Abstract
This review focuses on the chemistry of benzo-annulated tropones and tropolones reported since the beginning of the 20th century, which are currently used as tools by the synthetic and biological communities.

Review
1. Introduction
Tropone (1) and tropolone (2) have fascinated organic chemists for well over one hundred years. The carbocycles 1 and 2 are a special variety of organic compounds and represent a nonbenzenoid type of aromatic system (Scheme 1). Their dipolar resonance structures such as tropylium oxide form 1B and 2B have been reported to provide a Hückel sextet of electrons that is necessary for aromaticity (Scheme 1) [1-9].

The tropone core is the ubiquitous structural motif in the alkaloid colchicine and in a number of other natural compounds that have shown a highly diverse range of biological activity [1-9], like the inhibitory activity of inositol monophosphatase [10,11], antitumor [12], antibiotic [12,13], and antibacterial activity [14] and lipooxygenase inhibitor activity [14-16]. Tropomoids 3–10 have been reported in the literature in a number of natural forms (Figure 1) [1-8]. These compounds have a structural class spacing from the simple monocyclic tropones, such as the potent antifungal and antibiotic monoterpane β-thujaplicin (4) [17-23] (isolated from the heartwood and essential oils of trees of the family Cupressaceae), to complex macrocyclic analogues, such as harringtonolide (5) [24-26], which was found to have antineoplastic and antiviral properties, and caulersin (6) [26], which is a biologically active natural tropone fused to indole rings (Figure 1). Benzo-annulated cycloheptanones (as colchicine [8], allocolchicine), benzo[7]annuleneones, or benzotropones (as purpurogallin) and their analogues are present in a great variety of pharmacologically relevant natural products [27-29]. Colchicine (7, from Colchicum autumnale) is
a medication most commonly used to treat gout and familial Mediterranean fever (Figure 1) [30]. Colchicine and its analogues are potent microtubule-polymerizing agents and they inhibit growth of human cancer cell lines and show antimitotic activity [31-36]. Purpurogallin (8), which is biogenetically produced by oxidation of pyrogallol, and its analogues (like 9) are natural pigments (Figure 1) [37-44]. Theaflavin (10) and its derivatives, named theaflavins, are antioxidant benzotropones that are formed by the enzymatic oxidation of black tea and have been found to have numerous biological activities such as antipathogenic and anticancer activity, and they prevent heart disease, hypertension, and diabetes (Figure 1) [39,43]. Because of the pharmacological relevance of benzotropon analogues, the development of new and efficient synthetic methods is one of the major goals for future research in chemistry. Perhaps most importantly, the continued interest in troponoid systems originates from the fact that such compounds can be used as both building blocks and starting materials in the synthesis of complex natural products [1-9].

To date, the chemistry of tropone (1) and tropolones 2 has been reviewed [1-9], but there have been no surveys covering benzotropones and benzotropolones completely. Tang’s group published a recent review limited to the synthesis of naturally occurring tropones and tropolones [9]. In addition to this, chemistry of dibenzosuberenone, which is one of the dibenzotropone isomers, has already reviewed by us [45].

There are three possible benzotropon isomers: 4,5-benzotropon (11), 2,3-benzotropon (12), and 3,4-benzotropon (13, Figure 2). The present review focuses on the chemistry of parent benzotropones and their hydroxy analogues (benzotropolones) in the hundred years from the beginning to the present day, because these classes of molecules still attract noticeable attention from the synthetic and biological communities due to emerging reports of their interesting chemical struc-
tures and potential biological activities. Historically, many efforts have been devoted to the chemistry of benzotropones/benzotropolones and a plethora of benzotropone-type molecules have been produced over 100 years. Furthermore, the scope of this review includes the chemistry of halo-benzotropones, halo-benzotropolones, dibenzotropones, dibenzotropolones, tribenzotropone, and tropoquinones in addition to parent benzotropones and benzotropolones. The numerous functionalized benzotroponoids are excluded from the review.

2. Chemistry of 4,5-benzotroponone (11)

Several research studies have been reported on the synthesis and properties of 4,5-benzotropones since they were first prepared by Thiele and Weitz nearly a century ago [46,47]. Similar approaches of this method was independently studied by Cook [48] and Föhlisch [49] groups. In 1975, the crystal and molecular structure of 4,5-benzotroponone (11) was determined by Hata’s group [50]. X-ray diffraction analysis showed that the molecule is approximately planar and the bond alternation in the seven-membered ring and C=O bond length support satisfactory aromaticity.

2.1. Synthesis of 4,5-benzotroponone (11)

2.1.1. Oxidation of benzo[7]annulenes: 4,5-Benzotroponone (11) was synthesized for the first time via oxidation with selenium dioxide of 7H-benzo[7]annulene (14, Scheme 2) [39-45]. Furthermore, the direct oxidation of 5H-benzo[7]annulene to benzotropones was examined by Srivastava and Dev [37]. The selenium dioxide oxidation of 5H-benzo[7]annulene (15) furnished not only 4,5-benzotroponone (11; 27%) but also 2,3-benzotroponone (12; 13%, Scheme 2).

Pomerantz and Swei [51] investigated the oxidation of benzotropylium cation (16) with several oxidants. The oxidants used and results obtained are summarized in Table 1 and Scheme 3. Oxidation of benzotropylium fluoroborate (16) with Na$_2$O$_2$ and KO$_2$ gives benzotropones as the major products, whereas oxidation with m-chloroperbenzoic acid (m-CPBA)
produces a small amount of ring-contracted naphthaldehydes along with benzotropones. The oxidation with Na$_2$O$_2$ gives slightly higher amounts of benzotropones than of naphthaldehydes. As shown in Table 1, the most suitable reaction conditions to obtain 4,5-benzotropone (11) with the Pomerantz and Swei procedure include Na$_2$O$_2$/Me$_2$SO.

Mechanistic and synthetic aspects of the reaction of 7-bromo-5H-benzo[7]annulene (22) with CrO$_3$ and SeO$_2$ as oxidation reagents were studied (Scheme 4) [52]. All reactions provided 4,5-benzotropone (11) in addition to a few benzotroponoid compounds 23–26, the structures of which were determined by means of spectral data and chemical transformations. It is deemed that the dibromides 24 and 25 are the result of the addition of HBr, which is formed under the reaction conditions.

2.1.2. Multistep synthesis of 4,5-benzotropone (11): The first multistep synthesis for 4,5-benzotropone (11) is the original procedure described by Thiele, Schneider, and Weitz, which involves the condensation of o-phthalaldehyde (27) with diethyl 1,3-acetonedicarboxylate (28), followed by hydrolysis and decarboxylation steps [46,47] (Scheme 5). Similar syntheses were made by Cook’s [48] and Föhlisch’s [49] groups. Nevertheless, for performing large-scale synthesis, the cost of 27 make deterrent and an autoclave environment at 200–250 °C for final stage are an unattractive feature (Scheme 5).

Ranken’s group reported a novel synthetic route to 4,5-benzotropone (11) via an acid-catalyzed bridge cleavage reaction of 7-chloro-6,9-dihydro-5H-5,9-epoxybenzo[7]annulene (34) (Scheme 6) [53]. Transformation of adduct 31 to 11 starts with the synthesis of the stable cyclopropanoid tricyclic 32 from the reaction of the 7-oxabenzonorbornadiene 31 with dichlorocarbene, generated by the phase-transfer method. The thermalysis of chlorocarbene 32 in nitrobenzene at 165 °C resulted in the formation of ring-expanded product 33. After the reduction of the allylic position with LiAlH$_4$, the treatment of monochloride 34 with concentrated sulfuric acid in ice water afforded a quantitative yield of 4,5-benzotropone (11).

The above researchers also proposed a mechanism for the formation of 11 from 31 as shown in Scheme 7. The acid-catalyzed cleavage of the oxo-bridge of 34 gives benzylic carbocation 35. Consequently, after deprotonation and dehydration, chloro benzotropilium cation 37 undergoes hydrolysis to give 4,5-benzotropone (11) in aqueous reaction media.
Using \( o \)-xyylene dibromide (38) as starting material, Ewing and Paquette designed and synthesized benzotropone 11 by an especially reliable route [54]. For this purpose, bisalkylation of \( o \)-xyylene dibromide (38) with tert-butyl lithioacetate (Rathke’s salt) and subsequent Dieckmann cyclization provided simple access to 40 in 51% overall yield (Scheme 8). After bromination of 40 with molecular bromine in carbon tetrachloride, direct dehydrobromination with lithium chloride in dimethylformamide gave 11 in 85% isolated yield.

Müller’s group reported an alternative synthesis for 11 starting from the carbene adduct 41 over two or three steps [55]. Firstly, dichloride 41 was reduced with LiAlH\(_4\) in ether to give the monochloride 42. The reaction of 42 with DDQ produced 4,5-benzotropone (11) in 24% yield together with 28% of starting material. The key step for 11 from 42 is the electrocyclic ring expansion of dehydrogenation product 44 to the benzotropylium ion 45. Secondly, 11 is obtained in 18% yield after benzylic bromination of 42 with NBS, followed by in situ elimination reaction of the labile bromide 43 mediated by 1-t-BuOK (Scheme 9).

Palladium-catalyzed C–C bond-formation reactions such as Heck and Sonogashira couplings are employed in a wide variety of areas in organic chemistry [56, 57]. Recently, Shaabani’s group synthesized and characterized palladium nanoparticles supported on ethylenediamine-functionalized cellulose (PdNPs@EDACs) as a novel bio-supported catalyst for Heck and Sonogashira couplings in water [58]. Shaabani’s group reported the efficient synthesis of benzotropone 11 in a good isolated yield (83%) via PdNPs@EDACs-catalyzed Heck coupling and intramolecular condensation of 2-bromobenzaldehyde (46) and methyl vinyl ketone (47) (Scheme 10) [58].

2.2. Reactions of 4,5-benzotropone (11)

2.2.1. Reactions via the carbonyl group: Fulvalenes are typical cross-conjugated carbocyclic unsaturated compounds and are of theoretical and synthetic interest [59]. Several
Researchers have studied the synthesis of benzofulvalenes via the carbonyl group of 4,5-benzotropone (11) (Scheme 11). Halton’s group applied the Peterson olefination reaction to the synthesis of benzofulvalenes 49 and 50 from the reaction of 4,5-benzotropone (11) with corresponding cyclopropanes [60,61]. While the reaction of 4,5-benzotropone (11) with malononitrile afforded 8,8-dicyano-3,4-benzoheptafulvalene (51) [62], the condensation of 4,5-benzotropone (11) with dimethyl malonate and its nitro analogue gave benzoheptafulvalene derivatives 52 and 53 [50,63]. The condensation of 4,5-benzotropone (11) and anthrone (10H-anthracen-9-one) also afforded 4,5-benzo-tropylen-anthron 54 in 65% yield [63]. Kitahara reported the synthesis of 1,2,3,4-tetrachloro-7,8-benzo-alexafulvalene 55 via condensation of 1,2,3,4-tetrachlorocyclopentadiene and 4,5-benzotropone (11) [64]. The thia-heptafulvalene 56 was synthesized by Wittig–Horner reaction of 4,5-benzotropone (11) with 2-dioxyphosphinyl-1,3-benzodithiole [59]. The reactants used for the synthesis of benzoheptafulvalene derivate 57 were
As polycyclic conjugated π systems can endow new properties to the original π system, conjugated systems are important in terms of both theoretical and experimental aspects. Nitta’s group extensively studied the synthesis and structural and chemical properties of a new kind of cycloheptatrienylium ions using aromatic π systems (Figure 3) [66-70]. In this context, Nitta and colleagues reported the synthesis, properties, and oxidizing ability of the novel $61^+\cdot\text{BF}_4^-$ [71]. A condensation reaction of 4,5-benzotropone (11) with dimethyl barbituric acid (62) and subsequent oxidative cyclization reaction using DDQ-Sc(OTf)$_3$ or photoirradiation under aerobic conditions afforded $61^+\cdot\text{BF}_4^-$ (Scheme 12). The $pK_{R^+}$ value and reduction potential of the cation 61 were studied. The relative stability of a carboxication can be expressed by the $pK_{R^+}$ value, which is the affinity of the carbocation toward hydroxide ions. The $pK_{R^+}$ value for cation 61 was determined to be 4.7 spectrophotometrically. The reduction potential of the cation 61 was determined as $-0.46$ and $-1.07$ V by cyclic voltammetry in acetonitrile. The oxidizing ability toward alcohols of $61^+\cdot\text{BF}_4^-$ in the auto-recycling process was also reported. However, to test the reactivity, the reactions of $61^+\cdot\text{BF}_4^-$ with a nucleophile such as NaBH$_4$, diethylamine, and methanol were carried out to afford $7$-adducts 64–66. Compound 64 was oxidized by DDQ to regenerate $61^+\cdot\text{BF}_4^-$ in good yield, whereas the treatment with $42$% aq HBF$_4$ of the compounds 65 and 66 regenerated $61^+\cdot\text{BF}_4^-$ in good yields.

Integrins are transmembrane α/β heterodimers that bind to extracellular matrix ligands, cell-surface ligands, and soluble
Perron-Sierra’s group prepared substituted benzo[7]annulenes as a novel series of potent and specific α₅ integrin antagonists starting from 4,5-benzotropone (11) (Figure 4 and Scheme 13) [73].

Figure 4: A novel series of benzo[7]annulenes prepared from 4,5-benzotropone (11).

TBS-enol ether intermediate 68 was first formed by the Mukaiyama–Michael reaction of O-silyl ketene acetal to 4,5-benzotropone (11) at low temperature in the presence of catalytic mercury iodide; it is a critical step for the formation of the compound 72. Hydrolysis of intermediate 68 led to ketone 69 in high yield containing an acetic acid residue β to the carbonyl group. A sequence of the one-carbon homologation of ketone 69 is followed by isomerization into the α,β-unsaturated aldehyde 71. A series of reductive amination and amidation reactions then led to the formation of the targeted substituted benzo[7]annulene 72 (Scheme 13). Moreover, the structure–activity study revealed that some of the compounds showed nanomolar IC₅₀ values on α₅β₃ and α₅β₅ integrins.

Scheme 13: Preparation of substituted benzo[7]annulene 72 using the Mukaiyama-Michael reaction.

Benzo[7]annulenylidenes 73–75 and their rearrangements have attracted much interest due to their thermal and photochemical transformations (Figure 5) [74-76]. For the first time, Jones reported the chemical trapping of thermal and photochemical decomposition of the tosylhydrazone sodium salt of 4,5-benzotropone (11) and defined carbene–carbene rearrangements of 77–79 before finally it was verified by trapping of unstable intermediates 77–79 (Scheme 14) [77]. In 2002, McMahon reported obtaining the naphthylcarbene rearrangement manifold via the carbonyl groups of the isomeric benzotropones 11 and 12 (Scheme 14 and Scheme 33) [78]. Diazo compound 76 was prepared from 4,5-benzotropone hydrazone under oxidative conditions. Irradiation of matrix-isolated 7-diazo-7H-benzo[7]annulene (76) afforded a mixture of triplet

Figure 5: Possible benzo[7]annulenylidenes 73–75.
Scheme 14: Thermal and photochemical decomposition of 7-diazo-7H-benzo[7]annulene (76) and the trapping of intermediates 77–79.

Scheme 15: Synthesis of benzoheptafulvalene 86.

7H-benzo[7]annulenylidene (77), 2,3-benzobicyclo[4.1.0]heptatriene (78), and triplet 2-naphthylcarbene (79). Formation of allene 83 as an alternative carbene rearrangement product was not detected under the studied photolysis conditions (Scheme 14).

Kitahara’s group reported the one-step synthesis of heptafulvalenes and benzoheptafulvalenes from monocyclic tropones and benzotropones [79]. The reaction of 4,5-benzotropane (11) and 8-oxoheptafulvene (85), prepared in situ via the reaction of cycloheptatriene-7-carboxylic acid chloride (84) with NEt₃, afforded 3,4-benzoheptafulvalene 86 in 50% yield as fairly stable deep brown crystals (Scheme 15). The structure of 86 was confirmed by the spectroscopic data. The formation of the heptafulvalenes could be explained via an intermolecular [2 + 2] cycloaddition product such as 87 between the carbonyl group of tropones and the ketene C=C double bond of 8-oxoheptafulvene (85) followed by decarboxylation.

In a similar manner, the synthesis of 7-(diphenylmethylene)-7H-benzo[7]annulene (89) was reported in two different ways (Scheme 16). First, the addition of diphenylketene (88) to 11...
resulted in the formation of benzoheptafulvalene \(89\) [80,81]. 7-(Diphenylmethylene)-7\(\text{H}\)-benzo[7]annulene \((89)\) was also prepared via the oxaphosphetane \(92\) intermediate by treating 4,5-benzotropane \((11)\) with (diphenylmethylene)(phenyl)phosphine oxide \((91)\) generated thermally or photochemically from \(90\) [82]. Furthermore, dimeric byproduct \(93\) is also formed under photochemical conditions.

2.2.2. Ring expansion reactions via a tropone unit: In 1975, Franck-Neumann and Martina reported the reaction of dimethyl diazomethane with tropone and benzotropones [83]. This reaction gave benzo-4,5-dimethyl-8,8-cyclooctatrienone \((94)\), 30\% isolable yield) as an insertion product via a carbonyl group and pyrazoline \(95\) as 1,3-dipolar addition product via double bonds (Scheme 17).

Azocine derivatives, eight-membered nitrogen heterocycles, exist as the core structure in many natural and non-natural products [84]. Nevertheless, 2-methoxyazocine \((96)\) reduces related aromatic 10\(\pi\)-electron dianion \(97\) (Scheme 18). Paquette’s group investigated benzo-annelation effects on azocine reactivity and the chemical and polarographic reduction of several methoxy azocines [85,86]. 4,5-Benzotropane \((11)\) was used as the logical starting material for the synthesis of benzomethoxyazocine \(101\) (Scheme 18). Treatment of \(101\) with potassium at \(-40\text{ °C}\) in \(\text{NH}_3–\text{THF}\) (5:1), subsequent quenching by the addition of methanol, yielded dihydro derivative \(103\) (Scheme 18).

In 1978, in order to examine heteroatomic influences on the possible generation of 9C–10\(\pi\) homoaromatic dianions, Paquette’s group described the synthesis and reducibility of benzo-fused-homo-2-methoxyazocines from benzotropones (Scheme 19) [87]. Firstly, dimethylsulfoxonium methylide addition to 4,5-benzotropane \((11)\) provided the introduction of the cyclopropane ring required for two benzohomoazocines. Beckmann rearrangement of \(104\) resulted in a mixture of ring expansion products \(105\) and \(106\) in nearly equal proportions. This lactam mixture was then converted into the desired imidates and the imidates \(107\) and \(108\) were separated. Reduction of benzohomoazocine \(107\) proceeded without cleavage of its three-membered ring, whereas the internal cyclopropane \(\sigma\) bond of \(108\) underwent cleavage to form \(110\) (Scheme 19). Paquette’s group were unable to determine the formation of homoazocinyl dianion intermediates due to the added benzene ring in \(107\) and \(108\) and concluded that the presence of imino ether does not enhance the homoaromaticity of 9C–10\(\pi\) dianions.

Homoaromaticity, homotropylium cations, and homotropones have been extensively studied [88-123]. Merk’s group obtained with \(\text{H}_2\text{SO}_4\) benzohomotropylium cation \(111\) starting from benzocyclooctatetraene and investigated its homoaromaticity (Scheme 20) [124]. Sugimura’s group attempted to prepare an alternative benzohomotropylium cation \(112\) and reported the synthesis of 4,5-benzohomotropones \(104\) and \(115\) from 4,5-benzotropones (Scheme 20). Although the conversions of 4,5-
benzohomotropones to hydroxytropylium ions 117 and 118 in sulfuric acid were presumed, benzohomotropylium cation 112 was not detected from the reactions of the corresponding alcohol 114 in sulfuric acid [125].

2.2.3. Reduction-based studies: To define the stereochemical, conformational, and dynamic properties of both benzo[7]annulenones (and related compounds) and monosubstituted tetrahydro-7H-benzo[7]annulenone, St-Jacques' group benefited ex-
tensively from the use of dynamic nuclear magnetic resonance (DNMR) techniques [126,127]. A catalytic deuterogeneration of 4,5-benzotroponone (11) followed by deuteration led to deuterated 5,6,8,9-tetrahydro-7H-benzo[7]annulen-7-one 119-d$_6$ with the presence of appreciable quantities of d$_4$ and d$_5$ species (Scheme 21). The compounds 120-d$_6$ and 121-d$_6$ were prepared from 119-d$_6$ as shown in Scheme 21. NMR studies for these molecules show that the chair conformation 122 is predominant over the boat. Several 5-monosubstituted benzo[7]annulenes 123–128 were prepared using 4,5-benzotroponone (11) as starting material and $^1$H and $^{13}$C NMR studies in each series of compounds revealed strikingly different substituent effects (Scheme 21).

In order to perform reactions with alkyl Grignard reagents, Bertelli’s group realized the synthesis of 7-methoxy-7H-benzo[7]annulene (129) (Scheme 22) [128]. Reduction of 4,5-benzotroponone (11) with LiAlH$_4$ followed by etherification gave

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**Scheme 20:** Synthesis of 4,5-benzohomotropones 104 and 115 from 4,5-benzotropones 11 and 113.

**Scheme 21:** A catalytic deuterogeneration of 4,5-benzotroponone (11) and synthesis of 5-monosubstituted benzo[7]annulenes 123–128.
the corresponding ether 129. Treatment of the ether 129 with MeMgI afforded an approximately equal mixture of two methyl benzo[7]annulenes, 131 and 132. An intermediate, 130, formed via the coordination of the Grignard reagent with ether was proposed to be operative in the reaction (Scheme 22).

2.2.4. Miscellaneous reactions: a. Halogenated benzo[7]annulenes and their synthetic potentials: In 1978, Föhlisch’s group reported the synthesis and ambident reactivity of benzo[7]annulenylium cations 133a and 133b (Scheme 23) [49]. While the reaction of 11 with oxalyl bromide yielded bromobenzo[7]annulenenylium bromide 134a as a stable carbenium salt, the reaction of oxalyl chloride or phosgene with 11 afforded 7,7-dichloro-7H-benzo[7]annulene (135b) as a covalent compound that ionizes in liquid SO$_2$ to the cation 134b. Treatment of cations with nucleophiles that are preferably added to the benzylic position (C-5 or C-9) yielded chloro- and bromo-5H-benzo[7]annulenes 136–143. According to Hückel molecular orbital (HMO) calculations, this observed regiochemistry is attributed to the highest positive charge density at the benzylic position, which is the favored process under kinetic conditions. During the attempted preparation of 4,5-benzotropone diaziridine 144, the synthesis of 7,7-dichloro-7H-benzo[7]annulene (135b) was also carried out from the reaction of 4,5-benzotropone (11) with SOCl$_2$ in a quantitative yield (Scheme 23) [77,78]. However, all attempts to synthesize 144 from 135 have failed.

7-Bromo-5H-benzo[7]annulene (22) was also used as a key molecule in the synthesis of benzo[7]annulenylidene–iron complexes 147 and 148 (Scheme 24) [129]. The monobromide 22 obtained from the reaction of oxalyl bromide with 11 fol-
lowed by \( n\)-BuLi-reduction converted into 146 and then into yellow-brown complex 147 by treatment with a cold solution of \((\eta^5\text{-C}_5\text{H}_5)\text{(CO)}_2\text{FeI}\) (FpI). After chromatography of 147 over alumina with a pentane–benzene mixture, the complex 147 oxidized to 148 as a fairly air-stable red-brown solid.

b. Nucleophilic addition to 4,5-benzotropone (11): Ried’s group realized the reaction of 4,5-benzotropone (11) and its derivatives with lithium acetylide as a nucleophile between \(-50\) and \(-32\) °C [130]. While the possible 1,4-conjugate addition product 149 was oxidized to 1-ethynylbenzotropone 150 in situ, the etheric compound 152 was obtained from the reaction of 1,2-addition product 151 with HCl (Scheme 25).

c. Decarbonylation of 4,5-benzotropone (11): The mechanism for the neutral and radical-cationic decarbonylation of tropone and benzannulated tropones was compared by both experimental techniques and by means of MNDO calculations (Scheme 26) [131]. While the key steps for the thermal decomposition of tropones are electrocyclic ring closure and cheletropic CO extrusion to give an aromatic system, the cationic reactions occur with ring closure followed by the opening to a benzoyl-type ion, which is the actual precursor of the CO loss (Scheme 26).

d. Ketalization of 4,5-benzotropone (11): Cavazza’s group reported their unsuccessful attempts to obtain tropone dithioketal like 155 [132]. The treatment of 4,5-benzotropone (11) with 1,2-ethanedithiol and BF\(_3\)Et\(_2\)O in MeOH gave the expected dithioketal 154, whereas the reaction of tropone under similar conditions presented complications from rapid [1,7] sigmatropic shifts of unhindered alkylthio groups to give bicyclic 1,7-disubstituted cycloheptatrienes like 156 (Scheme 27). Leitich’s group reported the synthesis and cycloaddition of tropone ethylene acetal and benzotropone ethylene acetal 157 (Scheme 27) [133]. The ketal 157 was prepared from the reaction of 4,5-benzotropone (11) with ethylene glycol in the presence of triethyloxonium tetrafluoroborate. The cycload-
Scheme 27: Reaction of 4,5-benzotropone (11) with 1,2-ethanediol and 1,2-ethanedithiol.

dition of 157 with 4-phenyl-1,2,4-triazoline-3,5-dione (158) gave the cycloadducts 159 and 160 via the cycloheptatriene form. However, usually the norcaradiene type product 161 observed with cycloheptatrienes was not formed (Scheme 27).

3. Chemistry of 2,3-benzotropone (12)

3.1. Synthesis of 2,3-benzotropone (12)

Several procedures relating to the synthesis of 2,3-benzotropone (12) were reported. The vast majority of these procedures utilize commercially available 1-benzosuberone (6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one, 162) (Scheme 28).

3.1.1. Synthesis using 1-benzosuberone (162): In 1959, Buchanan’s group realized a nontedious method for the synthesis of 2,3-benzotropone (12) starting with 1-benzosuberone (162) (Scheme 29) [134]. First, the unsaturated ketone 163, which is called Julia’s ketone, was prepared by NBS-bromination in the presence of a trace of benzoyl peroxide (BPO) and followed by dehydrobromination. Another synthesis of Julia’s ketone was achieved by dehydration of the known keto-alcohol 164 by boric acid. Oxidation of Julia’s ketone with selenium dioxide gave 2,3-benzotropone (12). An alternative synthesis for 12, which represents a feasible route to avoid the disadvantage of selenium dioxide, is also bromination of Julia’s ketone 163 followed by spontaneous elimination of hydrogen bromide at the temperature of the reaction.
Scheme 30: Oxidation-based synthesis of 2,3-benzotropone (12) via 1-benzosuberone (162).

Hypervalent iodine(V)-based reagents such as IBX (or 2-iodoxybenzoic acid) and Dess–Martin periodinane (DMP) are commonly used in organic synthesis as oxidizing agent to form both unsaturated carbonyl compounds and conjugated aromatic carbonyl systems. Nicolaou’s group reported a general method for the mild, swift, and highly efficient oxidation of alcohols, ketones, and aldehydes to unsaturated compounds in one pot (Scheme 30) [138,139]. Accordingly, an IBX-controlled dehydrogenation through single-electron-transfer-based oxidation processes of 162 gave 12 in 60% yield.

3.1.2. Other synthetic approaches: A convenient synthesis of 2,3-benzotropone (12) from α-tetralone (171) by ring expansion was performed by Sato’s group (Scheme 31) [140]. First, 1-ethoxy-3,4-dihydronaphthalene (172) was prepared by reacting α-tetralone (171) with ethyl orthoformate in the presence of an acid catalyst. Subsequent successive reactions are dihalocarbene addition to enolether 172, ring expansion of the adduct 173 to halocycloheptadienone 168, and dehydrohalo-
3.2. Reactions of 2,3-benzotropone (12)

3.2.1. Reactions via a carbonyl group: Among the most common reactions for 2,3-benzotropone (12) are condensation reactions with active methylenic compounds, resulting in the formation of benzoheptafulvenoids (Figure 6). For example, Machiguchi reported that the condensation reaction of deuterium tracer 2,3-benzotropone 177 with malononitrile to yield 8,8-dicyano-2,3-benzoheptafulvene 178 via reaction paths including the choice of a Michael-type attack of the nucleophile at the C-4 position to Knoevenagel-type attack at the C-1 position [143]. Benzannulated quinotropylidene 180 was produced by the condensation reaction of 2,3-benzotropone (12) and 10H-anthracen-9-one [63]. 2,3-Benzotropone (12) was transformed into the corresponding benzoheptafulvalene 181 using the ketene addition protocol illustrated in Scheme 15 and Figure 6.

The thermal decomposition of the obtained tosylhydrazone salt 182 from 2,3-benzotropone (12) afforded a trapping product of 1-naphthylcarbene (185) [128], while the allenic rearrangement product 183 for the carbene 75 was not detected in the photolysis of a diazo compound (Scheme 33) [78]. 2,3-Benzotropone
(12) was converted to gem-dichloride 187 to achieve diazirine as carbene precursor (Scheme 33) [77,144].

3.2.2. Ring-expansion reactions via a tropone unit: The ring-expansion product 188, which is a net insertion of a diazomethane unit into the tropone, was prepared from the reaction of 2,3-benzotropone (12) with dimethyl diazomethane (Figure 7) [83]. Benzohomoazocines 191–193 and benzo-methoxyazocines 195–197 were prepared using a similar protocol illustrated in Scheme 18 and Scheme 19 (Figure 7) [84-87,145]. The cyclopropane ring in 192 was reduced to the corresponding dihydroazonine 193.

Additionally, Ogliaruso’s group prepared 2,3-benzo-6,7-mono-homotropone (189) and trans-2,3-benzo-4,5,6,7-bishomotropone (190) from the nonselective reaction of 2,3-benzotropone (12) with dimethyloxosulfonium methyld in yields of 35% and 28% and investigated the structural characterization of these compounds by extensive NMR analysis (Figure 7 and Scheme 34) [146]. In addition, carbonium ions 198–201, prepared via the protonation of 2,3-benzotropone (12), homotropone 189, and bishomotropone 190, and their deuterated analogues using fluorosulfuric acid–antimony pentafluoride were investigated using NMR spectroscopy (Scheme 34) [147]. NMR investigation of the carbonium ion formed from 189 indicated the formation of the carbonium ion 199 with complete electron delocalization, whereas the carbonium ion 200 (and 201) formed from 190 indicated considerably less electron delocalization (Scheme 34).

3.2.3. Cycloaddition reactions: 2,3-Benzotropone (12) possesses a high functional tolerance towards both the diene and dienophile and undergoes the Diels–Alder reaction. Ghosh’s group reported an exclusive peri-, regio-, and stereoselective cycloaddition reaction of 5H-benzo[7]annulen-5-one (Scheme 35) [137]. The intermolecular [4 + 2] cycloaddition of 2,3-benzotropone (12) with cyclopentadiene (202) in the presence of boron trifluoride occurred totally periselectively, regioselectively, and exo-diaselectively to afford the adduct 203 in 75% yield. The Diels–Alder reaction of 2,3-benzotropone (12) with various dienophiles has also been reported. In the first example, Rennhard’s group realized the cycloaddition of benzotropone 12 with maleic anhydride (204) to give a tricyclic adduct 207 (in 90% yield) (Scheme 35) [141,142]. Later, Middlemiss’ group also used dienophiles such as maleic anhydride (204), N-methylmaleimide (205), and N-phenylmaleimide (206) to give endo-adducts 207–209 [148]. Furthermore, these ethenobenzocycloheptenones 207–209 underwent di-π-methane photo-rearrangement to 210–212 exclusively.
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Scheme 35: Cycloaddition reactions of 2,3-benzotropone (12).

(Scheme 35). Moreover, Dastan’s group prepared bicyclic
dendoperoxide 213 in 74% yield from 2,3-benzotropone (12) via
tetraphenylporphyrine (TPP)-sensitized photo-oxygenation
(Scheme 35) [149].

3.2.4. Miscellaneous transformations: Machiguchi reported
that the oxidative amination of 2,3-benzotropone (12) with
methylcopperamine sulfate in aqueous methylamine at room
temperature afforded 4-methylamino-1-naphthalene carbalde-
hyde (215) with a trace amount of 4-methylamino-2,3-benzotro-
pone (214) via reaction paths including the dishing of Michael-

4. Chemistry of 3,4-benzotropone (13)
4.1. Generation, characterization, and reaction
3,4-Benzotropone (13) is of considerable interest for both theo-
retical and preparative reasons. The aromaticity of 3,4-
benzotropone (13A) is considered to depend on the contribu-
tion of electronically polarized form 13B such as tropone 1A
(Figure 8) [153,154]. Kurihara’s group reported the calculated
resonance energies and bond currents for benzotropenes and
troponoid compounds [155]. Although benzotropenes 11 and 12
have been isolated, 3,4-benzotropone (13) is rather unstable and
has not been isolated. This instability is attributed to the
o-quinoidal structure of 13 because it has no sextet electron

Considering the known reactivity of benzocyclobutenes, i.e.,
their isomerisation to o-quinodimethanes, Tsuji’s group used
6,7-benzobicyclo[3.2.0]hepta-3,6-dien-2-one (230) as a precur-
sor to produce 13. They reported the first generation and spec-
troscopic characterization of this elusive molecule obtained by
electrocyclic ring-opening reaction of 230 through irradiation
in a rigid medium at low temperature or by thermolysis at high

temperature [153]. As shown in Scheme 37, compound 230 was
synthesized through the addition of benzene to 2-cyclopen-
tenone acetel (228) followed by hydrolysis and subsequent oxi-
dation of the resultant ketone 229 with DDQ. Irradiation
(>300 nm) of 230 in EPA (a 5:5:2 mixture of ether, isopentane,
and ethanol) at −196 °C led to the formation of 13, which
exhibited the development of characteristic UV–vis absorption
in the range 300–550 nm. In addition to product 13, two

48 (3%), and 225 (28%) [152].

IR spectroscopic results showed a substantial contribution of
13B to 13A in the ground state. Moreover, it was found that the
Scheme 36: Reaction of 2,3-benztropone (12) with various reagents and compounds.

Figure 8: 3,4-Benztropone (13) and its resonance structure.

photochemical behavior of 230 depended on the state of the irradiation medium. For example, the smooth \([\pi 10 + \pi 10]\) dimerization of 13 to give dimeric product 233 was realized with the irradiation (>420 nm) of 13 in a fluid EPA solution below \(-100 \, ^\circ C\) [154]. Furthermore, the IR spectra of 3,4-benztropone (13) generated in matrices at 13 K by the photoisomerization of 230 were directly observed [156]. In addition, the thermal generation of 13 from 230 was investigated [153,154]. When 230 with 10 equiv of maleic anhydride in benzene at 220 °C was reacted, \([\pi 2 + \pi 8]\) cyclo-adduct 234 as a single product was isolated in 52% yield (Figure 9) [153,154]. The thermolysis of 230 in the presence of ethyl vinyl ether gave three volatile products 235–237 in GLC yields of 10%, 7%, and 15%, respectively (Figure 9) [154].

5. Benzotropolones

Benzannulation to the tropolone scaffold can give numerous tautomeric hydroxybenzotropolones or benzotropolones. Figure 10 shows 238A (or 241A–240) as single tautomers, whereas 239 and 174 are depicted as a mixture of tautomers. Moreover, benzenoid structures as 238A are more stable than \(o\)-quinoidal structures as 238B due to Clar’s \(\pi\)-sextet rule.
Scheme 37: Synthesis of 6,7-benzobicyclo[3.2.0]hepta-3,6-dien-2-one (230).

Figure 9: Photolysis and thermolysis products of 230.

Figure 10: Benzotropolones and their tautomeric structures.
5.1. 2-Hydroxy-4,5-benzotropone (238)

5.1.1. Synthesis of 2-hydroxy-4,5-benzotropone (238):
Tarbell’s group reported the first synthesis of 2-hydroxy-4,5-benzotropone (238) starting from phthalaldehyde (27) in two steps (Scheme 38) [157]. Condensation of 27 with methoxycetone in the presence of NaOH and then cleavage of the methyl ether 243 by strong acid afforded 2-hydroxy-4,5-benzotropone (238). Turner’s group reported a new method for the synthesis of 4,5-benzotropolone (238) via the cycloaddition of dichloroketene (generated in situ from trichloroacetyl chloride) with indene followed by hydrolysis of the adduct 244 with sodium acetate in aqueous acetic acid (Scheme 38) [158]. In addition, Stevens’ group reported a method for the synthesis of 238 using a strategy similar to that of Turner’s group (Scheme 38) [159]. One-step synthesis for 238 was described by Christol’s group through the oxidation of benzocycloheptene 245 with SeO$_2$ in 35% yield (Scheme 38) [160].

Galantay’s group described a novel synthetic protocol for benzotropolones using the oxazole-benzo[7]annulenes 247 and 248, which may be easily obtained from the reaction of α-oximino-benzosuberone 246 with Ac$_2$O/AcOH/HCl (Scheme 39) [161]. The olefin 249, derived from reduction, chlorination, and elimination of 247, was converted by SeO$_2$ in refluxing dioxane or xylene to the acetamido-benzotropone 250, which in turn can be hydrolyzed to 2-hydroxy-4,5-benzotropone (238).

5.1.2. Reactions of 2-hydroxy-4,5-benzotropone (238):
Some quinoxaline and pyrazine derivatives 254–256 were synthesized from 1,2-phenylenediamine (251), 1,2-diaminocyclohexane (252), and ethylenediamine (253) with 4,5-benzotropolone 238 (Figure 11) [162]. Compound 256 can be converted to methylated 257.

Tarbell’s group also reported 4,5-benzotropolone 238 and its methyl ether do not give the characteristic aromatization reactions as colchicine and monocyclic tropolones, and explained that 238 is a weaker acid than colchicine or tropolone [157]. However, the conversion of 238 to 1-nitro-2-naphthoic acid...
5.2. 6-Hydroxy-2,3-benzotropone (239)

5.2.1. Synthesis of 6-hydroxy-2,3-benzotropone (239): Takahashi and co-workers described a route for 6-hydroxy-2,3-benzotropone (239) starting from benzosuberone (162) [163]. Firstly, a mixture of isomeric dibromides 261 was prepared with excessive bromination of 162 followed by subsequent dehydrobromination. By treatment of dibromides 261 with hydroxylamine in pyridine, 5- and 4-bromo-6-hydroxylamino-2,3-benzotropone oximes 262 were obtained. Hydrolysis of these oximes 262 with sulfuric acid gave 5-bromo-6-hydroxy-2,3-benzotropone and the 4-bromo isomer 263, which were debrominated with catalytic hydrogenation to give 239 (Scheme 41). Although 239 is capable of existing as two tautomeric mixture tautomers, 239A and 239B, which predominates is not clear, and the formation of a single methyl ether,
acetate, and 2,4-dinitrophenylhydrazone has been reported [163].

5.2.2. Reactions of 6-hydroxy-2,3-benzotropone (239): Hoshino’s group reported the synthesis and chemical transformations of azo, nitro, and amino derivatives of 6-hydroxy-2,3-benzotropone (239) (Scheme 42) [164]. While 7-amino derivative 264 was prepared via diazo coupling of 239 with diazotized $p$-toluidine in a pyridine solution followed by hydrogenation, the nitration of 239 in acetic acid solution afforded nitro compound 267. Nitro compound 267 was also hydrogenated to produce 7-amino derivative 264. Diazoketone 265 was prepared from 264 with sodium nitrite in fluoroboric acid (HBF$_4$) and its Wolff rearrangement under reflux conditions in water gave 1-hydroxy-2-naphthoic acid (266). Acetylation of 264 with sodium acetate in acetic anhydride at 100 °C for 30 min afforded an unusual product, 269 or 270 via intermediate 268. The hydrolysis of 269 (or 270) provided a compound that is assumed to be an oxazolobenzotropone based on its infrared absorption spectrum. In fact, the authors reported that the correct structures for both pairs (271 or 272) are not clear. However, the oxidation of both 239 and 264 to $o$-carboxycinnamic acid (273) was also reported under alkaline hydrogen peroxide conditions (Scheme 42) [163,164]. Furthermore, bromination of 6-hydroxy-2,3-benzotropone (239) and corresponding transformations will be covered in the next sections.

Scheme 42: Various reactions via 6-hydroxy-2,3-benzotropone (239).
Photoreaction of 6-hydroxy-2,3-benzotropone (239) was reported by Yoshioka and Hoshino (Scheme 43) [165]. The irradiation of 239 in methanol with Pyrex-filtered light gave the products 274 and 275 in 25% and 2% yields, respectively, accompanied by undefined materials.

5.3. 7-Hydroxy-2,3-benzotropone (241)

5.3.1. Synthesis of 7-hydroxy-2,3-benzotropone (241): The first synthesis of 7-hydroxy-2,3-benzotropone (241) was described by Cook’s group (Scheme 44) [166,167]. 7-Hydroxy-2,3-benzotropone (241) was prepared from benzosuberone (162) by oxidation with selenium dioxide in boiling ethanol, followed by dehydrogenation with bromine in acetic acid at 100 °C. Another method for the synthesis of 7-hydroxy-2,3-benzotropone (241) starting from the reaction of diketone 276 with boiling acetic anhydride was achieved by Maignan (Scheme 44) [168]. The reaction of enol-acetate with NBS led to 277, which was heated in water–dioxane at 100 °C to give 7-hydroxy-2,3-benzotropone (241) by an elimination process. Galantay’s group also reported the synthesis of 7-hydroxy-2,3-benzotropone (241), which was similar to the synthesis of 2-hydroxy-4,5-benzotropone (238) as depicted in Scheme 38 (Scheme 45) [161].

Sato’s group reported the synthesis of 7-hydroxy-2,3-benzotropone (241) via the ring expansion pathway of β-naphthoquinone (280) with diazomethane under various conditions and hydrolysis steps (Scheme 46) [169]. The boron trifluoride etherate-promoted ring expansion reactions were carried out at various quinone/BF$_3$OEt$_2$/CH$_2$N$_2$ molar ratios in a different solvent under an atmosphere of nitrogen and with cooling in an ice bath and 3,4-benzotropolonoboron difluoride 281 was obtained in 2–25.5% yield. The hydrolysis of chelate compound 281 was performed with dilute sulfuric acid to afford 241 in almost quantitative yield.

Bicyclic endoperoxides generated from the cycloaddition of singlet oxygen to 1,3-dienes serve as excellent synthetic precursors and have led to developments in tropone chemistry [170-172]. Taking advantage of the endoperoxide transformation, the synthesis of 7-hydroxy-2,3-benzotropone (241) was successfully realized by Dastan’s group (Scheme 47) [149]. Thiourea reduction of the peroxide linkage of 213 to the diol 282 and then simultaneously dehydration in situ gave the corresponding benzotropolone 241 in nearly quantitative yield.

Recently, Arican and Brückner reported the synthesis of 7-hydroxy-2,3-benzotropones by ring-closing metathesis (Scheme 48) [173]. 7-Hydroxy-2,3-benzotropone (241) was synthesized in four steps starting from a Br/Li exchange reaction of o-bromostyrene (283) followed by the addition of aldehyde 284 to give the benzyl alcohol 285. Oxidation with Dess–Martin periodinane of the alcohol 285 followed by ring-closing metatheses in the presence of 1 mol % of the second generation Grubbs catalyst (287) gave the 5H-benzo[7]annulene-5,6(7H)-dione monoketal 288 in nearly quantitative yield. The hydrolysis of 288 with excess p-TsOH in aqueous acetonitrile at 75 °C for 4 h afforded the benzotropolone 241.

5.3.2. Reaction of 7-hydroxy-2,3-benzotropone (241): Various monosubstitution products 289–291 of 7-hydroxy-2,3-benzotropone (241) were readily prepared by Nozoe’s group (Figure 12) [174]. The synthesis of bromo-derivative 290 from 241 was also reported by Cook’s group [166]. The coupling of 241 with aryl diazonium chlorides resulted mainly in the forma-
Scheme 45: Synthesis strategy for 7-hydroxy-2,3-benzotropone (241) from ketone 276.

Scheme 46: Synthesis of 7-hydroxy-2,3-benzotropone (241) from β-naphthoquinone (280).

Scheme 47: Synthesis of 7-hydroxy-2,3-benzotropone (241) from bicyclic endoperoxide 213.

Scheme 48: Synthesis of 7-hydroxy-2,3-benzotropone (241) by ring-closing metathesis.

Catalytic hydrogenation of 241 over Adams's catalyst (PtO₂·H₂) gave the diol 295 (Scheme 49) [162,165,174]. Treatment of 241 with alkaline hydrogen peroxide caused degradative fission to give o-carboxycinnamic acid (296) [165], while nitration of 241...
with nitric acid in an acetic acid solution afforded 2,4-dinitro-1-naphthol (297) [175] (Scheme 49). Yoshioka’s group studied the photochemical behavior of benzotropolone 241 (Scheme 49) [176]. Irradiation of a dilute solution of 241A in methanol with Pyrex-filtered light led to the formation of l-hydroxy-6,7-benzo-bicyclo[3.2.0]hepta-3,6-dien-2-one (299) in good yield as a major product. The formation of this product has been described either by the initial formation of 298 followed by rearrangement or by a mechanism with 241B as an intermediate. Also, Aihara’s group reported excited-state intramolecular proton transfer (ESIPT) and aromaticity studies for 241A and 241B [177].

5.4. 4-Hydroxy-2,3-benzotropone (174)

5.4.1. Synthesis of 4-hydroxy-2,3-benzotropone (174):

Benzotropolone 174 was prepared through intermediate bis-enol acetate obtained from reaction between benzo[7]annulene-3,7-dione (300) and isopropenyl acetate followed by dehydrogenation using N-bromosuccinimide, and its properties were compared with those of benzotropolone 241A (Scheme 50) [178]. The benzotropolone 174 could also be prepared from diester 301 in a similar way (Scheme 50) [179]. The simultaneous hydrolysis and decarboxylation of benzotropolone-diester 304 to 174 were catalyzed by NaOH.
5.4.2. Reaction of 4-hydroxy-2,3-benzotropon (174): The structure of 174 was confirmed by the reduction of both benzotropolone 174 and diketone 300 into the diol 305 with catalytic hydrogenation (Scheme 51) [178].

![Scheme 51: Catalytic hydrogenation of diketones 300 and 174.](image)

6. Halobenzotropones
6.1. Monohalobenzotropones
6.1.1. One-step synthesis via dihalocarbene addition: Probably one of the most useful methods for the synthesis of halo-benzotropones is the formation of a three-membered intermediate by addition of halocarbenes to alkoxynaphthalenes. The carbene addition step is then a simultaneous ring-opening step to give the corresponding halobenzotropon (Scheme 52). In 1969, two research groups independently reported the preparation of 2-bromo-4,5-benzotropon via adduct 308 starting from 2-methoxynaphthalene (306) using different dibromocarbene reagents (Scheme 52) [180,181]. The results for the synthesis of halo-benzotropones via carbene addition are shown in Table 2.

As shown in Table 2, the reported yields were extremely low. To further improve the yields of the products, different carbene sources and reaction conditions were tested. Parham’s group reported treatment of 2-methoxynaphthalene (306) with 0.75 equivalents of the carbene source (ethyl trichloroacetate) and sodium methoxide to give the chlorobenzotropon 309 in 13% yield [184]. Uyehara’s group also performed the same reaction by changing the ratios of the carbene sources and the

![Scheme 52: Synthesis of halo-benzotropones from alkoxynaphthalenes 306, 307 and 310.](image)

| entry | alkoxy-naphthalene | carbene source | product | yield (%) | reference(s) |
|-------|--------------------|----------------|--------|----------|--------------|
| 1     | 306                | CHBr₃, t-BuOK  | 26     | 11       | [181]        |
| 2     | 306                | PhHgCBr₃       |        | 20       | [182]        |
| 3     | 306                | PhHgCCl₃       | 37     |          | [180]        |
| 4     | 306                | CHCl₃, t-BuOK  | 37     |          | [183]        |
| 5     | 306                | CHCl₃, t-BuOK  | 18     |          | [181]        |
| 6     | 306                | Cl₂CCO₂Et, NaOMe | 13–33 |          | [184,185]    |
| 7     | 307                | Cl₂CCO₂Et, NaOMe | 66     |          | [185]        |
| 8     | 307                | CHBr₃, t-BuOK  | 15–25  |          | [180,181]    |
| 9     | 310                | PhHgCBr₃       | 33     |          | [181]        |
| 10    | 310                | PhHgCCl₃       | 17     |          | [183]        |
| 11    | 310                | Cl₂CCO₂Et, NaOMe | 11     |          | [184]        |

Table 2: Synthesis of some mono-halobenzotropones via carbene addition.
base to the substrate [185]. When 7 equivalents of the carbene source and sodium methoxide were used, however, 309 was obtained in lower yield (33%) and unexpected byproducts 313–315 were isolated in 6%, 23%, and 0.2% yields, respectively (Figure 13).

Several methods for the synthesis of 7-bromo-2,3-benzotropon (316) via dibromocarbene addition to 1-methoxynaphthalene (310) were reported (Figure 14) [180,181]. However, Moncur and Grutzner repeated the reaction as described and their studies led to the structural revision of the previously published structure of 7-bromo-2,3-benzotropon (311) to that of 5-bromo-2,3-benzotropon (311, Scheme 52, Figure 14) [186]. The structure of 311 has also been confirmed by independent extensive experiments and NMR data [182,187]. The chloro-derivative 312 was synthesized from the addition of dichlorocarbene to 310 in the same manner [187]. The results indicated that the dihalocarbenes prefer the addition of the 3,4-double bond rather than the 1,2-double bond to 1-methoxynaphthalene (310). The position of the halogen substituent in 311 and 312 was also determined by the cycloadducts 320 and 321 between 5-halo-2,3-benzotropes and maleic anhydride (Figure 14) [185,187].

6.1.2. Multistep synthesis via dihalocarbene addition: As shown in Scheme 6, the synthesis of the bicyclic ring 33 from the dichlorocarbene adduct of oxobenzonorbormadiene 31 has also been reported by Ranken’s group in two steps [53]. Hydrolysis of 33 in water under acidic conditions led to 2-chlorobenzotropon 309 in 20% yield (Scheme 53) [53].

A multistep method for the synthesis of 2-bromobenzotropon 26 starting from dihydrobenxalene (322) was also realized by Balci’s group (Scheme 54) [188]. After addition of dibromocarbene to 322, the obtained dibromocyclopropane 323 was submitted to silver ion-catalyzed ring expansion/hydrolysis in aqueous acetone (autoclave, 7.5–8.5 atm, 120–124 °C) to yield a mixture of products, 324, 325, and 326 in 53%, 3%, and 8% yields, respectively. Bromo-alcohol 325 can be converted readily to unsaturated ketone 324 by MnO₂ oxidation. Finally, the NBS-mediated bromination of 324 followed by dehydrobromination on silica gel led to the corresponding bromobenzotropon 26 in 80% yield.

6.1.3. Synthesis using benzosuberone: Jones’ groups reported two synthetic ways for obtaining 7-bromo-2,3-benzotropon (316) starting from benzosuberone (162) (Scheme 55) [135,136]. As shown in Scheme 30, brominations of 162 were investigated using both molecular bromine and NBS conditions. On the other hand, excess bromination of benzosuberone 162 with NBS resulted in the formation of tribromide 328. Treatment of tribromide 328 with LiCl in DMF yielded 7-bromo-2,3-benzotropon (316) in high yield. The results have shown that lithium chloride can be used as a mild dehydrobromination base to obtain the corresponding tropones from the multihalo-benzosuberones. Alternatively, 7-bromo-2,3-benzotropon (316) was
prepared in situ from benzotropone 12 and bromine in DMF followed by dehydrobromination (Scheme 55). The synthesis of benzotropone 12 from benzosuberone (162) is shown in Scheme 30. Benzosuberone (162) was also used as starting material for the synthesis of 5-bromo-2,3-benzotropone (311) (Scheme 55) [187,189].

6.1.4. Synthesis via oxidation: As shown in Scheme 4, bromobenzotropones 23 and 26 were obtained and characterized during the oxidation of both benzylic and allylic positions in 7-bromo-5H-benzo[7]annulene (22) [52]. To the best of those authors’ knowledge, this is the first synthesis of 23. With the reaction conditions established, Balci’s group next turned their attention to evaluating the scope and limitations of the oxidation reaction with different types of benzo[7]annulene (Scheme 56) [190]. Thus 8-bromo-5H-benzo[7]annulene (329) was oxidized with different oxidants to give a mixture of bromobenzotropones such as 23, 316, and 26. Formation of naphthaldehyde derivative 330 was also reported by SeO2-oxidation reaction (Scheme 56).

6.1.5. Synthesis via benzotropone precursors: Suzuki reported the formation and reactions of 2-carboxylic acid and 2,7-dicarboxylic acid derivatives 331 and 332 of 4,5-benzotropone (Scheme 57) [191]. 2-Carboxylic acid-substituted 4,5-benzotropone 331 was converted to 2-bromo-4,5-benzotropone (26) via bromination in acetic acid followed by decarboxylation at 240 °C.

The first synthetic methods for 6-chloro-2,3-benzotropone (335) were presented by Balci’s group (Scheme 58) [52]. When dibromide 334 was dehydrobrominated by lithium chloride in N,N-dimethylformamide, the chloro derivative 335 was formed as a sole product without any other halo derivatives. Independently, the reaction of 6-bromo-2,3-benzotropone (23) with lithium chloride under the same reaction conditions gave 6-chloro-2,3-benzotropone (335) in 96% yield. The proposed mechanism involves the intermediate 336 formed by Michael addition of a chloride ion to the β-position of the carbonyl group followed by the elimination of a bromide ion as a better leaving group.

6.2. Reactions of monohalo-benzotropones

6.2.1. Reactions with nucleophiles: Crabbé’s group reported the reactions of 7-bromo-2,3-benzotropone (316) with several primary and secondary amines (Scheme 59) [192]. Amines such as ammonia, dimethylamine, and morpholine analogous amines afforded the corresponding cine-substitution products such as 337, whereas the reactions of compound 316 with various amines such as methylamine, ethylamine isopropylamine, and ethanolamine gave aromatic lactams such as 338 and tricyclic amino derivatives as 339, in addition to the desired cine-substitution products, under similar reaction conditions. It was proposed that the aromatic lactam was formed via cleavage of the
**Scheme 56:** Oxidation reactions of 8-bromo-5H-benzo[7]annulene (329) with some oxidants.

**Scheme 57:** Synthesis of 2-bromo-4,5-benzotropone (26).

**Scheme 58:** Synthesis of 6-chloro-2,3-benzotropone (335) using LiCl and proposed intermediate 336.

**Scheme 59:** Reaction of 7-bromo-2,3-benzotropone (316) with methylamine.
troponoid ring. The tricyclic ring was derived by a sequence of 1,6-addition reaction of the amine to the tropone and intramolecular displacement of the bromine by an attack from the nitrogen.

Namboothiri and Balasubrahmanyam showed that the ipso/cine regioselectivity in the amination of some bromobenzotropones 26 and 311 was dependent upon the temperature at which the reaction was conducted (Scheme 60) [182]. The reactions of 2-bromo-4,5-benzotropone (26) and 5-bromo-2,3-benzotropone (311) with dimethylamine were carried out at a high temperature and ipso-products (340 and 342) were more favorable than cine-products (341 and 343).

Namboothiri and Balasubrahmanyam also investigated transformations in bromo- and alkoxybenzotropones (Scheme 61) [182]. The treatment of bromobenzotropones 26 and 311 with sodium methoxide in methanol under reflux led to a mixture of ipso and cine products. While the ipso product 344 in the case of 311 is dramatically favored over the cine product 345 (96:4), the ipso/cine ratio 346/347 in the case of 26 is 22:76. However, a small (2%) amount of 4,5-benzotropone (11) was formed under these conditions via presumably reductive removal of the bromine. In addition, a trapping experiment with 1,3-diphenylisobenzofuran (DPIBF) furnished evidence for the formation of benzodehydrotropones 348 and 350, generated by the reaction of 26 and 311 with t-BuOK (Scheme 62).

6.2.2. Miscellaneous reactions: The direct functionalization of important motifs such as benzotropones, cycloheptenones, azepanes, and piperidines is of ubiquitous importance. In 2015, Beng’s group focused on the cobalt-catalyzed reductive cross-coupling of versatile α-bromo enones with cyclic α-bromo enamides under mild conditions (Scheme 63) [193]. The coupling of bromo enecarbamate 352 and 7-bromo-2,3-benzotropone (316) was efficiently accomplished at room temperature.

**Scheme 60:** Reactions of bromo-2,3-benzotropones 26 and 311 with dimethylamine.

**Scheme 61:** Reactions of bromobenzotropones 311 and 26 with NaOMe.
using the conditions described in Scheme 61. The coupling product 354 was also prepared by this method. Treatment of imino diene 355 with the corresponding ester-quinone as an activated dienophile resulted in the formation of the highly functionalized pentacyclic 356 (Scheme 63). As illustrated in Scheme 35 and Figure 14, benzotropones can be used to afford cycloadducts and their photochemical products. In this context, the cycloaddition of 7-bromo-2,3-benzotropone (316) to maleic anhydride was reported by Hassner’s group (Figure 15) [148]. The direct and sensitized photolysis of the cycloadduct 357 afforded di-π-methane rearrangement product 358, which was confirmed by X-ray diffraction.

Simple and practical routes to 5,6,8,9-tetrahydro-7H-benzo[7]annulen-7-one (40) were reported by Uyehara’s group [184]. Catalytic hydrogenation of 2-chloro-4,5-benzotropone...
with 5% palladium on activated charcoal in methanol gave the ketone 40 in 97% yield (Scheme 64).

Scheme 64: Catalytic hydrogenation of 2-chloro-4,5-benzotropane (311).

6.3. Dibromobenzotropones

6.3.1. Synthesis from benzotropones: Decarboxylation of both diacid-332 and monoacid-benzotropane 333 by Hunsdiecker–Simonini reaction gave 2,7-dibromo-4,5-benzotropane (359) in 31% and 12% yield, respectively (Scheme 65) [191]. Bromination of 2,3-benzotropane (12) afforded tetrabromide 260 only, which underwent dehydrobromination to yield 5,7-dibromo-2,3-benzotropane (261A, Scheme 65) [134].

6.3.2. Synthesis from benzosuberone: An alternative protocol for the preparation of the dibromobenzotropones 261A and 261B was bromination/dehydrobromination starting from benzosuberone (162) (Scheme 66) [134,163,189].

6.3.3. Reactions of dibromobenzotropones: The transformations of isomeric dibromo-benzotropones 261A and 261B are summarized in Scheme 67 [163,189]. Dibromo-benzotropane 261A was treated with KOH in methanol at room temperature for 24 h followed by acidification using HCl to yield 6-methoxy- and 6-hydroxybromobenzotropones 360 and 361 and an uncharacterized product. Tribromide 362 was prepared by treating 162 with refluxing bromine. Treatment of dibromobenzotropones with hydroxylamine caused a cine-reaction to give oximes 363 and 364. The Diels–Alder adducts 365 and 366 of 261A and 261B with maleic anhydride were used to elucidate the position of the bromo substituents. The reduction of 261B in acetic acid with 4 mol equivalent of hydrogen in the presence of 5% palladium-on-charcoal and anhydrous sodium acetate, and by subsequent treatment with 2,4-dinitrophenylhydrazine, resulted in the formation of hydrazone 367. Moreover, the hydrazone 368 was prepared in an analogous manner using 2 equivalents of hydrogen.

6.4. Halobenzotropolones

6.4.1. Synthesis of halogenated benzotropolones: The benzotropolones undergo electrophilic substitution in the form of halogenation and their reactions towards halogens are similar. Hoshino and Ebine reported the formation and reaction of bromo derivatives 369 and 370 of benzotropolone 239B with
bromine in acetic acid under various conditions (Scheme 68) [194]. Bromobenzotropolones 372–376 and 290 were also synthesized by bromination/dehydrobromination of the corresponding benzotropolones (Figure 16) [165,179,194-197].

A short communication describing how 3,4-benzotropolone (241A) can be chlorinated to yield monochloro-3,4-benzotropolone was presented by Nozoe’s group [174]. Ebine studied in more detail the chlorination and iodination of 241A (Scheme 69, Scheme 70 and Figure 17) [194,198]. Treatment of the benzotropolone 241A with one or two equivalents of chlorine in acetic acid afforded 5,7-dichloro-3,4-benzotropolone (378) in low to fair yield. When reacted with a concentrated hydrochloric acid, both 290 and 375 underwent halogen exchange to give 289 and 378, respectively. A similar substitution was also observed when 375 was reacted with thionyl chloride. Bromo-chloro-3,4-benzotropolones 379–381 were prepared using similar procedures (Figure 17). 7-Iodo-3,4-benzotropolone 290 was also synthesized by bromination/dehydrobromination of the corresponding benzotropolones (Figure 16) [165,179,194-197].

Scheme 67: Some transformations of isomeric dibromo-benzotropones 261A/B.

Scheme 68: Transformations of benzotropolone 239B to halobenzotropolones 369–371.
tropolone (382) was also obtained in 40% yield by the reaction between benzotropolone 241A and sodium iodide/sodium iodate in acetic acid (Scheme 70) [195].

6.4.2. Reaction of halobenzotropolones: Dehalogenation of halobenzotropolones: Hoshino and Ebine reported that palladium-catalyzed hydrogenation of bromobenzotropolones 369 and 370 resulted in debromination of halogen atoms to give 239B as depicted in Scheme 71 [194]. However, hydrogenation of 375 gave 241A in low yield (Scheme 72) [195]. Debromination of monobromide 290 with hydrobromic acid in acetic acid afforded 241A in 73% yield, whereas the reaction of dibromide 375 under the same conditions provided monobromide 383 in 85% yield as the debromination product (Scheme 72) [198].

Oxidation of halobenzotropolones: Oxidation reactions of halo-benzotropolones were often used to determine the structures of benzotropolones [194,198,199]. For clarification of the positions of substituents in the final compounds, Ebine reported that oxidation of dihalo-benzotropolones 370 and 381 with alkaline hydrogen peroxide gave phthalic acid (385) in 40% and 35% yields, respectively, while that of monohalo-benzotropolones 369, 384, and 290 afforded o-carboxycinnamic acid (273) in 47%, 33%, and 33% yields, respectively (Figure 18) [194]. Bromobenzotropolones 290 and 375 were nitrated in acetic acid to yield the same nitration product 386 in 29% and
16% yields (Figure 18) [199]. 5-Nitro-7-bromo-3,4-benzotropolone (386) rearranged to 2-bromo-4-nitro-1-naphthoic acid (387) in 80% yield with alkali (Figure 18). When reacted with exhaustive bromination (or chlorination) in acetic acid, dibromobenzotropolone 375 gave 2,3-dibromo-1,4-naphthoquinones (388) in 81% yield (or 389 in 35% yield) as an unexpected product (Figure 18). The nitration of 375 in concentrated sulfuric acid also produced the corresponding 388 in 29% yield (Figure 18). A reaction of 5,7-dichloro-3,4-benzotropolone (378) under the same conditions gave dichloronaphthoquinone 389 in 16% yield (Figure 18). The author proposed possible tentative mechanisms for the formation of naphthoquinones.

Azo-coupling reaction of halo-benzotropolones: The azo-coupling reaction of 7-bromobenzotropolones 294 with diazonium cations, which are generated by treatment of aromatic amines with nitrous acid and a stronger mineral acid in acetic acid, resulted in 5-phenylazo-7-bromo-3,4-benzotropolone (390) in 28% yield (Scheme 73) [175]. However, when the same reaction was carried out in a pyridine solution, the formation of rearrangement products 391 and 392 in 29% and 9% yields was reported (Scheme 73). Azo-coupling reactions of 5,7-dihalo-3,4-benzotropolones 375 and 378 under similar conditions provided the corresponding naphthols 393–395 in
low yields (Scheme 73). The possible courses for the formation of coupling products were discussed [175].

7. Dibenzotropones

There are four possible dibenzotropane isomers: 2,3;4,5-dibenzotropane (396), 3,4;5,6-dibenzotropane (397), 2,3;5,6-dibenzotropane (398), and 2,3;6,7-dibenzotropane (399, Figure 19). We reported comprehensive syntheses and applications of dibenzosuberones [45]. Thus, this section does not cover the chemistry of dibenzotropones.

8. Tribenzotropane (400)

Tribenzotropane, or 9H-tribenzo[a,c,e][7]annulen-9-one (400A), has a tetracyclic structure, consisting of a seven-membered ring fused to benzene rings (Figure 20). Based on experimental observations, it is suggested that tribenzotropane (400) shows structural resistance against planarity arising from an angular strain of a planar 7-membered ring as well as the unfavorable steric interactions between the ortho-hydrogen atoms (Figure 20) [200]. As a measure of the characteristics of tropone, the calculated circuit resonance energies show that tribenzotropane (400) among the other benzotropones has a small circuit resonance energy associated with the number of benzene rings [155]. The charge density for the corresponding uniform reference frame of 400 shows that the oxygen atom occupies the site of the largest charge density.

Figure 19: Four possible isomers of dibenzotropones 396–399.

Figure 20: Resonance structures of tribenzotropane (400).

8.1. Synthesis of tribenzotropane

The first synthesis of tribenzotropane (400) was simultaneously reported by two groups in 1957. Stiles’ group reported the synthesis of 400 in 24% yield via the rearrangement of the diazonium salt of 9-(2-aminophenyl)-9H-fluoren-9-ol (402) in two steps (Scheme 74) [200]. A multistep preparation with difficulties or poor yields of 400 was reported by Bergmann’s group starting from cycloaddition of butadiene and cinnamaldehyde (403) in 12 steps (Scheme 74) [201]. Moreover, Diels–Alder trapping with furan of an alkyne derivative from benzotropane 399 followed by catalytic hydrogenation and polyphosphoric acid (PPA)-assisted dehydration steps provided an excellent approach to the synthesis of tribenzotropane (400) in a 31% overall yield over five steps (Scheme 75) [202]. Wan’s group also reported the deoxygenation with Fe$_2$(CO)$_9$ of the cycloadduct 404 to 400 [203].

Koo’s group reported a challenging method for the synthesis of 400 in 38% overall yield by ring-expansion method as a key step starting from readily available 9,10-phenanthraquinone (406, Scheme 76) [204]. A mild and selective indium-mediated nucleophilic addition of allyl bromide followed by the addition...
of vinylmagnesium bromide led to the formation of diol 407 with allyl and vinyl substituents, which underwent an oxidative ring-opening reaction to form diketone 408. Then the reaction of 408 with triisopropyl triflate (TIPSOTf) in the presence of triethylamine afforded the desired silyl enol ether 409, which contains the required electron-rich diene and electron-deficient dienophile units for intramolecular cycloaddition. Unexpectedly, the intramolecular Diels–Alder reaction of 409 at room temperature followed by filtration from silica gel gave an inseparable mixture of tribenzotropone (400) and dihydro analogue of 400. The crude mixture was reacted with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in order to complete the oxidation (DDQ).

Papaianina and Amsharaov demonstrated that thermally activated γ-aluminum oxide can be very effective for C–F bond activation in trifluoromethyl-substituted arenes to yield either cyclic ketones or the respective carboxylic acids in good to excellent yields (Scheme 77) [205]. The condensation of trifluoromethyl-substituted arene 411 on activated alumina at 150 °C resulted in the formation of the intramolecular Friedel–Crafts products 400 (52% yield) and 412 (8% yield),
whereas formation of the possible acid 413 was not observed. The prevention of side reactions and the regiochemistry of the process were attributed to the confined space of alumina pores. Furthermore, the non-activated alumina-mediated hydrolysis of 412 at 200 °C afforded o-terphenyl-1,2-carboxylic acid (413) in close to quantitative yield. A presumable mechanism was also proposed for the formation of acylation and hydrolysis products with C–F activation in trifluoromethylated arenes in alumina nanopores.

8.2. Reactions of tribenzotropone (400)

Herold’s group reported ESR and ENDOR/TRIPLE resonance studies of ion pairs derived from the reduction of tribenzotropone (400), dibenzotropone 399, and dibenzosuberone 414 (Figure 21) with different alkali metals, which may be evidence of the existence of three different stereoisomers [206]. The INDO calculations of the spin densities at the lithium cation also supported the geometries proposed for the three stereoisomers.

An experimental study on the excited-state carbon acidity of several dibenzosuberene derivates was reported by Wan’s group (Figure 22) [203]. To this end, tribenzotropone (400) from the selected substrate was reduced with both LiAlH₄ (with AlCl₃) and LiAlD₄ (with AlCl₃) to give 415 and 415-d₂, respectively. The detectable deuteration (proton) incorporation for photolysis of 415 in D₂O–MeCN (1:1) (or 415-d₂ in H₂O–MeCN (1:1)) was not observed. Photolysis of 416 under similar conditions resulted in mono- (21%) and dideuterium (3%) incorporation at the methylenic position. These results were explained by the fact that benzannelation of the vinyl moiety affects the excited-state carbon acidity for 415 (or 415-d₂). Subsequent photolysis of 415 using 1 M NaOD/EtOD gave mono- and dideuterium exchange products 415-d (15%) and 415-d₂ (3%). 9H-Tribenzo[a,c,e][7]annulene (415) as one of the model compounds for conformational studies with dynamic NMR was prepared from tribenzotropone (400) via Wolff–Kishner reduction (Figure 22) [207]. Tochtermann’s group prepared tribenzotropone dimethyl ketal 417 from 400 and studied the conversion of the boat form of the 7-membered ring by means of the NMR spectra (Figure 22) [208]. The free activation enthalpy for 417 was 23 kcal/mol. The treatment of 400 with polyphosphoric acid (PPA) at 200 °C yielded 4-phenylfluorenone (412) in 60% yield via a proposed intermediate, 418 (Figure 23) [202].

Bergmann and Klein reported the synthesis of the condensation product 419a by the reaction of 400 with benzylmagnesium chloride (Figure 24) [201]. The UV absorption spectrum for 419a was measured and it was evaluated that 419a has no fulvenic properties. Later, Tochtermann’s group reported the synthesis of the racemic 9-methylene-9H-tribenzo[a,c,e][7]annulenes such as 420 via Wittig reaction followed by carboxylation of vinylic bromide using lithium/carbon dioxide (Figure 24) [209]. The classical resolution of the vinyl carboxylic acids as its brucine salt was also studied and the thermal racemization barrier was 31 kcal/mol at 139 °C. Udayakumar and Schuster were the first to show the direct asymmetric synthesis of a series of 9-benzylidene-9H-tribenzo[a,c,e][7]annulenes 419a–e and they examined the photochemistry of optically active potential triggers for physical amplification of a photoresponse in liquid crystalline media (Figure 24) [210]. The optically active compounds were prepared from the reaction of 400 with chiral phosphonamides 421a–d as an application of the Hanessian chiral olefination reaction. The acetyl derivative 419e was prepared by reaction of 419c with methyl lithium. The optical purities of the compounds were determined to be 92% and 5% by NMR spectroscopy in the presence of chiral shift reagents. While UV irradiation of the benzylidene-9H-tribenzo[a,c,e][7]annulenes resulted in the formation of the possible acid 413, the prevention of side reactions and the regiochemistry of the process were attributed to the confined space of alumina pores. Furthermore, the non-activated alumina-mediated hydrolysis of 412 at 200 °C afforded o-terphenyl-1,2-carboxylic acid (413) in close to quantitative yield. A presumable mechanism was also proposed for the formation of acylation and hydrolysis products with C–F activation in trifluoromethylated arenes in alumina nanopores.
in high-efficiency photoracemization, thermal racemization was not observed at temperatures below 100 °C.

Figure 24: Structures of benzylidene- and methylene-9H-tribenzo[a,e,j][7]annulenes 419 and 420 and chiral phosphonamides 421.

Although the Grignard reaction between tribenzotropane (400) and 4-methoxyphenylmagnesium bromide provided the alcohol 422 in good yield (72%), O-dealkylation of the tetracyclic alcohol 422 gave the corresponding \( \text{p}-\text{quinone methide} 423 \) in low yield (23%, Figure 25) [211]. This result was attributed to the relatively low stability of the formed cation 424 due to the aromatic system twisted out of plane. Tribenzotropane (400) was also used as starting material for host molecules 425–427 (Figure 26) [212,213].

As outlined in Scheme 78 with regard to the synthesis of a series of non-helical overcrowded derivatives, syn-431 was also prepared using 400 in four steps, which covered pinacol coupling and then pinacol rearrangement, carbonyl reduction, and Wagner–Meerwein rearrangement occurred [214]. Isomers syn-431 and anti-431 were converted as quantitative to each other at thermal and photochemical conditions as shown in Scheme 78. At the same time, the unambiguous characterization of syn-431 and anti-431 revealed that the previously claimed synthesis of hexabenzooctalene 432 by Tochtermann [215] was incorrect (Figure 27).

9. Naphthotropones

Although eight isomers 433–440 for naphthotropane, which possess an \( \text{XH-cyclohepta[\text{y}]naphthalen-Z-one} (\text{X} = \text{Y} = 7, 8, 9 \text{ or } 10; \text{y} = \text{a}, \text{b}) \) skeleton system, are possible, only five isomers 433–437 were found experimentally (Figure 28). Sudoh’s group reported the annulation effects of benzene rings to tropone (1) on the ground-state dipole moment, which can be useful for the study of molecular interactions in solution and excited states, as both the experimental and computational for the first time [216]. The ground-state dipole moments of a series of annulated tropones were computationally calculated using the Hartree–Fock (HF), density functional theory (DFT), and Möller–Plesset second-order perturbation (MP2) methods. While the ground-state dipole moment for 4,5-naphthotropane (433) was experimentally determined as 5.19 D, the MP2 method gave the result corresponding best to the experimental one for 433 among the three methods. The electronic transitions observed in tropone and tropolone derivatives condensed with benzene and naphthalene were studied experimentally and

Figure 25: Structures of tetracyclic alcohol 422, \( \text{p}-\text{quinone methide} 423 \) and cation 424.

Figure 26: Structures of host molecules 425–427.
Scheme 78: Synthesis of non-helical overcrowded derivatives syn/anti-431.

Figure 27: Hexabenzooctalene 432.

theoretically [217-219]. Ohkita’s group characterized the aromaticity of \( \pi \)-extended \( \sigma \)-quinoidal tropone derivatives 433–435 along with five other tropone derivatives via the nucleus-independent chemical shifts (NICS), which is a computational method proven to be the most reliable probe of aromaticity due to its simplicity and efficiency [220,221]. Interestingly, the NICS(1) value calculated for the tropone ring in 433 is negative (−7.4), and indicates significantly increased aromatic character relative to the parent system. Moreover, NICS calculations demonstrated that the annulation of a benzene or naphthalene ring to the 2,3- or 4,5-position of tropone resulted in diminution of aromaticity. Furthermore, the elongations of the calculated C=O bond in the studied molecules as 433 were attributed to substantial contributions of polar resonance structures to these molecules.

9.1. Synthesis and characterization studies of naphthotropones

Elad and Ginsburg reported the synthesis of a naphthotropone isomer for the first time (Scheme 79) [222]. Catalytic reduction of the key diketone 442, which was prepared by multi-stage
Synthesis of 1-phenylcycloheptene (441), removed the carbonyl group conjugated to the benzene ring and stepwise bromination and dehydrobromination of ketone 443 afforded the desired 11H-cyclohepta[a]naphthalen-11-one (437) [222,223]. Treibs and Herdman [224] reported the synthesis of 10-hydroxy-11H-cyclohepta[a]naphthalen-11-one (448) in very low yield starting from 2-naphthaldehyde and diethyl 2-ethylidenemalonate as outlined in Scheme 80 [224]. The condensation product 445 was converted to the ketone 444 in four steps: hydrolysis, catalytic hydrogenation, decarboxylation, and Friedel–Crafts acylation. After hydrolysis of oxime 446 derived from ketone 444, diketone 447 was subjected to an oxidation reaction with elemental sulfur, Pd/C, or SeO₂ to give naphthotropolene 448 in very low yield.

Naville’s group completed the series of benzologue tropylium cations up to C15 by preparing some tropylium cations [225]. This context with synthesis of 8H-cyclohepta[b]naphthalen-8-one (433) was reported featuring condensation of 2,3-naphthalenedicarboxaldehyde (449) with diethyl 1,3-acetonedicarboxylate (28) followed by decarboxylative hydrolysis of diester 450 (Scheme 81). Ito’s group reported the simple synthesis of two naphthotropono isomers utilizing the cycloaddition of tropone (1) (Scheme 82) [226]. Cycloaddition of exocyclic diene 451a, obtained from o-xylene 154 with excess 1 in DMF resulted in the formation of the [6 + 4] adduct 452 and [4 + 2] adduct 453. After separation by silica gel chromatography, both of the cycloadducts were independently subjected to dehydrogenation with triphenylcarbinol in trifluoroacetic acid under reflux to yield naphthotropones 433 and 434 as the sole product in each respective reaction. Multistep synthesis of these naphthotropones was also performed through the reaction of dibromo-o-xylene 451b generated in situ from 1,2-bis(dibromomethyl)benzene at 80 °C with 1 (Scheme 82). The proposed mechanism for the transformation of 452 to 434 includes dehydrogenation, disrotatory electrocyclic ring-closing, thermal [1,5]-sigmatropic rearrangement, and again dehydrogenation steps as depicted in Scheme 83. Kanematsu’s
group reported a selective reaction at the 2,3-position of tricarbonyl(tropone)iron 458a with \( o \)-quinodimethane 451a using the masking effect of tricarbonyliron complex to yield exclusively [4 + 2] adduct 459a with no formation of other cycloadducts (Figure 29) [227]. The reaction of 459a with \( o \)-chloranil in refluxing methylene chloride to remove the tricarbonyliron moiety afforded the previously unobtainable product 460a, whereas treatment of 459b with trimethylamine oxide provided naphthotropone 434 in 15% yield along with 460a and its isomers. While a similar reaction of tricarbonyl(2-chlorotropone)iron 458b and 451a yielded the sole product 459b (55%), 2-chlorotropone reacted poorly with 451a to afford naphthotropones 433 (13%) as the only isolable product via [4 + 2] cycloaddition reaction followed probably by dehydrobromination and aromatization.

Jones’ group prepared naphthotropone 436 using published procedures and known intermediates (Scheme 84) [228-231]. The ketone 461 prepared in 11 steps starting from naphthalene (17) was converted to 462 through ring-opening of cyclopropane with a base followed by oxidation. After previous successful generation of 13 from the corresponding benzocyclobutene 230, Ohkita’s group also reported the synthesis of 465 as a precursor for naphthotropone 435 (Scheme 85) [220,221]. Photopromoted [2 + 2] cycloaddition of 2-cyclopentenone with (\( E \))-1,4-dichloro-2-butene followed by protection of the carbonyl group and subsequent dehydrohalogenation afforded diene 463, which was converted to 465 after a series of reactions including the Diels–Alder reaction with benzyne, dehydrogenation with DDQ, bromination, dehydrobromination, and acid-catalyzed hydrolysis of the ketal group. Irradiation of 465 in a rigid class at \(-196^\circ C\) resulted in the formation of the hitherto unknown...
7H-cyclohepta[b]naphthalen-7-one (435), which displayed characteristic UV–vis absorption extending to 700 nm and underwent rapid dimerization to give the dimers 467 and 468 (Scheme 86). However, Okhita’s group applied this strategy to generate the corresponding anthracene-tropon from 466 under the same reaction conditions (Scheme 85). However, anthrocyclobutene derivative 466 failed to result in ring-opening for the expected tropone and the starting material 466 was recovered quantitatively. The products were unambiguously characterized as syn-[π12 + π14] dimers 467 and 468 by X-ray crystallography, and the preferential syn-dimerization was attributed to the extended secondary orbital interactions. Sato’s group also reported the IR spectra of 435 generated in nitrogen matrices at 13 K by monochromatic irradiation with a XeCl excimer laser to investigate medium effects on the molecular structures of tropones [156].

9.2. Applications of naphthotropones

In connection with the completion of the benzologue tropylium series, Naville’s group also prepared the tropylium cations 469 and 470 from the corresponding naphthotropones 433 and 436 and described the absorption spectra and the relative acidities of all cations (Figure 30) [225]. After hydride reduction of tropones, the alcohols in sulfuric acid provided the corresponding cations.
Due to encouraging initial results obtained regarding the synthesis, properties, and reactivity of catacondensed aromatic π-systems as well as their photoinduced autorecycling oxidizing reactions toward some alcohol and amines [66-71], Nitta’s group focused on novel tropylium ions $471^+\text{BF}_4^-$, $472^+\text{BF}_4^-$, and $473^+\text{BF}_4^-$ containing heterocyclic moieties (Figure 31) [232]. The synthesis of $471^+\text{BF}_4^-$ was achieved by three-step reactions in modest yield (19%) starting from naphthotropone 433 while generation of $479^+\text{ClO}_4^-$ was not observed (Scheme 87). The naphthotropylium cation $479^+\text{ClO}_4^-$ was prepared in 64% yield by the reduction of 433 with NaBH₄ in EtOH in the presence of CeCl₃ followed by subsequent treatment of 474 with 60% aqueous HClO₄ in Ac₂O. The synthesis of $472^+\text{BF}_4^-$ and $473^+\text{BF}_4^-$ as a mixture was carried out in similar ways starting from benzotropone 11 and its separation was performed by fractional recrystallization from MeCN/EtOAc to give pure samples. While the compounds $471^+\text{BF}_4^-$, $472^+\text{BF}_4^-$, and $473^+\text{BF}_4^-$ were fully characterized on the basis of spectroscopic methods as well as elemental analysis and X-ray analysis, their chemical shifts provided quite noteworthy information for determining structural properties such as diatropicity and bond alternation. The carbocation stability is expressed in terms of its $pK_{R^+}$ value, which is the affinity of the carbocation toward hydroxide ions, and this value is the most common criterion for carbocation stability. Although the $pK_{R^+}$ values for cations $471^+$, $472^+$, and $473^+$ were determined spectrophotometrically as the values of ca. 0.5–9.0, the $pK_{R^+}$ value of naphthotropylium ion $479^+$ was clarified as much lower, at <0. Autorecycling oxidation properties of some amines as well as
the reduction potentials and the reactions with some nucleophiles of the compounds $471^+\text{BF}_4^-$, $472^+\text{BF}_4^-$, and $473^+\text{BF}_4^-$ were also reported. The oxidations of benzylamine, 1-phenylethylamine, hexylamine, and cyclohexylamine with $471^+\text{BF}_4^-$, $472^+\text{BF}_4^-$, and $473^+\text{BF}_4^-$ produced the corresponding imines under aerobic and photoirradiation conditions.

The napthotropones 433 and 436 were also used to prepare tosylhydrazones and their salts in the usual manner as precursors of the corresponding carbenes. Hackenberger and Dürr reported the generation and chemistry of naphtho[b]tropolylidene 483 (Scheme 88) [233,234]. Carbone 483 generated by flash solvolysis from the salt 480 in the gas-phase led to the formation of 1- and 2-methylanthracene (481 and 482) via carbene–carbene rearrangement to anthrylcarbene 486 to 487 as a decisive step (Scheme 88). In the condensed phase, while the trapping of the carbene 483 with olefins yielded cycloaddition products 488 and insertion products 489, the cycloadducts 490 through intermediate anthrylcarbene 486 also occurred as byproducts (Figure 32). However, if electron-deficient alkenes were used, the amount of cycloadduct 490 increased. The intermediate 485 was trapped by 2,3-dimethylbut-2-ene to afford 491 (Figure 32). The reactions and products described were attributed to an equilibrium mixture of singlet 483, triplet 483, and bicycle 485.

Jones’ group also reported the generation and properties of a naphtoannelated cycloheptatrienylidene-cycloheptatetraene intermediate from both the corresponding salt 492 derived from 436 or a mixture of bromocycloheptatrienes 499 and 500 (Scheme 89) [228]. While thermolysis of salt 492 in cyclohexane or benzene afforded only a mixture of napthoannelated heptafulvalenes 493 and 494, thermolysis in the presence of dimethyl fumarate 495 yielded the expected spirocyclopropane 496 along with trace amounts of the same two dimers. Thermolysis of 492 in the presence of diphenylisobenzofuran (DBI, 497) gave a new adduct, 498. Dehydrobromination of a mixture of bromocycloheptatrienes 499 and 500 with potassium tert-butoxide in the presence of 497 resulted in the formation of the rearranged adduct 498 along with carbenedimer products 493 and 494. Valance isomerization of carbene 501 to allene 502 plays a critical role in the proposed mechanism for the formation of the adduct 500, which was formed by Diels–Alder addition of 497 to the allene 502 followed by rearrangement as depicted in Scheme 90. Based on INDO calculations of a number of the carbenes and allenes, Jones’ group deduced that while the chemistry of cycloheptatrienyldiene and in some its aneled relatives are dominant in some cases by the allene form and in others by triplet carbene, the role of singlet carbene is uncertain.
Jang and Kelley studied the exited-state intramolecular proton transfer (ESIPT) and relaxation of 7-hydroxy-8H-cyclohepta[b]naphthalen-8-one (505) in room temperature solutions studied using static and time-resolved absorption as well as emission spectra for the equations indicated in Scheme 91 [235,236]. Dual fluorescence (normal and tautomer fluorescence) is observed in the protic solvent (ethanol), while only tautomer fluorescence is observed in the nonpolar solvent (cyclohexane). The dual green and red fluorescence arise from the intermolecular hydrogen-bonded normal molecules and the tautomer molecules with proton transfer in the excited state (ESIPT), respectively. The observed fluorescence lifetimes and quantum yields in ethanol and cyclohexane solutions could be attributed to competition between intersystem crossing and proton transfer in the first excited singlet state.

10. Miscellaneous benzotroponoids
10.1. Benzoditropones
Although benzoditropane has many isomeric possibilities, only two isomers 506 and 507 of the benzoditropane system have
been reported (Figure 33). The X-ray diffraction studies for benzo[1,2,4,5]di[7]annulene-3,9-dione (506e) as the main skeleton revealed a nearly planar geometry [237]. The intermolecular distances confirmed good agreement with normal van der Waals interactions, while the intramolecular distances led to a significant bond alternation within the seven-membered rings.

Aldol-type cyclizations provide an expedient access to the benzoditropones in a single step. Föhlisch and Widmann applied aldol-type cyclization for the synthesis of benzoditropones 506c–e (Scheme 92) [238]. In an analogous manner, Soyer and Kerfento, and subsequently Soyer, attempted Aldol-type condensations of benzene-1,2,4,5-tetracarbaldehyde with the corresponding acetone derivatives to give the benzoditropones derivatives 506a–k (Figure 33) [237-239]. An increasing bathochromic effect was observed for 506e (R1–R4 = H) < 506c (R1–R4 = CO2Et) < 506a (R1–R4 = Me) < 506b (R1–R4 = Ph).

Kato’s group reported the synthesis of benzoditropones 507 via cycloaddition between tropone (1) and 7,7-dibromo-3,4-dimethylenebicyclo[4.1.0]heptane (512, Scheme 93) [240]. To this end, diene 512 reacted with 1 to give a mixture (77% yield, syn/anti = 3.8:1) of [6 + 4] cycloadducts 513 in refluxing toluene, while the reaction proceeded with high regioselectivity (90% yield, syn/anti = 9:1) in benzene in a sealed tube at 100 °C. Epoxidation of 513 with m-chloroperbenzoic acid (mCPBA) afforded a mixture containing epoxide 514 as a major product. This epoxide was then converted to benzoditropones 507 after direct or indirect steps. Bromination of 515 with molecular bromine followed by dehydrobromination by heating at 100 °C in N,N-dimethylformamide (DMF) also provided an improved route to 507 (56% yield). Formation of 507 and 516 from 515 occurs by the three mechanisms depicted in Scheme 94. Firstly, the protonated 517 may undergo two different 1,2-cationic rearrangements via 518 and 519 intermediates to yield 516 and 507. Secondly, tropone-ketone 515 undergoes
Scheme 93: Synthetic approaches for dibenzotropone 507 via tropone (1).

A thermal [1,5]-sigmatropic shift followed by successive dehydrogenation to give benzoditropone 507. Lastly, initial dehydrogenation of 515 to bistropone 522 followed by 6π-electrocyclic ring-opening and a [1,5]-sigmatropic shift of the carbonyl carbon results in norcaradienone 524, which undergoes 6π-retrocyclization followed by oxidation to give 507.

Scheme 94: Formation mechanisms of benzoditropane 507 and 516 via 515.

Agranat and Avnir reported the synthesis of the benzoditropane systems 525 and 526, which may be considered double dibenzotropones (Scheme 95) [241]. Double Perkin condensation between pyromellitic dianhydride (527) and phenylacetic acid gave a mixture of the two isomeric lactones, 528 and 529, in the ratio of 5:3, which were separable by repeated fractional crystallization. The reduction of 528 and 529 with red phosphorus in boiling hydroiodic acid led to the formation of isophthalic acid derivatives (such as 530), which underwent intramolecular Friedel–Crafts acylation by polyphosphoric acid (PPA) to construct a seven-membered ring. The synthesis of benzoditropones 525 and 526 involved the dehydrogenation of the corresponding Friedel–Crafts products with N-bromosuccinimide (NBS) in the presence of benzoyl peroxide followed by treatment with trimethylamine.

10.2. Benzocyclobutatropones

Cyclobutadiene (532), the smallest annulene, is an unstable hydrocarbon with an extremely short lifetime in the free state and has attracted much attention from both experimental and theoretical viewpoints (Figure 34). Although 532 rapidly dimerizes via a Diels–Alder reaction, its dibenzo-derivative 533 (biphenylene) is thermally stable and shows many of the properties associated with aromatic compounds (Figure 33) [242-246]. Three possible isomeric benzocyclobutatropones, 534–536, which are analogues of biphenylene in which one benzenoid ring has been replaced by the tropone ring, are of significant interest due to the question of the extent of π-electron delocalization in the seven-membered ring (Figure 34). Benzo-
cyclobutatropones 535 and 534, which possess a formal benzo-
cyclobutadienoid double bond, are also of particular interest.

Wege’s group attempted to prepare the main analogues 534-536 of a benzocyclobutatropone system [247-249]. Allylic oxidation of diene 537 with chromium trioxide–pyridine complex in dichloromethane occurred to afford dienone 538 in 21% yield, which was exposed to DDQ in refluxing benzene to give 534 in low yield (9–10%) as a stable and crystalline solid at room temperature along with some of the starting material 537 (Scheme 96) [247,248]. Deuterated derivative 539 was prepared to confirm structural assignments. NMR results showed that the seven-membered ring of 534 has a more localized π-bond system than tropone itself [248]. The CrO₃-oxidation product 542 of the benzyne-cycloheptatriene adduct 540 was also converted to 534 after a sequence of NBS-bromination and dehydrobromination with DBU. However, the major oxidation product 542 did not react with DDQ in refluxing benzene.
All attempts to prepare the other benzocyclobutatropone, 545, have failed so far (Scheme 97). The potential precursor 543 of 545 was verified to be extremely acid-sensitive, and ketone 543 was rearranged to afford the bridged ketone 545 in high yield via cationic intermediates [247,248]. Another attempt then aimed to introduce a second double bond into the seven-membered ring of ketone 546, which reacted with N-bromosuccinimide followed by treatment with tetrabutylammonium bromide to yield fluoren-9-ol (547) as the only isolable product [248]. After unsuccessful attempts resulting from the propensity of reaction intermediates to undergo skeletal rearrangements, Wege’s group attempted the preparation of ketone 548, in which π-electrons binding to the iron carbonyl moiety as the driving force for isomerization should be suppressed [248]. However, attempts towards the preparation of the complex 548 were not successful.

To access the symmetrical tropone derivative 536, the cycloadduct 537 was again used as a starting material since this compound contains the necessary ring skeleton of 536 and possesses the diene function permitting the introduction of the essential carbonyl group (Scheme 98) [248,249]. Compound 537 was transformed to monobromo 549 in 8 steps, which reacted with trimethylamine in the presence of cyclopentadiene (202) in dichloromethane at 0 °C to give the trapping product 550 in 20% yield as [6 + 4] cycloadduct. This result was attributed to the formation of benzocyclobutatropone 536. The reaction performed without 202 gave no recognizable product.

Ebine’s group were the first to report the addition reaction between 1-methoxybiphenylene (551) and dichlorocarbene generated from chloroform to give chloro-benzocyclobutatropone 552 (1.7%) together with two fluorenones with chloro and methoxy substituents, similar products were obtained with dibromocarbene. The formation of these products was attributed to unequivocal chemical evidence for bond fixation of 1,2-dimethoxybiphenylene. Furthermore, cleavage of the ether functionality with boron tribromide in dichloromethane at −65 °C provided the first example of tropolone analogue 559a (93%) of biphenylene (Scheme 100). Electronic spectra and NMR coupling constants of the compound showed that 559a exists as only one tautomer due to instability of the antiaromatic cyclobutadiene structure in the central four-membered ring of 559b.

At the same time, Ebine’s group reported the reaction of biphenylene-2,3-quinone (560) with diazomethane in the presence of boron trifluoride etherate to give another tropolone analogue 561 and its boron difluoride chelate 562, which was hydrolyzed in acidic aqueous ethanol to 561 quantitatively (Scheme 101) [252,253]. On the other hand, some electrophilic reactions, including nitration, bromination, and azo coupling for 561 yielded only 7-substituted tropolones.

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Scheme 97: Synthesis attempts for benzocyclobutatropone 545.
10.3. Benzotropoquinones

Benzene annulations to o- and p-tropoquinone rings (563 and 564) have also attracted interest due to their unique quinone characteristics as in benzoquinone series of o- and p-tropoquinones (Figure 35). Both 566 and 567 of possible benzo analogues containing tropoquinone rings were synthesized, and their properties were described (Figure 34) [254,255]. Oxidation of hydroxybenzotropone 568 with DDQ in acetone at room temperature followed by addition of water provided 1,2,3-benzotropoquinone hydrate 569 in 85% yield, which was carefully sublimated to afford the desired 1,2,3-benzotropoquinone 566 in low yield (18%, Scheme 102) [254]. The synthesis of starting 568 was reported by Hartwig’s group [197]. Benzotropoquinone 566 is gradually decomposed in dry air and is highly hygroscopic, giving 569. 1,2,5-Benzotropoquinone 567 was prepared by starting from the Diels–Alder reaction between 1-acetoxy-1,3-butadiene (570) and p-tropoquinone (564) in a four-step synthesis (Scheme 103) [255]. The acetylation of cycloadduct 571 or 572 provided the diacetoxybenzotropone 573, which was converted to benzotropoquinone 567 after acid hydrolysis and oxidation steps.

Due to the highly hygroscopic nature of 566, chemical reactions of hydrated 569 were studied [254]. The reaction of 569 with o-phenylenediamine at room temperature afforded the quinoxaline derivative 575 (15%) along with
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Scheme 102: Synthesis of benzo[α]phenazine (13%, Figure 36). While the reaction between NaN₃ and 569 gave 576 through conjugate addition followed by dehydration (Figure 36), treatment of 569 with concentrated HCl at room temperature provided 568 in 80% yield. Furthermore, the corresponding diacetate 577 was obtained in 87% yield from the acetylation of 569 in the presence of H₂SO₄ (Figure 36). Acetylation of 569 with BF₃ catalyst resulted in the formation of 1,2-diacetoxy-naphthalene (25%) and 3,3’,4,4’-tetraacetoxy-1,1’-binaphthyl (15%) together with 577 (15%).

Although 1,2,5-benzotropoquinone 567 is highly sensitive to moisture, it is stable under anhydrous conditions in the dark and, its hygroscopic form returns to 567 when dried under a vacuum. While the reaction of tropoquinone 567 with o-phenylenediamine gives a quinoxaline derivative 578, the reduction of 567 to 579 was realized via catalytic hydrogenation with Pd/C (Scheme 104) [252]. A naphthaldehyde derivative 580 was derived from Thiele acetylation (Ac₂O, H₂SO₄, room temperature) of 567 in 11% yield. Treatment of tropoquinone 567 with hydrogen chloride in ethanol gave the adduct 581 (74% yield), which was oxidized with silver carbonate-celite to yield the indigoid 582 (30%). Upon the addition of methanol, 567 reversibly forms a mixture of the corresponding methyl acetals through adjacent diketone.

10.4. Dibenzotropoquinones

Two possible structures for dibenzotropoquinone, 5H-dibenzo-[a,c][7]annulene-5,6,7-trione (583) and 5H-dibenzo-[a,d][7]annulene-5,10,11-trione (584), are already known (Figure 37). Firstly, triketone 583 was prepared by oxidation of

Scheme 103: Synthesis of benzo[α]phenazine 566.
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Scheme 104: Structures 578–582 prepared from tropoquinone 567.

Figure 37: Two possible structures 583 and 584 for dibenzotropoquinone, and precursor compound 585 for 583.

the activated methylene group of diketone 586 with selenium dioxide [256,257]. Oxidative degradation of diketone 585 with nitric acid also provided 583 (Figure 36) [258,259]. The synthesis of dibenzotropoquinone 584 was realized via SeO$_2$-mediated oxidation of 5H-dibenzo[a,d][7]annulen-5-one (399, Figure 19) [260,261].

Conjugated carbon nanomaterials such as fullerenes, carbon nanotubes, and graphene have received tremendous attention and have great potential application in nanoscience due to their exceptional electrical, thermal, chemical, and mechanical properties. Starting from dibenzotropoquinone 584, Miao’s group reported the synthesis of saddle-shaped ketone 592 containing two tropone subunits embedded in the well-known framework of peri-hexabenzo coronene as depicted in Scheme 105 [261]. However, bistropone 592 was used as a precursor for the successful synthesis of two novel large aromatic saddles (C$_{70}$H$_{26}$ and C$_{70}$H$_{30}$) by reactions on the carbonyl groups. Local aromaticity and nonplanarity of individual rings in these saddle-shaped π-backbones were confirmed by crystal structure analysis. Moreover, preliminary studies on semiconductor properties were performed.

Conclusion

Tropones and tropolones are an important class of seven-membered aromatic compounds. In addition, hundreds of tropone or tropolone derivatives are known in the literature. These kinds of products have a wide range of biological activity and are building blocks in the synthesis of many molecules. All these factors have made these molecules a focus of intense interest among both organic chemists and medical chemists for nearly a century. This chemistry is one of the milestones leading to a deeper understanding of static, dynamic, and multidisciplinary aspects of organic chemistry such as spectroscopic studies, mechanistic and synthetic investigations, theoretical calculations, aromaticity, evolution, and design of bioactive molecules and molecular materials.

In this review, we have described the numerous efforts concerning synthesis and applications in benzotropon chemistry spanning over 100 years, from the first works up to the most recent. The review covers isomeric benzotropones and tribenzotropones as well as their benzotropolone analogues. As it is well known, halogenated compounds are very valuable as they are the key compounds for many functionalizations. Therefore, halogenated benzotropones and benzotropolones are also included in this review. Tropoquinones are a topic of interest in organic research and these compounds are used for many functionalization reactions. Works on benzo analogues of tropoquinones are also summarized in this review. Carbene–carbene and carbene–allene rearrangements on benzo[7]annulene-derived benzotropones are investigated in detail in the literature and discussed in this review. Carbene insertion reaction, synthesis of azocine, synthesis and physical properties of homo- and bis-homobenzotropones, and their conversation to corresponding homotropolium cations are also other well-investigated issues reviewed in this work. Knowledge of the chemistry of benzocyclobutenotropones, naphthotropones, and their tropolone analogues is limited and more research on those compounds is required in the future.

Numerous synthetic efforts towards the synthesis and chemical reactivity of benzotropones and benzotropolones were reported from the 20th century to date. In addition to being natural products, many benzotropon derivatives can be prepared directly by oxidation of seven-membered rings. They can also be derived from cyclization, ring expansion, or cycloaddition of appropriate precursors followed by elimination or rearrangement. The oxidation of seven-membered rings generally gives a mixture, whereas cyclization of suitable acyclic compounds or ring expansion reactions generally produces one isomer in high yield. Although 2,3- and 4,5-benzotropon have been investigated in detail, research on 3,4-benzotropon is rather limited due to instability of this kind of compound, which is attributed
to the \(\alpha\)-quinoidal structure, and because it does not have a sextet electron system in the benzene ring.

In general, two kinds of reactions on benzotropone and their analogues are common: i) reaction on the carbonyl group, which is generally a nucleophilic addition or condensation, ii) reaction on the double bond in the seven-membered ring, which is generally with a nucleophile since the tropone ring is behaving as an electrophile. The double bonds in the seven-membered ring give a cycloaddition reaction as both a diene and a dienophile. Although many reactions on this hydrocarbon have been reported, we think that there is still a need for the scientific community to develop many synthetic methods and investigate their possible interesting synthetic applications in various fields. We consider the objectives of this review as helping in the systematization of the literature data collected to date and allowing a better understanding of them, and possibly bringing new ideas to the field. We strongly believe that the synthetic potential and applications of this chemistry have not yet been fully revealed, and there are certainly further challenges and opportunities for reinvestigation, and plenty of room for further studies on the chemistry of benzotropones for medicinal, material, and synthetic organic chemists. Based on the progress in benzotropone chemistry including synthesis and applications summarized in this work, we feel certain that this review will find broad interest and will continue to attract much attention in

**Scheme 105**: Synthesis of saddle-shaped ketone 592 using dibenzotropoquinone 584.
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