter, H. *J. Org. Chem.* **1970**, *35*, 295.
(31) Adlington, R. M.; Baldwin, J. E.; Bottaro, J. C.; Perry, M. W. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1040.
(32) Schollkopf, U.; Hanssle, P. *Justus Liebigs Ann. Chem.* **1972**, *763*, 208.
(33) Baldwin, J. E.; Hofle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125.
(34) Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694.
(35) Takeda, T.; Furukawa, H.; Fujiwara, T. *Chem. Lett.* **1982**, 593.
(36) Sevrin, M.; Denis, J. N.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 526.
(37) Raucher, S.; Koolpe, G. A. *J. Org. Chem.* **1978**, *43*, 3794.
(38) Comasseto, J. V. *J. Organomet. Chem.* **1983**, *253*, 131.
(39) Nemoto, H.; Kubota, Y.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 4515.
(40) Cookson, R. C.; Parsons, P. J. *J. Chem. Soc., Chem. Commun.* **1976**, 990.
(41) Harirchian, B.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 522.
(42) Parham, W. E.; Kalnins, M. A.; Theissen, D. R. *J. Org. Chem.* **1962**, *27*, 2698.
(43) Katritzky, A. R.; Yang, Z.; Lam, J. N. *J. Org. Chem.* **1991**, *56*, 2143.

Table I. Preparation of Disubstituted 1-Carbazol-9-ylmethylbenzotriazole Derivatives

compd	electrophile [R]	mp (°C)	yield (%)	crystal form (recryst solv)	molecular formula	found (required) C	H	N
14	4-Me-C_6H_4CHO	156–158	87	needles (EtOH)	$C_{34}H_{28}N_4O$	79.92 (80.29	5.74 5.55	11.08 11.02)
16	PhSSPh	170–172	95	plates (MeOH)	$C_{32}H_{24}N_4S$	77.54 (77.39	4.88 4.87	11.32 11.28)
18a	$PhCHO/ClSiMe_3$ [Ph]	130–131	67	plates (*a*)	$C_{36}H_{34}N_4OSi$	75.97 (76.29	6.13 6.05	9.71 9.89)
18b	$Me_3CCHO/ClSiMe_3$ [Me_3C]	175–177	85	microcrystals (*a*)	$C_{34}H_{38}N_4OSi$	75.05 (74.69	7.09 7.00	9.82 10.25)
22a	$PhCH_2Br$ [$PhCH_2$]	145–147	86	needles (MeOH)	$C_{33}H_{26}N_4$	82.53 (82.84	5.51 5.44	11.45 11.71)
22b	MeI [Me]	89–91	88	prisms (*a*)	$C_{27}H_{22}N_4$	80.78 (80.57	5.68 5.51	13.56 13.92)
22c	BuI [Bu]	101–103	78	plates (*a*)	$C_{30}H_{28}N_4$	81.05 (81.39	6.35 6.53	12.60 12.48)
24	ClCOOEt	212–214	87	plates (MeOH)	$C_{29}H_{24}N_4O_2$	75.64 (75.63)	5.36 5.25	12.03 12.17)
25a	PhNCO [Ph]	115–117	88	plates (*a*)	$C_{33}H_{25}N_5O$	77.71 (78.09	4.98 4.96	13.62 13.80)
25b	Me_3CNCO [Me_3C]	165–167	84	plates (MeOH)	$C_{31}H_{29}N_5O$	76.10 (76.36)	5.97 5.97	14.30 14.36)
26a	2-cyclopentenone [*n* = 1]	105–107	76	microcrystals (*a*)	$C_{31}H_{26}N_4O$	79.20 (79.12	5.98 5.57)	
26b	2-cyclohexenone [*n* = 2]	187–189	81	plates (*a*)	$C_{32}H_{28}N_4O$	78.90 (79.31	5.80 5.82	11.39 11.56)

[a] Column chromatography (silica gel; $CHCl_3$–hexane, 1:2).

Scheme II



their trimethylsilyl derivatives (**18a,b**) by addition of trimethylsilyl chloride to the reaction mixture prior to workup. With *p*-tolualdehyde, the alcohol (**14**) was obtained and was stable enough to be isolated without such addition.

The structures of **14**, **16**, **18a,b**, **22a–c**, **24**, and **25a,b** were confirmed by the ^1H and ^{13}C NMR spectra and by their CHN microanalyses data. Proton spectra are recorded in Table II. The presence of the chiral center rendered the adjacent methylene protons of the benzyl group nonequivalent and they appeared as an AB pattern between 4 and 5 ppm. The difference in the chemical shifts for the two protons varied from 0.14 ppm (for **22c**) to 0.62 ppm (for **18b**). The aromatic signals were generally uninformative, but the signal patterns of the substituents and the integral ratios confirmed the structures of the products.

In the ^{13}C NMR spectra all the compounds showed the characteristic six peaks for the benzotriazole group, the six peaks for the carbazole group, the five peaks of the benzyl group, and the quarternary carbon which resonated between 82 and 91 ppm (Table III). The remaining resonsances were characteristic of the substituents intro-

Table II. ^{1}H NMR Data of the Benzyl Derivatives

compd	aromatic CH signals	dd for CH^AH^B δH^A	δH^B	J (Hz)	other signals
14	8.15–7.90 (m, 3 H), 7.26–6.83 (m, 12 H), 6.81–6.57 (m, 5 H), 6.18 (d, J = 8.3 Hz, 2 H)	4.54	4.11	13.4	3.44 (d, J = 4.6 Hz, 1 H), 2.21 (s, 2 H)
16	8.11–7.91 (m, 3 H), 7.30–6.50 (m, 9 H)	4.69	4.54	14.0	
18a	7.66 (d, J = 8.4 Hz, 1 H), 7.09–6.35 (m, 21 H)	4.19	3.93	13.7	5.76 (d, J = 8.4 Hz, 1 H), −0.18 (s, 9 H)
18b	8.08 (d, J = 7.8 Hz, 1 H), 7.92 (d, J = 8.8 Hz, 1 H), 7.82 (d, J = 7.8 Hz, 1 H), 7.73 (d, J = 8.3 Hz, 1 H), 7.38–6.60 (m, 10 H), 6.08 (d, J = 7.1 Hz, 2 H), 5.66 (d, J = 8.5 Hz, 1 H)	4.73	4.11	12.7	5.24 (s, 1 H), 0.82 (s, 9 H), −0.01 (s, 9 H)
22a	8.15–7.92 (m, 3 H), 7.28–6.85 (m, 14 H), 6.76–6.42 (m, 5 H)	4.58[a]	4.33	13.5	
22b	8.12–8.01 (m, 3 H), 7.24–6.92 (m, 11 H), 6.60–6.51 (m, 3 H)	4.85	4.66	13.0	2.53 (s, 3H)
22c	8.12–8.01 (m, 3 H), 7.30–6.91 (m, 11 H), 6.67–6.46 (m, 3 H)	4.70	4.57	13.5	3.15–3.00 (m, 2 H), 1.60–1.17 (m, 4 H), 0.78 (t, J = 7.3 Hz, 3 H)
24	8.10–7.97 (m, 3 H), 7.25–6.68 (m, 12 H), 6.07 (d, J = 8.3 Hz, 2 H)	4.99	4.65	14.0	4.30–4.12 (m, 2 H), 0.97–0.91 (m, 3 H)
25a	11.11 (s, 1 H), 8.15–8.06 (m, 3 H), 7.63–6.97 (m, 17 H), 6.43 (d, J = 7.1 Hz, 2 H)	4.87	4.64	12.0	
25b	9.04 (s, 1 H), 8.06–8.03 (m, 3 H), 7.35–6.92 (m, 12 H), 6.45 (d, J = 7 Hz, 2 H)	4.83	4.53	12.0	1.25 (s, 9 H)
26a[b]	8.09 (d, J = 7.9 Hz, 2 H), 8.01 (d, J = 8.4 Hz, 1 H), 7.2–7.0 (m, 8 H), 6.91 (t, J = 7.9 Hz, 3 H), 6.45 (d, J = 7.1 Hz, 2 H), 6.20 (d, J = 8.5 Hz, 1 H)	4.74	4.45	13.3	4.16 (m, 1 H), 3.06 (dd, J = 6.8, 17.4 Hz, 1 H), 2.67 (m, 1 H), 2.47 (dd, J = 11.2, 18 Hz, 1 H), 2.3–1.8 (m, 3 H)
26b	8.15–8.04 (m, 3 H), 7.30–6.81 (m, 12 H), 6.46–6.29 (m, 3 H)	4.77	4.43	12.0	3.67–3.38 (m, 2 H), 2.66–2.35 (m, 2 H), 2.10–1.65 (m, 4 H), 1.33–1.16 (m, 1 H)

[a] Multiplet (2 H). [b] Spectrum run at 45 °C.

Table III. ^{13}C NMR Data of the Benzyl Derivatives

	benzotriazole						carbazole									
compd	C_4	C_5	C_6	C_7	C_{3a}	C_{7a}	C_1	C_2	C_3	C_4	C_{4a}	C_{9a}	>C<	Ph	CH_2	electrophile
14	120.0	124.4	127.6	111.4	145.7	133.8	114.0	125.2	119.8	119.0	125.4	138.5	86.9	133.2* 129.1 128.0* 127.9	43.8	133.3* 129.7 128.6* 76.8 21.0
16	119.5	124.2	127.1	112.7	145.8	132.0	112.9	123.7	120.4	119.6	125.5	139.1	90.8	132.3 130.0 128.4 127.7*	44.3	136.6 130.6 127.2* 125.4
18a	119.9	124.7	127.5	111.4	145.7	133.3	114.2	123.5	119.5	118.5	126.9	138.4	87.2	133.9 130.0 128.0 127.9*	43.9	129.6 128.6 127.7* 123.5 77.8 0.09
18b[a]	119.6	124.7	126.9	111.1	145.6	133.3	114.9	123.6	120.8	120.3	125.9	139.1	89.0	133.6 129.7 127.9 127.3	45.4	82.2 38.2 28.9 1.53
22a	120.1	124.3	127.5	110.6	146.5	132.9	112.5	124.1	120.3	120.1	126.1	139.8	83.5	133.2 130.3 128.1 127.8	41.5	
22b	120.0*	124.2*	127.3	110.7	146.8	132.1	112.3	124.3*	120.3	120.1*	126.2	139.9	82.2	134.0 130.4 128.0 127.7	43.7	27.9
22c	120.1	124.2*	127.4	110.7	146.7	132.3	112.6	124.3*	120.2	120.1	126.2	139.9	85.3	134.0 130.1 128.1 127.6	40.6	37.0 25.7 22.3 13.8
24	119.6	124.4	127.1	111.4	146.5	132.8	114.3	123.7	120.2	119.8	125.6	139.5	82.5	133.2 131.3 127.5 127.4	40.2	165.6 63.3 13.5
25a	121.1	124.9	128.1	111.4	145.4	131.7	112.0	125.2	120.6	120.5	126.7	140.6	86.4	132.8 130.0 128.3 128.1	45.6	164.3 136.4 129.2 128.9 128.2 125.2 121.1
25b	120.1	124.2	127.2	112.4	143.9	131.2	112.4	125.3	119.7	118.6	126.9	140.2	87.5	133.5 131.2 127.7 127.2	39.8	163.7 52.3 28.0
26a[b]	120.6	124.2	127.7	112.1	146.3	134.0	113.1	126.2	120.1	120.1	*c*	*c*	86.6	133.5 129.9 128.2	45.1	214.1 42.8 42.0 37.8 26.4
26b	120.7	124.2*	127.4*	112.4	146.2	134.4	113.0	124.2*	120.1	119.9	126.1	139.8	87.5	133.4 130.3 128.1 127.4*	44.9	208.8 40.7 40.1 28.9 23.8

[a] Some extra peaks were also observed due to the existence of isomers: 141.6 120.2 118.4 117.6. [b] Spectrum run at 45 °C. [c] Signals not observed due to low intensity. * Tentative assignments, could be interchanged.

duced. Thus for the amides (**25a,b**), the carbonyl resonance was observed at about 164 ppm, while the carbonyl group for the ester (**24**) was found at 165.6 ppm.

With cyclohexanone, the unreacted starting material (**20**) was recovered. However, anion **21** added regiospecifically 1,4 to the α,β-unsaturated ketone 2-cyclopentenone to yield **26a** (76%) as was shown by its NMR spectra. At room temperature, the ^{1}H NMR spectrum of the product displayed broad signals for the aliphatic protons indicating restricted rotation. However at 45 °C, the signals were sharp and the pattern indicated formation of **26a**. In addition to the expected signals for carbazole, benzotriazole, and the benzyl group, the resonance at 214.1 ppm indicated that a carbonyl group was present. In the ^{1}H NMR spectrum, the absence of the vinylic protons indicated that exclusive 1,4-addition had occurred. Similarly, 2-cyclohexenone also afforded the corresponding 1,4-addition product **26b** (81%). The ketone resonance was observed at 208.7 ppm. With ethyl acrylate, an uncharacterizable mixture was obtained.

When the anion **21** was treated with phenyl isothiocyanate, the product isolated displayed no benzotriazole resonances in the NMR spectra. Furthermore, the absence of the AB pattern for the benzylic protons and of the corresponding carbon between 82 and 90 ppm in the ^{13}C NMR spectrum as well as the presence of a signal at 192 ppm, indicated that electrophilic addition with concomitant elimination of benzotriazole had occurred to afford

Table IV. Preparation of Ketones

compd	R	mp (°C) or bp (°C/mmHg)	lit. mp (°C) or bp (°C/mmHg)	yield (%)	molecular formula	found (required) C	H	N
15a	Ph	77–79	–	57	$C_{15}H_{14}O_2$	79.56 (79.62	6.23 6.24)	
15b	4-Me-C_6H_4	90–91	–	51	$C_{16}H_{16}O_2$	80.21 (79.97	6.72 6.71)	
23a	$PhCH_2$	oil	118–120/0.1[a]	63	$C_{15}H_{14}O$	–	–	–
23b	Me	107–109/24	109–112/24[b]	77	$C_9H_{10}O$	–	–	–
23c	Bu	112–114/5	110–112/5[c]	82	$C_{12}H_{16}O$	–	–	–
27a	(n = 1)	oil	–	51	$C_{13}H_{14}O_2$	HRMS calcd 202.0994, found 202.0985		
27b	(n = 2)	oil	–	67	$C_{14}H_{16}O_2$	HRMS calcd 216.1150, found 216.1131		
29	–	127–129	–	62	$C_{15}H_{13}NO_2$	75.42 (75.30	5.31 5.48	6.26 5.89)
36a	Me	126–127/760	127/760[d]	86	$C_6H_{12}O$	–	–	–
36b	Bu	49–51/0.5	88/22[e]	89	$C_9H_{18}O$	–	–	–
37	–	99–101	–	82	$C_{12}H_{15}NO_2$	70.63 (70.23	7.46 7.37	6.78 6.82)

[a] Olah, G. A.; Mehrotra, A. K.; Narang, S. C. *Synthesis* **1982**, 151. [b] Julian, P. L.; Oliver, J. J. *Org. Synth.* **1938**, *18*, 54. [c] Niinobe, S. *J. Pharm. Soc. Jpn.* **1943**, *63*, 204. [d] *Dictionary of Organic Compounds*, 5th ed.; Bucking, J., Ed.; Chapman and Hall: New York, 1982; p 2932. [e] Briese, R. R.; McElvain, S. M. *J. Am. Chem. Soc.* **1933**, *55*, 1697.

Table V. ^{1}H NMR Spectral Data of Ketones

15a	7.46–7.20 (m, 8 H), 7.06–6.95 (m, 2 H), 5.18 (d, J = 4.4 Hz, 1 H), 4.25 (d, J = 4.4 Hz), 3.63 (s, 2 H)
15b	7.30–7.24 (m, 3 H), 7.20 (s, 4 H), 7.05–6.98 (m, 2 H), 5.15 (d, J = 4.2 Hz, 1 H), 4.21 (d, J = 1 H), 3.63 (s, 2 H), 2.37 (s, 3 H)
23a	7.31–7.20 (m, 6 H), 7.15–7.05 (m, 4 H), 3.66 (s, 4 H)
23b	7.40–7.13 (m, 5 H), 3.69 (s, 2 H), 2.15 (s, H)
23c	7.35–7.14 (m, 5 H), 3.66 (s, 2 H), 2.43 (t, J = 7.4 Hz, 2 H), 1.53 (quintet, J = 7.4 Hz, 2 H), 1.24 (sextet, J = 7.5 Hz, 2 H), 0.85 (t, J = 7.3 Hz, 3 H)
27a	7.36–7.19 (m, 5 H), 3.79 (s, 2 H), 3.33 (quintet, J = 8.3, 1 H), 2.50–1.95 (m, 6 H)
27b	7.32–7.09 (m, 5 H), 3.68 (s, 2 H), 2.98–2.86 (m, 1 H), 2.50–2.38 (m, 1 H), 2.32–2.14 (m, 3 H), 2.05–1.87 (m, 2 H), 1.70–1.52 (m, 2 H)
29	8.74 (bs, 1 H), 7.67–7.61 (m, 2 H), 7.43–7.14 (m, 8 H), 4.31 (s, 2 H)
36a	2.43 (t, J = 7.2 Hz, 2 H), 2.13 (s, 3 H), 1.60–1.51 (m, 2 H), 1.36–1.28 (m, 2 H), 0.91 (t, J = 7.3 Hz, 3 H)
36b	2.40 (t, J = 7.3 Hz, 4 H), 1.55 (quintet, J = 7.2 Hz, 4 H), 1.30 (sextet, J = 7.3 Hz, 4 H), 0.91 (t, J = 7.2 Hz, 6 H)
37	8.86 (bs, 1 H), 7.64 (d, J = 8.2 Hz, 2 H), 7.41–7.30 (m, 2 H), 7.19–7.10 (m, 1 H), 2.99 (t, J = 7.3 Hz, 2 H), 1.62 (quintet, J = 7.6 Hz, 2 H), 1.36 (sextet, J = 7.5 Hz, 2 H), 0.92 (t, J = 7.3 Hz, 3 H)

Table VI. ^{13}C NMR Spectral Data of Ketones

15a	206.9, 137.5, 132.8, 129.3, 129.1, 128.9, 128.6, 127.7, 127.2, 79.2, 44.6
15b	207.1, 138.7, 134.6, 132.9, 129.7, 129.3, 128.6, 127.6, 127.2, 78.9, 44.5, 21.2
23a	205.3, 133.8, 129.3, 128.4, 126.8, 48.9
23b	206.4, 134.2, 129.3, 128.7, 127.0, 51.0, 29.2
23c	208.6, 134.3, 129.3, 128.6, 126.8, 50.0, 41.6, 25.7, 22.1 13.7
27a	216.3, 208.0, 133.4, 129.3, 128.7, 127.1, 48.9, 46.7, 40.2, 37.3, 25.9
27b	209.8, 207.9, 133.4, 129.3, 128.8, 127.2, 49.2, 48.3, 42.6, 40.8, 27.3, 24.8
29	196.2, 157.3, 136.2, 132.4, 129.8, 129.2, 128.7, 127.3, 125.3, 119.7, 42.7
36a	208.9, 43.2, 29.5, 25.7, 22.1, 13.6
36b	211.4, 42.4, 25.9, 22.3, 13.7
37	199.4, 157.6, 136.3, 129.0, 125.1, 119.7, 36.0, 25.3, 22.1, 13.7

the styryl derivative **28**. This was confirmed by the combustion analysis. Elimination of benzotriazole only occurred when the electrophile was phenyl isothiocyanate. With electrophiles such as isocyanates or aldehydes (cases where electrophilic addition also led to an anionic intermediate), only the normal products **18** and **25** were obtained.

Hydrolysis of Intermediates. We found that products **14**, **18a**, **22a–c**, **25a**, and **26a–c** could easily be hydrolyzed under relatively mild conditions: treatment at 20 °C with tetrahydrofuran/0.9 M aqueous hydrochloric acid solution showed the complete disappearance (TLC) of the starting material after 24 h and afforded the corresponding carbonyl derivatives in moderate to good yields. Isolation of the ketones was readily achieved by extracting the reaction mixture with hexane since carbazole and benzotriazole were not soluble. The crude products thus obtained were purified by column chromatography.

In this way, the alkylated derivatives **22a–c** gave the corresponding simple ketones **23a–c** (63–82%). The product **25a** from the phenyl isocyanate reaction afforded the α-keto amide **29** (62%). The products **18a** and **14** from aldehydes, gave α-hydroxy ketones **15a,b** (51–57%). The 1,4-addition products yielded the γ-diketones **27a–c** (67–81%) (Table IV).

The ketone products were characterized by comparison with literature data or from CHN analysis/high-resolution mass spectroscopy and by their spectra (Tables V and VI). The ^{13}C NMR spectra of the ketones diplayed the carbonyl resonance between 205 and 208 ppm except for the α-caboxamido drivative **29** where the keto carbon was observed at 196 ppm while the amido carbon was further upfield at 157 ppm.

When **16** and **18b** were subjected to hydrolysis, loss of benzotriazole was accompanied by formation of the styryl derivatives **13** and **19**, respectively, which were resistant to further hydrolysis. This was confirmed by the absence of the benzotriazole, benzylic and keto resonances in the ^{13}C NMR spectra of the products, and correct combustion analyses for the postulated products. The reason for the formation of the styryl derivatives is not known. In both cases, only one isomer was obtained, the stereochemistry of which was not determined.

Pentanoyl Anion Equivalent 31: Reactions with Electrophiles. Similarly, the butyl analogue **30** reacted readily with butyllithium and the anion **31** was trapped with methyl iodide and butyl iodide to afford **33a** (91%) and **33b** (94%), respectively. Reaction with phenyl isocyanate afforded the amide **34** (86%), and with diphenyl disulfide, the phenylthio derivative **35** (87%) (Table VII). As in the phenacetyl case, reaction with phenyl isothiocyanate led to elimination of benzotriazole to give **32** (91%). The structures of the disubstituted derivatives **33–35** and of the alkene **32** were confirmed by the ^{1}H and ^{13}C NMR spectra (Tables VIII and IX) and by their CHN microanalyses data. For compounds **33a,b** and **34**, the methylene protons α to the quaternary carbons displayed complex patterns, again indicating that the hydrogens were nonequivalent. For the dibutyl derivative **33b**, the chem-

Table VII. Preparation of Disubstituted 1-Carbazol-9-ylmethylbenzotriazole Derivatives

compd	electrophile [R]	mp (°C)	yield (%)	crystal form	molecular formula	found (required) C	H	N
33a	MeI [Me]	138–140	91	needles[a]	$C_{24}H_{24}N_4$	77.97 (78.23)	6.59 6.57	15.10 15.20)
33b	BuI [Bu]	158–160	94	plates[a]	$C_{27}H_{30}N_4$	78.85 (78.99)	7.55 7.39	13.70 13.65)
34	PhNCO	122–124	86	prisms[b]	$C_{30}H_{27}N_5O$	75.96 (76.09)	5.95 5.75	14.51 14.79)
35	PhSSPh	159–161	94	plates[a]	$C_{29}H_{26}N_4S$	75.41 (75.29)	5.65 5.66	11.90 12.11)

[a] From MeOH. [b] Column chromatography (silica gel; $CHCl_3$–hexane, 1:2).

Table VIII. ^1H NMR Data of the Butyl Derivatives

33a 8.11–8.00 (m, 3 H), 7.27–7.13 (m, 7 H), 7.00–6.94 (m, 1 H), 6.60 (d, J = 8.5 Hz, 1 H), 3.57–3.45 (m, 1 H), 3.25–3.10 (m, 1 H), 2.66 (s, 3 H), 1.36–0.85 (m, 4 H), 0.75 (t, J = 6.9 Hz, 3 H)

33b 8.10–7.97 (m, 3 H), 7.29–7.13 (m, 7 H), 6.99–6.91 (m, 1 H), 6.61 (d, J = 8.5 Hz, 1 H), 3.50–3.17 (m, 4 H), 1.45–0.80 (m, 11 H), 0.75 (t, J = 7.3 Hz, 3 H)

34 11.04 (s, 1 H), 8.13–8.05 (m, 3 H), 7.67–7.58 (m, 2 H), 7.47–7.12 (m, 11 H), 6.81 (d, J = 7.6 Hz, 1 H), 3.60–3.25 (m, 2 H), 1.55–0.76 (m, 7 H)

35 8.01 (d, J = 7.3 Hz, 3 H), 7.30–6.80 (m, 13 H), 6.57 (d, J = 8.6 Hz, 1 H), 3.20 (t, J = 8.0 Hz, 2 H), 1.95–1.76 (m, 1 H), 1.44–1.21 (m, 2 H), 0.84 (t, J = 7.3 Hz, 3 H)

ical shifts for the two protons were quite similar. However, for **33a**, the difference in the chemical shifts for the two protons was about 0.3 ppm. Interestingly, for the phenylthio compound **35**, the signals appeared as a triplet, indicating the two protons were isochronous.

Hydrolysis of Intermediates. Hydrolysis of **33** and **34** under the conditions described previously afforded the corresponding ketones **36** and **37** (82–89%) (Table IV). As with the phenylthio derivative **16** where hydrolysis afforded the styryl derivative **13**, the corresponding butyl analogue **35** gave the alkene **38** (89%), which in this case was obtained as a mixture of the E and Z isomers.

Conclusions

The heterocyle-activated methane system employed here is a novel acyl anion equivalent. The variety of electrophiles that can be employed coupled with the mild single-step hydrolysis makes it an attractive system for the synthesis of functionalized ketones.

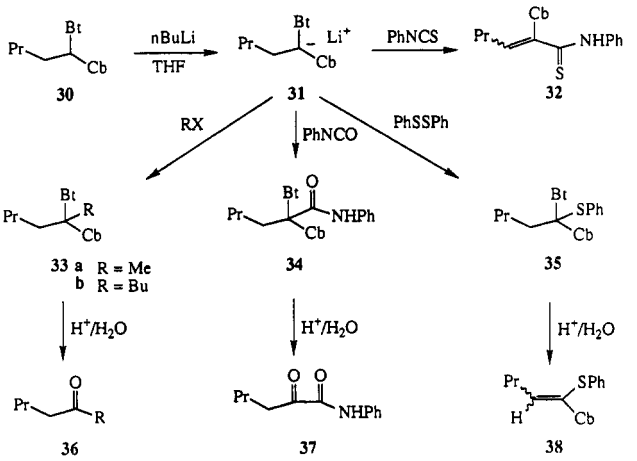
Experimental Section

Melting points were determined on a bristoline hot-stage microscope and are uncorrected. ^1H (300 MHz) NMR spectra were recorded on a Varian VXR-300 (FT mode) spectrometer with Me_4Si as internal standard. ^{13}C NMR spectra were recorded at 75 MHz on the same instrument using solvent peaks ($CDCl_3$, δ 77.0 or DMSO-d_6, δ 39.5) as references. IR spectra were run on a Perkin-Elmer 1600 FTIR spectrometer. High-resolution mass spectrometry was carried out on a Finnigan Mat 95. Elemental analyses (C, H, N) were carried out using a Carlo Erba 1106 elemental analyzer. Flash chromatography was run on EM Science silica gel 60 (230–400 mesh).

The following compounds were prepared by literature procedures: **1-(benzotriazol-1-yl)-1-(carbazol-9-yl)-2-phenylethane (20)**, mp 129–130 °C (lit.[44] mp 129–130 °C); **1-(benzotriazol-1-yl)-1-(carbazol-9-yl)-pentane (30)**, mp 135–137 °C (lit.[43] mp 135–137 °C).

General Procedure for the Lithiation of 20 and 30 and Subsequent Reaction with Electrophiles. To a solution of

Scheme III



20 or **30** (10 mmol) in THF (80 mL) was added butyllithium (2.5 M in hexanes; 4.4 mL, 11 mmol) at −78 °C. The solution was stirred at −78 °C for 2 h, and a solution of the corresponding electrophile (10 mmol) in THF (10 mL) was added (for **18b** and **18c** a solution of $ClSiMe_3$ (1.4 mL, 11 mmol) in THF (10 mL) was also added). The reaction was stirred at −78 °C for 4 h and at ambient temperature for 12 h. The reaction mixture was poured into saturated aqueous NH_4Cl (40 mL), and the aqueous layer washed with Et_2O (3 × 30 mL). The combined organic fractions were washed with H_2O (1 × 30 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure to afford the crude product, which was purified either by recrystallization or by column chromatography (see Table 1).

***N*,3-Diphenyl-2-(carbazol-9-yl)prop-2-enethioamide (28).** With phenyl isothiocyanate as the electrophile and **20** as the precursor, **28** was obtained as yellow needles from hexanes (91%), mp 145–147 °C: ^1H NMR ($CDCl_3$) δ 8.76 (s, 1 H), 8.48 (s, 1 H), 8.16 (d, J = 5.9 Hz, 2 H), 7.4–6.95 (m, 14 H), and 6.77 (d, J = 7.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 191.6, 141.4, 138.6, 138.1, 132.8, 132.1, 130.1, 129.9, 128.7, 128.5, 127.1, 126.8, 124.3, 123.9, 121.2, 120.7, and 110.5. Anal. Calcd for $C_{27}H_{20}N_2S$: C, 80.17; H, 4.98; N, 6.92. Found: C, 80.00; H, 4.98; N, 6.80.

***N*-Phenyl-2-(carbazol-9-yl)hex-2-enethioamide (32).** With phenyl isothiocyanate as the electrophile and **30** as the precursor, **32** was obtained as yellow needles from hexanes (87%), mp 126–127 °C: ^1H NMR ($CDCl_3$) δ 8.47 (s, 1 H), 8.2–8.0 (m, 3 H), 7.5–7.1 (m, 11 H), 1.8–1.7 (m, 2 H), 1.5–1.35 (m, 2 H), and 0.75 (t, J = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.7, 148.6, 140.0, 138.0, 134.8, 128.7, 127.1, 127.0, 126.7, 124.4, 123.5, 120.9, 120.8, 120.76, 120.7, 110.0, 31.2, 21.3, and 13.9. Anal. Calcd for $C_{24}H_{22}N_2S$: C, 77.80; H, 5.98; N, 7.56. Found: C, 77.90; H, 6.06; N, 7.45.

General Procedure for Hydrolysis. To a solution of the corresponding compound (2.5 mmol) in THF (20 mL) and H_2O (10 mL) was added aqueous HCl (10 M; 1 mL). The mixture was stirred at ambient temperature for 24 h and extracted with Et_2O (3 × 20 mL). The organic layer was washed with H_2O (1 × 10 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure to give the crude product. The ketone was extracted from the residue by washing with hexane (3 × 20 mL), and the solvent was evaporated to give the crude product, which was purified by column chromatography (see Table IV).

(44) Katritzky, A. R.; Drewniak-Deyrup, M.; Lan, X.; Brunner, F. *J. Heterocycl. Chem.* **1989**, *26*, 829.

Table IX. ^{13}C NMR Data of the Butyl Derivatives

	benzotriazole						carbazole								
compd	C_4	C_5	C_6	C_7	C_{3a}	C_{7a}	C_1	C_2	C_3	C_4	C_{4a}	C_{9a}	>C<	Bu	electrophile
33a	119.9	124.6	127.5	110.7	146.8	132.0	112.4	124.1	120.3	120.1	126.2	139.7	82.5	39.4 25.5 22.4 13.7	27.6
33b	119.9	124.6	127.4	110.7	146.7	132.1	112.6	124.1	120.2	120.1	126.2	139.9	85.7	35.9 25.5 22.5 13.7	
34	120.2	124.8	127.8	109.6	145.7	132.7	112.0	124.2	120.8	120.4	126.5	140.4	86.0	39.3 26.4 22.3 13.7	164.7 136.7 129.1 125.3 124.8
35	119.8	124.5	127.8	111.0	146.7	132.3	113.6	124.4	120.8	120.1	126.0	139.8	91.9	39.5 26.2 22.2 13.9	137.2 130.2 128.6 126.0

1-(Carbazol-9-yl)-1-(phenylthio)-2-phenylethylene (13). Hydrolysis of **16** under the above conditions afforded **13** as colorless plates (column chromatography; hexanes as elutent) (92%), mp 120–122 °C: ^1H NMR ($CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 2 H), 7.44 (d, J = 8.1 Hz, 2 H), 7.35–7.25 (m, 2 H), and 7.25–6.8 (m, 11 H); ^{13}C NMR ($CDCl_3$) δ 139.1, 134.2, 133.7, 129.0, 128.4, 128.38, 128.34, 128.04, 128.0, 127.9, 125.8, 123.8, 120.3, 119.8, and 111.6. Anal. Calcd for $C_{26}H_{19}NS$: C, 82.72; H, 5.07; N, 3.71. Found: C, 82.65; H, 5.01; N, 3.45.

1-Phenyl-2-(carbazol-9-yl)-3-hydroxy-4,4-dimethylpent-1-ene (19). Hydrolysis of **18b** under the above conditions afforded **19** as colorless needles from hexanes (79%), mp 155–157 °C: ^1H NMR ($CDCl_3$) δ 8.15–8.0 (m, 2 H), 7.55–6.85 (m, 11 H), 6.7–6.65 (m, 2 H), 4.65 (s, 1 H), and 0.86 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 139.1, 137.6, 137.4, 134.3, 128.1, 128.0, 127.9, 127.6, 125.9, 125.8, 125.5, 124.0, 123.7, 120.4, 120.3, 120.0, 119.6, 112.0, 110.9, 79.1, 36.6, and 25.9. Anal. Calcd for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 4.50. Found: C, 84.15; H, 7.19; N, 4.11.

1-(Carbazol-9-yl)-1-(phenylthio)pent-1-ene (38). Hydrolysis of **35** under the above conditions afforded a mixture of the *E* and *Z* isomers **38** as a colorless oil (column chromatography; hexanes as elutent) (89%). **Major isomer**: ^1H NMR ($CDCl_3$) δ 7.94 (d, J = 7.7 Hz, 1.33 H), 7.55–6.7 (m, 7.33 H), 6.27 (t, J = 7.3 Hz, 0.67 H), 2.64 (q, J = 7.3 Hz, 1.33 H), 1.30 (hex, J = 7.4 Hz, 1.33 H), and 0.72 (t, J = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 140.0, 134.7, 133.6, 131.2, 128.4, 128.14, 125.6, 123.2, 119.9, 119.8, 110.8, 30.8, 22.0, and 13.6. **Minor isomer**: ^1H NMR ($CDCl_3$) δ 7.88 (d, J = 7.7 Hz, 0.67 H), 7.55–6.7 (m, 3.67 H), 6.13 (t, J = 7.5 Hz, 0.33 H), 1.81 (q, J= 7.3 Hz, 0.67 H), 1.65 (hex, J = 7.2 Hz, 0.67 H), and 1.10 (t, J = 7.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 140.8, 135.2, 133.0, 130.3, 128.08, 127.7, 125.5, 122.9, 119.7, 119.6, 110.7, 31.3, 22.6, and 14.0. $C_{23}H_{21}NS$ requires M^+ m/z 343.1394, found M^+ m/z 343.1387.

Registry No. **13**, 136617-15-7; **14**, 136617-16-8; **15a**, 41049-36-9; **15b**, 136617-17-9; **16**, 136617-18-0; **18a**, 136617-19-1; **18b**, 136617-20-4; **19**, 136617-21-5; **20**, 124337-51-5; **22a**, 136617-22-6; **22b**, 136617-23-7; **22c**, 136617-24-8; **23a**, 102-04-5; **23b**, 103-79-7; **23c**, 25870-62-6; **24**, 136617-25-9; **25a**, 136617-26-0; **25b**, 136617-27-1; **26a**, 136617-28-2; **26b**, 136617-29-3; **27a**, 136617-30-6; **27b**, 136617-31-7; **28**, 136617-32-8; **29**, 6362-61-4; **30**, 132724-55-1; **32**, 136617-33-9; **33a**, 136617-34-0; **33b**, 136617-35-1; **34**, 136617-36-2; **35**, 136617-37-3; **36a**, 591-78-6; **36b**, 502-56-7; **37**, 52884-95-4; (*E*)-**38**, 136617-38-4; (*Z*)-**38**, 136617-39-5; 4-Me-C_6H_4CHO, 104-87-0; PhSSPh, 882-33-7; PhCHO, 100-52-7; Me_3CCHO, 630-19-3; $PhCH_2Br$, 100-39-0; ClCOOEt, 541-41-3; PhNCO, 103-71-9; Me_3CNCO, 1609-86-5; PhNCS, 103-72-0; 2-cyclopentenone, 930-30-3; 2-cyclohexenone, 930-68-7.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **27a** and **27b** (6 pages). Ordering information is given on any current masthead page.