The formation of 3-methylcoumarin 4 from the acid 1 has been observed only under the influence of a base.[9] Thermal rearrangement of acrylic acid 1 in *o*-DClB in the presence of a catalytic amount of PTS resulted only in the formation of dimer 2. In HMPA and *N*-methyl-2-pyrrolidone, considerable cleavage of the acid 1 to the corresponding phenol was observed apart from the formation of the 3-methylcoumarins in very poor yields. In DEA, apart from the formation of coumarin 4 a small amount of dimer 2 was also obtained.

The several features associated with PEG-200, viz., complete miscibility with water and consequently easy workup of the reaction mixture, high boiling point, polar nature, higher selectivity, nontoxicity, and low cost particularly, prompted us to investigate its utility in the field of Claisen and Cope rearrangements.

In our experience, we find PEG to be a superior solvent for Claisen rearrangement of α-(aryloxy)methylacrylic acids affording 3-methylcoumarins in high yields.

Experimental Section

Melting points (uncorrected) were taken with Toshnival Capillary apparatus. ^{1}H NMR spectra were recorded with Me_4Si as an internal standard in $CDCl_3$. Commercial SD'S sample of Polyethylene glycol-200 was used. Diethylene glycol and ethylene glycol were flame distilled before use.

General Procedure for Preparation of 3-Methylcoumarins in Polyethylene Glycol. A solution of 1 (200 mg 0.001 mol) in 10 mL of polyethylene glycol-200 was heated for exactly 30 min at a temperature of 220 °C under argon atmosphere. The reaction mixture was cooled and poured into water. The 3-methylcoumarins 4 separated out in most cases as a good solid in high yields and were crystallized from benzene–hexane (Table I). Table I lists the melting points of the various substituted 3-methylcoumarins: IR ($CHCl_3$) ν_{max} C=O at 1700 cm^{-1}; NMR ($CDCl_3$) values at 2.2 (s, 3 H), 7.4–7.6 (m, Ar H), 7.3 (s, 1 H, Ar C=).

The reactions in diethylene glycol and ethylene glycol were performed by following the same above procedure (Table II).

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Registry No. 1 (X = Y = Z = H), 57295-21-3; 1 (X = Y = H, Z = CH_3), 56634-11-8; 1 (X = Y = H, Z = Cl), 57295-22-4; 1 (X = H, Y,Z = CH=CHCH=CH), 57295-23-5; 1 (X = Y = H, Z = OCH_3), 95532-63-1; 1 (X = CH_3, Y = Z = H), 95532-64-2; 1 (X = CHO, Y = Z = H), 95532-65-3; 1 (X,Y = CH=CHCH=CH, Z = H), 95532-66-4; 1 (X = Y = H, Z = CHO), 95532-67-5; 1 (X = Y = H, Z = $COCH_3$), 95532-68-6; 1 (X = Y = H, Z = NO_2), 95532-69-7; 3 (X = Y = Z = H), 56783-44-9; 4 (X = Y = Z = H), 2445-82-1; 4 (X = Y = H, Z = CH_3), 57295-24-6; 4 (X = Y = H, Z = Cl), 57295-25-7; 4 (X = H, Y,Z = CH=CHCH=CH), 86818-99-7; 4 (X = Y = H, Z = OCH_3), 62399-35-3; 4 (X = CH_3, Y = Z = H), 95532-70-0; 4 (X = CHO, Y = Z = H), 95532-71-1; 4 (X,Y = CH=CHCH=CH, Z = H), 21315-40-2; 4 (X = Y = H, Z = CHO), 95532-72-2; 4 (X = Y = H, Z = $COCH_3$), 95532-73-3; 4 (X = Y = H, Z = NO_2), 95532-74-4; polyethylene glycol, 25322-68-3; ethylene glycol, 107-21-1; diethylene glycol, 111-46-6.

(2) Suzuki, N.; Ayaguchi, Y.; Izawa, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3349 and references cited therein.
(3) (a) Colombo, R. *Tetrahedron Lett.* **1981**, 4129. (b) Pillai, V. N. R.; Mutter, M.; Baeyer, C.; Gatfield, I. *J. Org. Chem.* **1980**, *45*, 5364 and references cited therein.
(4) Zupancic, B. C.; Kokaij, M. *Synth. Commun.* **1982**, *12* (11), 881.
(5) Rao, U.; Balasubramanian, K. K. *Tetrahedron Lett.* **1983**, 5023.
(6) Ramakanth, S.; Narayanan, K.; Balasubramanian, K. K. *Tetrahedron*, in press.
(7) Gopalan, B.; Rajagopalan, K.; Swaminathan, S.; Balasubramanian, K. K. *Tetrahedron Lett.* **1975**, 1507.
(8) Rhoads, S. J.; Raulins, N. R. *Org. React. (N.Y.)* **1975**, *22*, 1.
(9) Gopalan, B.; Rajagopalan, K.; Swaminathan, S.; Balasubramanian, K. K. *Synthesis* **1975**, 599.

Facile One-Step Synthesis of Phenyl-*tert*-butylnitrone (PBN) and Its Derivatives

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In recent years, the technique of spin trapping has provided detailed information on radical processes.[1] This is especially true for radical reactions occurring in the biological milieu.[2] Of the spin traps which have been utilized, phenyl-*tert*-butylnitrone (PBN) and its derivatives are some of the most important.[1-3] Indeed, derivatives of PBN that are water-soluble,[4] lipid-soluble,[5] and polymer-bound[6] have been prepared and shown to be effective trapping agents.

Currently, two methods for the preparation of these types of spin traps are known. The first involves conversion of an aldehyde into a *tert*-butyl imine followed by oxidation to the oxazirane and final rearrangement to the nitrone.[7] Overall yields are generally low and the oxidation step calls for 90% H_2O_2 although 30% may be used with a decreased yield.[7] The second method is direct addition of *tert*-butylhydroxylamine to the corresponding aldehyde.[5] This procedure results in relatively high yields. However, the hydroxylamine has typically been prepared by reduction of the nitro compound with Al/Hg amalgam[8] or activated zinc[9] and then is purified prior to condensation with the aldehyde. We now detail a simplified, one-step preparation of PBN and its derivatives.

An early report by Wiemann and Glacet on the synthesis of diaryl nitrones prompted us to investigate a similar procedure for arylalkylnitrones.[10] In this procedure, the hydroxylamine is prepared from the nitro compound in situ via reduction with metallic zinc. By modification of this procedure, high yields of nitrone have been achieved in a single step. The results for several nitrones are shown in Table I. Particularly useful is the high yield of the lipid-soluble dodecyloxy derivative.

The general procedure is to cool a mixture of 1 equiv of the appropriate aldehyde, 2 equiv of 2-methyl-2-nitropropane, and 3 equiv of activated zinc dust in 95% EtOH to 10–15 °C. Glacial acetic acid is then added dropwise while maintaining the sample temperature below 15 °C. After being stored in the refrigerator (~6 °C) for 24–48 h, the sample is filtered and the solvent removed. The NMR analysis of the crude nitrone indicates >95% purity with essentially no aldehyde contamination. A single recrystallization yields suitably pure nitrone (mp range <3 °C and no residual EPR signal).

All of the variables pertaining to this procedure have not been investigated through the best solvent appears to be

(1) Evans, C. A. *Aldrichimica Acta* **1979**, *12*, 23. Janzen, E. G. *Acc. Chem. Res.* **1971**, *4*, 31.
(2) Janzen, E. G. In "Free Radicals In Biology"; Pryor, W. A., Ed.; Academic Press: New York, 1980; Vol. IV, pp 115–154.
(3) Janzen, E. G.; Blackburn, B. J. *J. Am. Chem. Soc.* **1968**, *90*, 5909; **1969**, *91*, 4481.
(4) Janzen, E. G.; Dudley, R. L.; Shetty, R. V. *J. Am. Chem. Soc.* **1979**, *101*, 243.
(5) Janzen, E. G.; Coulter, G. A. *J. Am. Chem. Soc.* **1984**, *106*, 1962.
(6) Janzen, E. G.; Wang, Y. Y. *J. Phys. Chem.* **1979**, *83*, 894.
(7) Private communication: Church, D. F.; Pryor, W. A.
(8) Calder, A.; Forrester, A. R.; Hepburn, S. P. *Org. Synth.* **1972**, *52*, 77.
(9) Greene, F. D.; Pazos, J. F. *J. Org. Chem.* **1969**, *34*, 2269.
(10) Wiemann, J.; Glacet, Ch. *Bull. Chim. Soc. Fr.* **1950**, *17*, 176.

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Table I. Yield of Nitrone [ArCH=N(O)-t-Bu] Prepared from the Corresponding Aldehyde (p-XC_6H_4CHO)

X	yield,[a] %	mp, °C (lit.)
H	78	72-74 (75-76[12])
CH_3	77	70-72 (68-70[13])
OCH_3	79	94-96 (96-98[13])
O-n-$C_{12}H_{25}$	76	62-64 (60-62[5])

[a] After recrystallization.

95% EtOH and 2 equiv of the nitroalkane results in the highest yield. However, this procedure does allow for the rapid preparation of large quantities (>20 g) of PBN and its derivatives, especially the lipid-soluble derivative which is so useful in biological studies.

Experimental Section

[(Dodecyloxy)phenyl]-*tert*-butylnitrone. (Dodecyloxy)benzaldehyde[11] (11.7 g, 0.0403 mol), 2-methyl-2-nitropropane (8.31 g, 0.0806 mol), and activated zinc dust (7.91 g, 0.121 mol) are added to 300 mL of 95% EtOH that had been precooled to 10 °C. All three reagents were added in single portions. Under brisk stirring, glacial acetic acid (14.5 g, 0.242 mol) is added dropwise over a period of 1 h. The mixture is stirred for 2 h and stored in the refrigerator for 48 h (~6 °C). The sample is then filtered to remove the $Zn(OAc)_2$ and the solvent evaporated. The solid nitrone is taken up in 150 mL of Et_2O and washed once with water (100 mL). The solid $Zn(OAc)_2$ is also rinsed once with Et_2O. The combined Et_2O portions are dried, and the solvent is removed to yield the crude nitrone (12.9 g, 88.4% mp 58-63 °C). Recrystallization from acetone/water provided fluffy white crystals (11.1 g, 76.0% mp 62-64 °C, lit.[5] mp 60-62 °C): NMR ($CDCl_3$, Me_4Si) δ 8.24 (d, J = 9 Hz, 2 H), 7.42 (s, 1 H), 6.88 (d, J = 9 Hz, 2 H), 3.98 (t, J = 6.5 Hz, 2 H), 1.57 (s, 9 H), 1.40-0.67 (m, 23 H); IR (cm^{-1}) 2900, 2830, 1585, 1460.

Registry No. $PhCH{=}N(=O)C(CH_3)_3$, 3376-24-7; p-$CH_3C_6H_4CH{=}N(=O)C(CH_3)_3$, 40117-29-1; p-$CH_3OC_6H_4CH{=}N(=O)C(CH_3)_3$, 40117-28-0; p-$CH_3(CH_2)_{11}C_6H_4CH{=}N(=O)C(CH_3)_3$, 80311-20-2; PhCHO, 100-52-7; p-$CH_3C_6H_4CHO$, 104-87-0; p-$CH_3OC_6H_4CHO$, 123-11-5; p-$CH_3(CH_2)_{11}C_6H_4CHO$, 24083-19-0; 2-methyl-2-nitropropane, 594-70-7; zinc, 7440-66-6.

(11) Prepared from dodecyl bromide and p-hydroxybenzaldehyde by the Williamson procedure: Dietrich, H. J.; Steiger, E. L. *Mol. Cryst. Liq. Cryst.* **1972**, *16*, 263.
(12) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739.
(13) Bacon, W. E.; Neubert, M. E.; Wildman, P. J.; Ott, D. W. *Mol. Cryst. Liq. Cryst.* **1983**, *90*, 307.

Chemistry of Proximal Double Bonds: Reaction of 9,10-Benzotricyclo[4.2.2.2^{2,5}]dodeca-3,7,9-triene with Bromine

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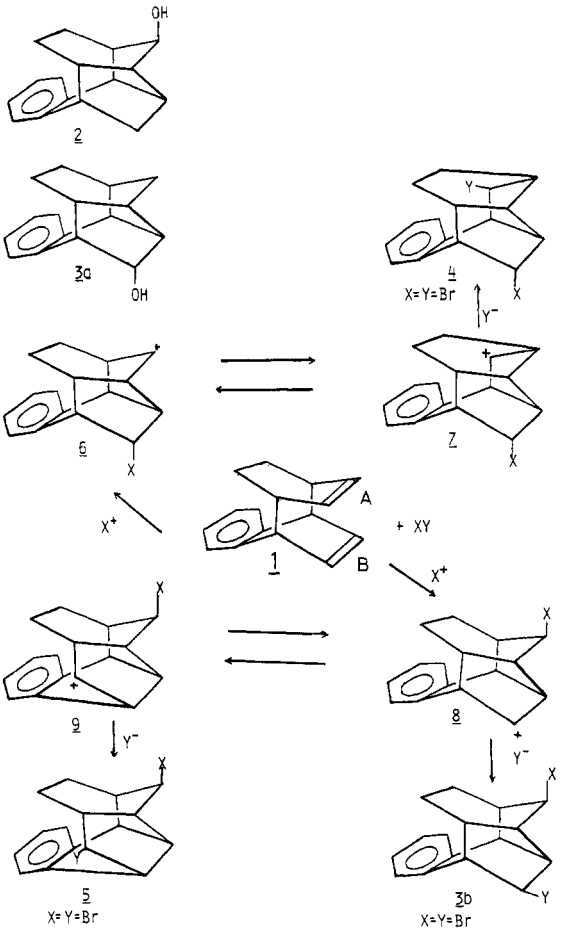
We have been interested in the chemistry of 9,10-benzotricyclo[4.2.2.2^{2,5}]dodeca-3,7,9-triene (**1**), which has a very strongly interacting nonconjugated π system (Scheme I, A and B). The addition of electrophilic reagents to proximal double bonds has been extensively studied to assess spatial interaction of π bonds.[1-3] Although the bromination of norbornadiene, which has typical proximal double bonds, gives mainly the corresponding dibromides without cross-bond formation,[4] the bromination of other compounds that have strongly interacting nonconjugated double bonds gives dibromides with cross-bond formation between the double bonds.[3] Yang et al. reported that **1** reacted with 1 equiv of bromine to give a mixture of saturated dibromides that had appropriate elemental analyses but that could not be separated by conventional methods.[1a] If the bromination was initiated by the attack of a bromonium cation, the structures of the bromides should be similar to those of the alcohols **2** and **3a** obtained from the oxymercuration of **1**.[1a] In the oxymercuration, there are no alcohols formed by skeletal rearrangement resulting from equilibria between the cations **6** ⇌ **7** and **8** ⇌ **9** (X = Hg, Y = OAc). We report the isolation of three dibromides, (5*RS*,9*SR*)-2,3-benzo-5,9-dibromotetracyclo[4.3.3.0^{4,8}.0^{7,10}]dodec-2-ene (**4**) and (9*RS*,12*RS*)-2,3-benzo-9,12-dibromotetracyclo[4.3.3.0^{4,10}.0^{8,11}]dodec-2-ene (**5**) (with skeletal rearrangement) and (8*SR*,12*RS*)-3,4-benzo-8,12-dibromotetracyclo[5.4.0.1^{2,6}.0^{5,6}]dodec-3-ene (**3b**) (without skeletal rearrangement) from the bromination products of **1**.

Treatment of **1** with 1 equiv of bromine in CCl_4 at 0 °C gave a mixture of brominated products, which were separated by fractional crystallization. Because the ^1H NMR

Scheme I



(1) (a) Yang, N. C.; Libman, J. *J. Am. Chem. Soc.* **1972**, *94*, 9228. (b) Kimura, M.; Sagara, S.; Morosawa, S. Abstracts, 4th International Conference on Organic Synthesis (IUPAC), **1982**, C-I-7107, p 186.
(2) Martin, H.-D.; Mayer, B. *Angew. Chem., Int. Ed. Engl.* **1983**, 283.
(3) (a) Underwood, G. R.; Ramamoothy, B. *J. Chem. Soc., Chem. Commun.* **1970**, 12; *Tetrahedron Lett.* **1970**, 4125. (b) Sasaki, T.; Kanematsu, K.; Kondo, A. *J. Org. Chem.* **1974**, *39*, 2246. (c) Tabushi, I.; Fujita, K.; Oda, R. *J. Org. Chem.* **1970**, 35, 2376. Uemura, S.; Onoe, A.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1975**, 210.
(4) Winstein, S.; Shatavsky, M. *J. Am. Chem. Soc.* **1956**, *78*, 592.

0022-3263/85/1950-1532$01.50/0