

Aqueous Micellar Medium in Organic Synthesis: Alkylations and Michael Reactions of Benzotriazole

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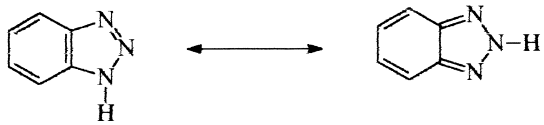
The feasibility of aqueous micelles of cetyltrimethylammonium bromide in catalyzing C–N bond formation has been studied with respect to *N*-alkylations of benzotriazole (Bt). Alkylations with various alkylating agents and the addition of Bt across activated double bonds in the Michael fashion occurred successfully in fair-to-good yields in the aqueous micellar regime. These reactions provided a mixture of N-1 and N-2 alkylated products, with a marked preference for N-1 over N-2 isomers. Micellar catalysis has been evaluated experimentally to indicate over a 50% micellar contribution to these alkylations in contrast to their aqueous counterparts. Since, *N*-alkyl benzotriazoles are of potential biological interest, the present micellar procedure offers a convenient alternative to other available methods.

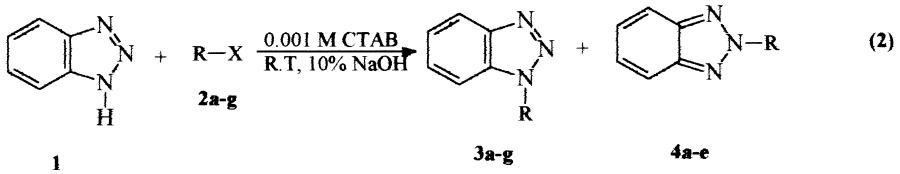
The *N*-alkylations of benzotriazole have been widely investigated under both homogeneous and PTC conditions using an assortment of basic catalysts and conditions.[1] These reactions invariable provide a mixture of both N-1 and N-2 alkylation products, though in many cases, marked preferences for N-1 over N-2 alkylations are observed. The formation of regioisomers in benzotriazole alkylations has been attributed to the existence of H-1 and H-2 tautomeric forms of benzotriazole (reaction 1, Scheme 1).[2]

In recent years, various organized media, such as micelles, zeolites and clays have been attracting interest as promising new reaction domains to study the reactivity, selectivity and catalysis in various chemical and biochemical processes.[3] According to literature, micelles have been used extensively to investigate the kinetic and thermodynamic aspects of chemical processes. However, relatively little attention has been devoted to exploiting micelles for synthetically useful processes. We have recently described the potential of aqueous micelles of the cationic surfactant, cetyltrimethylammonium bromide (CTAB), as an efficient and convenient medium for executing synthetically useful reactions, namely the aldol condensations, Michael reactions and C–S bond formations.[4–6] In a continuation to this work, we presently studied the micellar catalyzed alkylations (generalized reaction 2, Scheme 1) and Michael reactions of benzotriazole so as to offer a new reaction medium to carry out the synthesis of alkylated benzotriazoles, many of which are known to possess varied biologically activity,[3] and also to observe any favorable influence of micelles on the regioselectivity of these alkylations.

We first examined the alkylation of Bt **1** with benzyl chloride on the 10 mmol scale in weakly alkaline aqueous CTAB micelles (CTAB; 50 mg, 1.35×10^{-4} mol ($>$ cmc) in 100 mL of 0.02 M NaOH). Because of the high acidity of the N–H bond of benzotriazole (pK_a of 8.2),[7] a fairly dilute NaOH solution has been used to effect the complete *N*-deprotonation of benzotriazole. The above mentioned micellar reaction was vigorously stirred at room temperature until the reaction was judged by TLC to be complete (16 h, Table 1). The crude



(1)



(2)

Scheme 1.

Table 1. N-Alkylation of Benzotriazole[a)]

Entry	Alkyl halides: R–X	Products	Time/h[b)]	Ratio of N1/N2[e)]	Yield/%[f)]
1	2a; R = $PhCH_2$; X = Cl	3a/4a	16	70:30	84
2	2b; R = $PhCOCH_2$; X = Cl	3b/4b	4	80:20	88
3	2c; R = $CH_2COOC_2H_5$; X = Br	3c/4c	4	80:20	84
4	2d; R = $CH_2CH{=}CH_2$; X = Br	3d/4d	24	68:32	63
5	2e; R = $PhCH_2CH_2$; X = Br	3e/4e	48	55:45	69
6	2f; R = $CH_3CH_2CH_2$; X = Br	3f	48[c)]	100:0	55
7	2g; R = $CH_3CH_2CH_2CH_2$; X = Br	3g	48[d)]	100:0	35

a) All reactions were carried out at room temperature using 10 mmol scale of benzotriazole and alkyl halide. b) Reaction time refers to $>$ 90% conversion. c) Ca. 55% conversion. d) Ca. 35% conversion. e) Ratio determined by quantitative separation on SiO_2 column chromatography. f) Yields are not optimised.

product obtained upon a work-up showed two compounds, which were readily resolved by SiO_2 column chromatography to afford the known *N*-1-**3a** and *N*-2-**4a** benzylbenzotriazoles in 70:30 ratio, the combined yield being 84%. Although, the regioselectivity is moderate, the successful alkylation of Bt with benzyl chloride in high yield confirms the potential of micellar medium in catalyzing C–N bond formation. Additionally, the reaction condition is very mild, easy to execute and economical.

The highest regioselectivity for the *N*-benzylation of benzotriazole to date has been reported by Katritzky[8] in refluxing benzene solvent (91% of N-1 isomer) using an excess of Bt, itself, serving as the base. In other conditions, the N-1/N-2 ratio reportedly varies from 85:15 in KOH/xylene[9] to 73:27 in C_2H_5ONa/C_2H_5OH systems.[10] It may be noted that there is a close parallel in the regioselectivity of the *N*-benzylation of benzotriazole reported in the alcoholic medium and that observed by us in the aqueous CTAB micelles. This similarity in the regioselectivity in alcohol and micellar media promoted us to probe the comparative rates of alkylation in these two media. Thus, we performed *N*-benzylation of benzotriazole with benzyl chloride both in aqueous micelles (conc. ca. 1 cmc) and in the ethanol solvent, keeping the substrates and alkali concentrations identical. A product analysis after 4 h of reaction revealed ca. 47% and 52% conversion to *N*-benzylbenzotriazole, with the ratio of N1/N2 being 70: 30 and 74:26 in the micelles and alcohol medium, respectively. Such a close parallel in chemical yields and regioselectivity of the *N*-benzylation of benzotriazole in alcohol and micellar media at least qualitatively supports the proposed similarity in the polarity of these two reaction domains.[11]

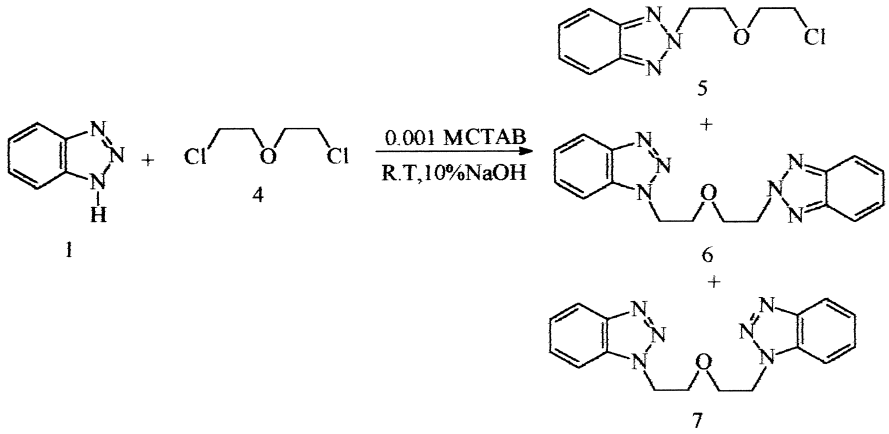
In order to evaluate and extend the scope, we carried out alkylations of Bt with a few activated as well as simple alkylating agents. Our results are collected in Table 1. The reaction of an activated alkylating agent, phenacyl chloride, with Bt in CTAB micelles, as expected, occurred relatively faster, producing a copious white precipitate of the product just after 4 h of reaction time. Two compounds, corresponding to *N*-1-**3b** and *N*-2-phenacylbenzotriazoles **4b** were isolated by SiO_2 column chromatography in 80:20 ratio, respectively, in yields of 88%. The micellar *N*-alkylation of Bt with ethyl bromoacetate, during 4 h of reaction led to *N*-1-**3c** and *N*-2-**4c** alkylated products in 80:20 ratio in good yield. The alkylation of Bt with allyl bromide furnished *N*-1-**3d** and *N*-2-**4d** allylbenzotriazoles in 63% yield in 68:32 ratio (entry 4, Table 1).

The micellar alkylations of Bt with simple alkyl halides, such as phenethyl bromide, propyl bromide, and *n*-butyl bromide, proceeded comparatively sluggishly (entries 5 to 7 Table 1) compared to the activated alkyl halides (entries 1 to 4, Table 1). Thus, the alkylation of Bt with phenethyl bromide in micelles required 48 h for complete conversion, giving *N*-1-**3e** and *N*-2-**4e** products in 55:45 ratio (entry 5, Table 1). However, alkylations with propyl bromide and butyl bromide were found to be incomplete even after 48 h, showing ca. 55% and 35% conversions, respectively. Interestingly, practically a single product, characterized as *N*-1-propylbenzotriazole **3f** and *N*-1-butylbenzotriazoles **3g**, was obtained in these reactions.

In order to assess micellar catalysis towards alkylation reactions, we simultaneously performed *N*-benzylation of Bt under micellar and plain aqueous conditions without added CTAB, keeping all other conditions identical. After 10 h of reactions, we found upon product analysis 75% and 35% conversions in micellar and aqueous media (N1/N2 ratio 67:33 in aqueous medium), respectively. A similar comparison of the slower reacting propyl bromide revealed ca. 28% reaction after 48 h in the presence of CTAB micelles, but only 9% in the aqueous medium during the same reaction time. These experiments clearly demonstrate the contribution of micellar catalysis to be in excess of 50% to the overall reaction. The comparatively slower reactions of low polar phenethyl bromide, propyl and butyl bromides (entries 5 to 7, Table 1) may in part be due their deeper residency in the hydrophobic domain of the micelles, rendering them relatively inaccessible to attack by polar *N*-benzotriazole anions.

In order to discern between the type of catalysis either being due to a phase-transfer effect or micellar aggregation, we performed *N*-benylation of benzotriazole in aqueous medium containing tetrabutylammonium bromide (TBAB), a conventional phase-transfer catalyst. An analysis of these reactions containing various concentrations of TBAB ranging from 1 to 5 wt% after 10 h revealed conversion to *N*-benzyl benzotriazole between 33–37%, which is nearly the same as observed in a pure aqueous medium. This result clearly rules out any involvement of phase-transfer type catalysis in the benzylation. We can therefore conclude that the much higher conversions observed in aqueous CTAB (ca. 75% *N*-benylation) after 10 h reaction time were due to micellar aggregation.

A reaction of benzotraizole with bis(2-chloroethyl) ether **4**



Scheme 2.

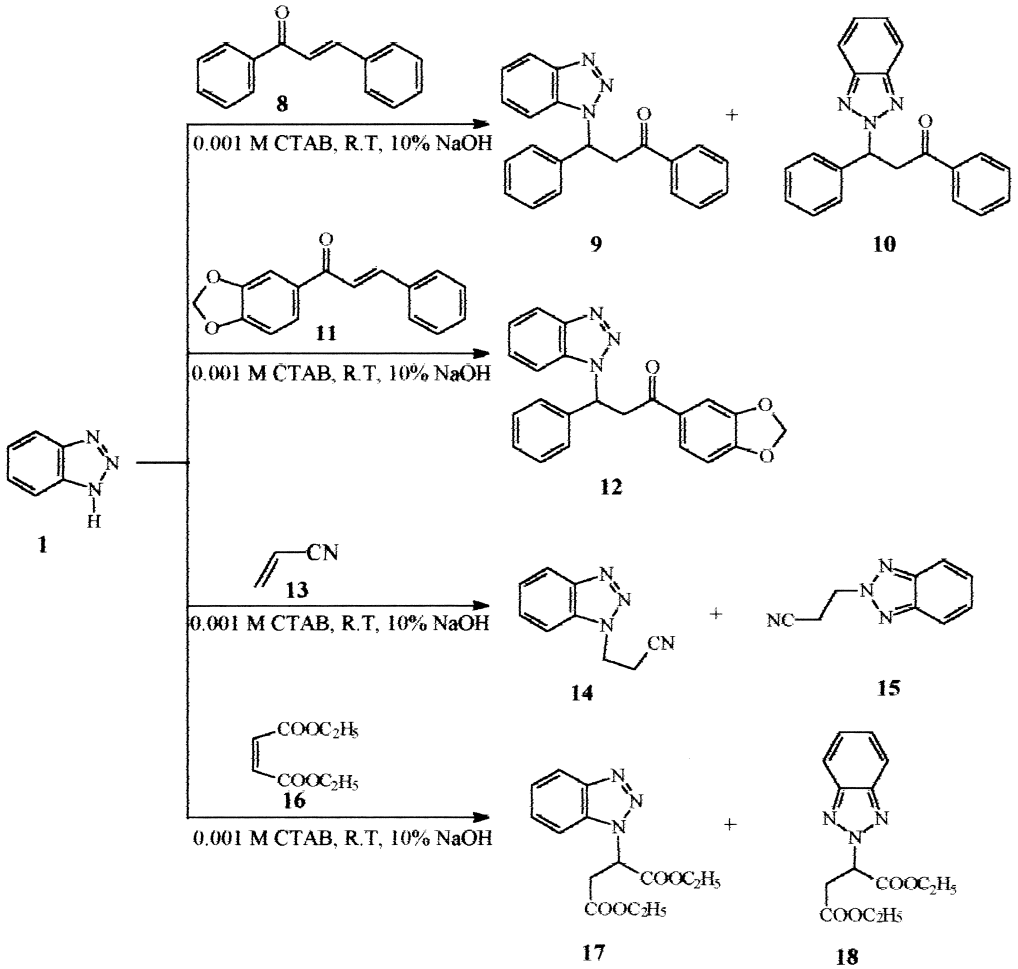
in 2:1 proportion was carried out in aq CTAB micelles so as to preferentially generate dialkylated products. Since only little conversion was discernible after 6 h at room temperature, we conducted the reaction at an elevated temperature of 70 °C, whereby the reaction proceeded smoothly. After 7 h, the reaction was extractively worked up to afford a complex mixture of products. The crude product was chromatographed on a SiO_2 column, resulting in the isolation of three compounds in pure form (Scheme 2).

A low polar compound obtained as an oil (mol formula $C_{10}H_{12}ClN_3O$) was assigned the structure N-2 mono-alkylation product **5** based on its 300 MHz ^{1}H NMR data. Triplets centered at δ 4.8 and 4.18 are due to N–C*H*$_2$ and –O–C*H*$_2$CH$_2$–N–, respectively. The remaining four methylene protons (ClC*H*$_2$CH$_2$O–) are seen as two overlapping triplets between δ 3.4–3.7. A characteristic A_2B_2 pattern for four aromatic protons appearing at δ 7.7 and 7.8 is indicative of the structure as the symmetrical N-2 alkylated product **5**. The second component, with intermediate polarity (mp 75–76 °C), was a dialkylated product to which we assign the structure as unsymmetrical *N*-1, *N*′-2-(oxydiethylene)bis(benzotriazole) **6**. The unsymmetrical nature of this compound is evident from the appearance of two overlapping multiplets, one between δ 3.8–4.4 and the other between δ 4.7–5.1, which could be assigned to the –C*H*$_2$OC*H*$_2$– and –N–C*H*$_2$CH$_2$OCH$_2$C*H*$_2$–N– groups, respectively. In the aromatic region, we noticed a downfield shifted multiplet (3H, δ 7.8–8.2) arising from the H-4 proton of the N-1 and H′-4 and the H′-7 protons of the N′-2 linked benzotriazole moieties of **6**. A complex multiplet integrating for 5H (δ 7.2–7.6) can be accounted for by the remaining aromatic protons (H-5, H-6, H-7 of N-1 and H′-5, H′-6 of N′-2 linked aromatic ring). The most polar compound (mp 80–82 °C) showed triplets centered at δ 3.8 and 4.6 (J = 8 Hz each) due to O–C*H*$_2$– and –N–C*H*$_2$– protons, respectively. A one-proton multiplet (δ 7.95) is for the H-4 proton, whereas an overlapping multiplet (3H) located between δ 7.0–7.3 is for the remaining H-5, H-6 and H-7 protons of the aryl ring. These data support the symmetric, bis*N*-1,*N*′-1-(oxydiethylene)bis(benzotriazole) **7** for this compound. The other possible product(s), such as *N*-1,*N*′-1-(oxydiethylene)bis(benzotriazole), though likely to be present in minor amounts in the crude product, could not be isolated.

Micellar Catalyzed Michael Addition to Benzotriazole: A few reports exist concerning the addition of Bt across electron-deficient alkenes under base catalysis. Good[12] and Moffat[13] have described the addition reactions of Bt with 1,4-naphthoquinone, chalcones, acrylonitrile, cinnamaldehyde etc. in the presence of pyridine or Triton B as a catalyst, and isolated the corresponding N-1 adducts in 25 to 65% yields. Euglero[14] has shown by NMR analysis that the addition of acrylonitrile on Bt gives both N-1 and N-2 products, the latter being the kinetically controlled product. We investigated the addition of Bt with a few representative examples of electron-deficient olefins under a micellar medium to ascertain the feasibility and regioselectivity of these additions (Scheme 3).

We first attempted a reaction between benzotriazole **1** and chalcone **8** in alkaline aqueous CTAB micelles on the 10 mmol scale. The resultant milky reaction was vigorously stirred for 24 h at room temperature. The crude product, upon SiO_2 column chromatography, gave two compounds, a major polar, N-1 adduct **9**, mp 106–107 °C (Ref. 13, 106 °C) and an unknown, less polar N-2 adduct **10** (mp 102–104 °C) in a combined yield of 79% (80:20 ratio). The minor product was assigned the structures as the N-2 adduct **10** based on its ^{1}H NMR data. A 4-proton multiplet due to H-4 and H-7 of the benzotriazole moiety and two ortho-protons of the phenacyl ring appeared together in the region of δ 7.8 to 8.2; the remaining 10 aromatic protons were found to be clubbed together between δ 7.2–7.7. A one-proton double doublet centered at δ 6.7 (J = 10 Hz and 4 Hz) can be assigned to N–C*H*–Ph, whereas two ethylene protons (diestereotopic in nature) adjacent to the carbonyl group appear individually at δ 3.7 (J = 18 and 4 Hz) and δ 5.0 (J = 18 and 10 Hz). Thus, the micellar process not only provides higher yields (79% compared to 65% reported in the literature[13]), but also affords hitherto unreported N-2 adduct **10**.

Consistent with the reduced electrophilicity of the 3′,4′-methylenedioxychalcone **11**, its micellar-catalyzed addition on Bt proceeded slower than that of the simple chalcone **8**. However, practically a single adduct (ca. 97% purity, 65% yield), characterized as the N-1 adduct **12**, was isolated from the 3′,4′-methylenedioxychalcone reaction. The structure follows from its ^{1}H NMR spectrum, particularly the appearance of a three-proton multiplet downfield located at δ 8.0 arising out of H-4 of



Scheme 3.

the benzotriazole moiety and two ortho protons of the phenacyl ring. The remaining aromatic protons (9H) appear as an overlapping multiplet in the range of δ 6.45 to 7.70.

In contrast to the highly successful micellar additions of Bt discussed above, the attempted addition of Bt on these 3′,4′-methylenedioxychalcone in aqueous medium without CTAB produced less than 10% of the corresponding Michael adducts. Therefore, these Michael reactions are also subjected to considerable micellar catalysis, affording much higher product yields. Further, in agreement with a literature report, we found these reactions to also be reversible in micelles. Thus, when pure N-1 adduct **9** was stirred under alkaline micellar condition for a period of 4 h, we detected by tlc both N-1 and N-2 adducts (**9** and **10**) as well as the starting chalcone **8**, which strongly supports the reversible nature of these processes.

The micellar-catalyzed reaction of Bt **1** with acrylonitrile **13** occurred smoothly, affording the known N-1 adduct **14** (mp 79 °C, Ref. 13 mp 79–80 °C) together the unknown N-2 adduct **15** being isolated for the first time (N-1/N-2 ratio 70:30; yield 69%) from the present micellar condition. The structure of the N-2 adduct **15** readily follows from the characteristic symmetrical A_2B_2-type coupling of aromatic protons (δ 7.5–7.75). The Michael addition of maleic ester **16** to **1**, a reaction which is not reported in the literature, was also investigated in CTAB micelles. Compared to the other Michael processes described above, this reaction was slower, giving only 50% conversion after 72 h. Adducts N-1 **17** and N-2 **18** were isolated by SiO_2 column chromatography in a 60:40 ratio. The structure of the N-1 adduct **17** is deduced from the unsymmetric multiplet in 1:3 proton ratio for its aromatic protons, whereas the structure of the N-2 **18** is based on its characteristic A_2B_2 type multiplet observed for its aromatic protons in ^{1}H NMR spectrum.

Conclusion: The present work clearly demonstrates the viability of aqueous CTAB micelles as a useful reaction domain in various alkylation reactions of benzotriazole. In spite of moderate regioselectivity, the procedure is mild, economical, and easy to execute. In addition, we have provided experimental evidence for micellar catalysis. In some micellar-catalyzed Michael additions, in addition to the N-1 adduct, we have also isolated for the first minor, N-2 adducts which have not been more easily isolated under the homogeneous conditions.

Experimental

The melting points (uncorrected) were determined on a Gallenkamp melting-point apparatus. IR spectral data were recorded on a Shimadzu FTIR-4200 Spectrophotometer as a KBr disk or oil film. ^{1}H NMR spectra were recorded on Varian EM-360-L, 60 MHz, and 300 MHz Spectrometers with TMS as internal standard.

General Procedure: Alkylation of Benzotriazole with Benzyl Chloride: Benzotriazole **1** (1.19 g, 10 mmol) and benzyl chloride **2a** (1.26 g, 10 mmol) were added to an alkaline CTAB solution (40 mg of cetyltrimethylammonium bromide, ca. 1 $\times 10^{-4}$ mol dissolved in 100 mL of distilled water containing 0.50 g NaOH). The reaction mixture was then stirred at room temperature for 16 h. Thereafter, it was diluted with water and extracted with a 4:1 v/v petroleum ether–ethyl acetate solvent system. The organic extract, after drying over anhyd. Na_2SO_4, was concentrated to give a semisolid residue, which was chromatographed by SiO_2 using hexane: ethyl acetate (90:10) to give a less-polar product, *N*-2-benzylbenzotriazole **4a** as a colorless oil (Ref. 15, oil) (0.531 g, 25%). IR (oil film) 3000 and 1560 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 5.8 (s, 2H), 7.1–7.5 (m, 7H), 7.84 (m, 2H). The more-polar, *N*-1-benzylbenzotriazole **3a** was obtained as a solid, and crystallised from ethanol to give white crystals, mp 114.0 °C (Ref. 15, mp 114 °C) (1.23 g, 59%). IR (KBr disk) 3000, 1620 and 1600 cm^{-1}, ^1H NMR (60 MHz, $CDCl_3$) δ 5.89 (s, 2H), 7.2–7.4 (m, 8H), 8.05 (m, 1H).

Preparation of *N*-1-3b and *N*-2-Phenacylbenzotriazoles 4b: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with phenacyl chloride **2b** (1.54 g, 10 mmol) was performed under the same condition as described in general procedure. The crude product obtained upon work-up was chromatographed over SiO_2 (hexane:ethyl acetate, 90:10) to separate the two isomers. The less-polar *N*-2 phenacylbenzotriazole **4b** eluted out first as a solid; mp 157 °C (Ref. 15, mp 156–158 °C) (0.42 g, 17%). IR (KBr disk) 3000, 1680 and 1560 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 6.0 (s, 2H), 7.1–7.7 (m, 5H), 7.9–8.2 (m, 4H). Further elution with the same solvent gave the more-polar *N*-1-phenacylbenzotriazole **3b** as a colourless solid; mp 116 °C (Ref. 15, mp 116–117 °C) (1.70 g, 71% yield). IR (KBr disk) 3000, 1680, 1620 and 1600 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 6.05 (s, 2H), 7.1–7.7 (m, 6H), 7.9 (m, 3H).

Preparation of *N*-1-3c and *N*-2-(Ethoxycarbonylmethyl)benzotriazoles 4c: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with ethyl bromoacetate **2c** (1.67 g, 10 mmol) was performed at room temperature for 4 h; thereafter, the reaction was extractively worked-up to give a crude product. This was subjected to SiO_2 column chromatography (eluent, petroleum ether–ethyl acetate, 80:20) to separate N-1 and N-2 isomers. The less-polar, ethyl 2-benzotriazolylacetate **4c** was isolated as a solid; mp 120–21 °C, (Ref. 15, mp 121 °C) in 16% yield (0.35 g). IR (KBr disk) 3000, 1760 and 1560 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.2 (t, J = 7 Hz, 3H), 4.2 (q, 2H), 5.4 (s, 2H), 7.3–7.6 (m, 2H), 7.6–7.9 (m, 2H). The more-polar, ethyl 1-benzotriazolylacetate **3c** was isolated in 68% yield (1.51 g) mp 81 °C (Ref. 15, mp 81–82 °C). IR (KBr disk) 3000 and 1760 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.1 (t, J = 7 Hz, 3H), 4.1 (q, 2H), 5.3 (s, 2H), 7.3–7.7 (m, 3H), 7.9–8.2 (m, 1H).

Preparation of *N*-1-3d and *N*-2-Allylbenzotriazoles 4d: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with allyl bromide **2d** (1.2 g, 10 mmol) was carried out for a period of 24 h. The crude product obtained upon the usual work-up was purified by SiO_2 column chromatography (petroleum ether:ethyl acetate, 80:20) to give the less-polar *N*-2-allylbenzotriazole **4d** (0.34 g, 21%) as an oil (Ref. 16, oil); IR (oil film) 3000, 1570, 980 and 920 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 5.0–5.4 (m, 4H), 5.5–6.0 (m, 1H), 7.0–7.3 (m, 2H), 7.5–7.7 (m, 2H). The more-polar *N*-1-allylbenzotriazole **3d** was obtained as colourless oil (Ref. 16, oil) (0.68 g, 42%). IR (oil film) 3000, 1620, 1600, 980 and 930 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 5.0–5.4 (m, 4H), 5.5–6.0 (m, 1H), 7.0–7.5 (m, 3H), and 7.8–7.9 (m, 1H).

Preparation of *N*-1-3e and *N*-2-Phenethylbenzotriazoles 4e: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with phenethyl bromide **2e** (1.85 g, 10 mmol) was stirred for 48 h. Purification of the crude product obtained upon a work-up was achieved by SiO_2 column chromatography (petroleum ether:ethyl acetate, 80:20) to separate the two isomers. The less-polar *N*-2-phenethylbenzotriazole **4e** was isolated as a solid; mp 70 °C (0.70 g, 31%) (Ref. 17, mp 71 °C); IR (KBr disk) 3000, 1600 and 1570 cm^{-1}, ^1H NMR (60 MHz, $CDCl_3$) δ 3.40 (t, J = 7 Hz, 2H), 4.9 (t, J = 7 Hz, 2H), 7.0–7.3 (m, 7H), 7.8 (m, 2H). The more-polar, *N*-1-isomer **3e** was isolated as an oil (Ref. 17, mp 37 °C) in 38% yield (0.858 g). IR (oil film) 3000, 1600 and 1620 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.20 (t, J = 7 Hz, 2H), 4.65 (t, J = 7 Hz, 2H), 6.8–7.3 (m, 8H), 7.8 (m, 1H).

Preparation of *N*-1-Propylbenzotriazole 3f: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with propyl bromide **2f** (1.23 g, 10 mmol) was carried out following the general procedure. The oil obtained after a work-up and purification afforded *N*-1-propylbenzotriazole **3f** in 55% yield (0.885 g) (Ref. 8, oil). IR (oil film) 3000, 1600 and 1620 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.9 (t, J = 7 Hz, 3H), 2.0 (m, 2H), 4.58 (t, J = 7 Hz, 2H), 7.36 (m, 3H), 7.8 (m, 1H).

Preparation of *N*-1-Butylbenzotriazole 3g: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with butyl bromide **2g** (1.37 g, 10 mmol) gave after a work-up and purification of the crude product *N*-1-butylbenzotriazole **3g** as oil (Ref. 1, oil) (0.613 g, 35%). IR (oil film) 3000, 1600 and 1620 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.0 (t, J = 7 Hz, 3H), 1.3–2.4 (m, 4H), 4.6 (t, J = 7 Hz, 2H), and 7.1–8.2 (m, 4H).

Preparation of Bis Alkylation Compounds: Reaction of Benzotriazole with Bis(2-chloroethyl) Ether 4: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with bis(2-chloroethyl) ether **4** (1.43 g, 10 mmol) was heated to 70 °C when the reaction was complete in 7 h. The oil obtained upon a work-up was chromatographed on SiO_2 (hexane:ethyl acetate, 90:10) to give three compounds. The less-polar product, 2-[2-(2-chloroethyl)ethyl]benzotriazole **5**, was obtained in 13% yield (0.28 g). IR (oil film) 3000, 1600, 1570, 1150 and 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.4–3.7 (tt, 4H), 4.18 (t, J = 7Hz, 2H), 4.8 (t, J = 7 Hz, 2H), 7.3 (m, 2H), 7.8 (m, 2H). Found: C, 52.9; H, 5.35; Cl, 15.54; N, 18.32%. Calcd for $C_{10}H_{12}ClN_3O$: C, 53.2; H, 5.32; Cl, 15.74; N, 18.62%.

An intermediate product, identified as 1,2′-(oxydiethylene)bis(benzotriazole) **6**, was obtained in 32% yield (0.986 g); mp 75–76 °C. IR (KBr) 3000, 1600, 1620, 1570 and 1150 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.8–4.2 (m, 4H), 4.7–5.1 (m, 4H), 7.2–7.6 (m, 5H), 7.8–8.28 (m, 3H). Found: C, 62.54; H, 5.05; N, 26.98%. Calcd for $C_{16}H_{16}N_6O$: C, 62.33; H, 5.19; N, 27.27%. A more-polar compound obtained as a solid, mp 80–82 °C, was identified as 1,1′-bis(oxydiethylene)bis(benzotriazole) **7** (yield 22%, 0.69 g). IR (KBr disk) 3000, 1600, 1620 and 1500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.8 (t, 4H), 4.6 (t, 4H), 7.0–7.3 (m, 6H), 7.9 (m, 2H). Found: C, 62.5; H, 5.35; N, 27.6%. Calcd for $C_{16}H_{16}N_6O$: C, 62.33; H, 5.19; N, 27.27%.

General Procedure for the Preparation of Michael Adducts with Benzotriazole: To an aqueous CTAB solution (100 mL, 0.001 M) were added benzotriazole **1** (1.19 g, 10 mmol), chalcone **8** (2.08 g, 10 mmol) and 1 mL of 10% NaOH solution. The reaction was stirred at room temperature for 24 h and extracted in diethyl ether, dried, and concentrated to give a semi-solid residue. The crude was subjected to SiO_2 column chromatography (80:20,

petroleum ether:hexane) to afford two isomeric adducts. The less-polar Michael adduct, N-2 **10**, was isolated in 16% yield (0.52 g); mp 102–104 °C. IR (KBr disk) 1680, 1600 and 1570 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.8–4.8 (m, 2H), 6.7–7.0 (m, 1H), 7.2–7.7 (m, 10H), 7.8–8.2 (m, 4H). MS *m/z* 327 (M^+), 222, 120, 105 (base peak), 91, 77. Found: C, 76.9; H, 5.23; N, 12.9%. Calcd for $C_{21}H_{17}N_3O$: C, 77.06; H, 5.19; N, 12.84%.

The major product, N-1 Michael adduct **9**, was obtained in 2.08 g, 63% yield, mp 106–107 °C (Ref. 13, mp 106 °C). IR (KBr disk) 1680, 1600 and 1620 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.5–5.8 (m, 2H), 6.5 (dd, 1H), 7.1–7.6 (m, 11H), 7.8–8.2 (m, 3H).

Reaction of Benzotriazole with 3′,4′-Methylenedioxychalcone: The reaction of benzotriazole **1** (1.19 g, 10 mmol) with 3′,4′-methylenedioxychalcone **11** (2.52 g, 10 mmol) under the same conditions as described above afforded after an extractive work-up a single component as the N-1 Michael adduct **12** (2.42 g, 65%) (mp 128–130 °C). IR (KBr disk) 1680, 1600, 1620 and 1020 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.6–5.1 (m, 2H), 5.9 (s, 2H), 6.3–6.7 (m, 1H), 6.8–7.7 (m, 9H), 7.8–8.2 (m, 3H). MS *m/z* 371 (M^+), 252 (base peak), 119, 91, 77; Found: C, 70.9; H, 4.72; N, 11.55%. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.58; N, 11.32%.

Reaction of Benzotriazole with Acrylonitrile: A micellar reaction of benzotriazole **1** (1.19 g, 10 mmol) with acrylonitrile **13** (0.53 g, 10 mmol) was carried under the same condition as described above. The oil obtained after extractive work-up was chromatographed on SiO_2 (petroleum ether:hexane, 80:20) to separate the N-1 and N-2 adducts. The N-2 adduct **15** obtained in 21% yield (0.361 g) mp 90–91 °C was crystallised from ethanol. IR (KBr disk) 3000, 2200 and 1570 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.2 (t, J = 7 Hz, 2H), 5.0 (t, J = 7 Hz, 2H), 7.2–7.5 (m, 2H), 7.7–8.0 (m, 2H). Found: C, 62.62; H, 4.67; N, 32.38%. Calcd for $C_9H_8N_4$: C, 62.79; H, 4.65; N, 32.55%.

The N-1 adduct **14** obtained in 48% yield (0.84 g) mp 79 °C (Ref. 13, mp 79–80 °C) was crystallised from ethanol. IR (KBr disk) 3000, 2250, 1620 and 1600 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.15 (t, J = 7 Hz, 2H), 4.9 (t, J = 7 Hz, 2H), 7.2–7.7 (m, 3H), 7.9–8.2 (m, 1H).

Reaction of Benzotriazole with Maleic Ester 16: Reaction of benzotriazole **1** (1.19 g, 10 mmol) with maleic ester **16** (1.72 g, 10 mmol) was proceeded slowly; after 72 h an extractive work-up gave an oil, which was chromatographed (hexane:ethyl acetate, 80:20) to afford three compounds. The unreacted starting material was recovered (0.86 g, 50%). The less-polar N-2 adduct **18** was obtained in 20% yield (0.58 g) (mp 68–70 °C). IR (KBr disk) 1740 and 1565 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.2 (t, J = 7 Hz, 6H), 3.5 (d, 2H), 4.2 (q, 4H), 6.05 (t, J = 7 Hz, 1H), 7.2–7.5 (m, 2H), 7.7–8.0 (m, 2H). MS *m/z* 291 (M^+), 246, 218 (base peaks), 146, 118, 91, 77; Found: C, 57.53; H, 5.76; N, 14.28%. Calcd for $C_{14}H_{17}N_3O_4$: C, 57.73; H, 5.84; N, 14.4%.

The N-1 adduct **17** was obtained in 29% yield (0.844 g) as a viscous oil. IR (oil film) 1740, 1620 and 1600 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.1 (tt, 6H), 3.4 (m, 2H), 3.9–4.3 (m, 4H), 5.8 (t, 1H), 7.2–7.5 (m, 3H), 7.8–8.0 (m, 1H); Found: C, 57.42; H, 5.59; N, 13.98%. Anal. Calcd for $C_{14}H_{17}N_3O_4$: C, 57.73; H, 5.84; N, 14.4%.

References

1 a) R. Boehm, *Pharmazie*, **33**, 83 (1978). b) J. Elguero, S. Julia, J. M. Del Mazo, and L. Avila, *Org. Prep. Proced. Int.*, **16**, 299 (1984). c) L. J. Mathias and D. Burkett, *Tetrahedran Lett.*, **49**, 4709 (1979). d) K. Sukata, *Bull. Chem. Soc. Jpn.*, **56**, 280 (1983). e) H. Aixi and Z. Zhaoqiong, *Goodeng Xuexiao Huaxue Xuebao*, **10**, 769 (1989); *Chem. Abstr.*, **112**, 198239g (1989). f) M. Searcey, J. B. Lee, and P. L. Pye, *Chem. Ind. (London)*, **1989**, 569.

2 a) "The Tautomerism of Hetreocycles, Adv. Heterocycl. Chem.," Supplement 1, ed by J. Elguero, C. Marzin, A. R. Katrizky, and P. Linda, Academic Press, New York (1976). b) N. K. Roberts, *J. Chem. Soc.*, **1963**, 5556. c) P. Mauret, J. P. Fayet, J. Elguero, and J. de Mendoza, *J. Chim. Phys.*, **71**, 115 (1974).

3 a) F. Sporatore, M. I. La Rotonda, G. Paglietti, E. Ramundo, C. Silipo, and A. Vittoria, *Farmaco, Ed. Sci.*, **33**, 901 (1978); *Chem. Abstr.*, **90**, 103903 (1978). b) R. E. Deal and R. V. Kendall, Jpn. Kokai., 78121762 (1978); *Chem. Abstr.*, **88**, 190843. c) American Cyanamid CO., Belg. Patent 853179 (1977); *Chem. Abstr.*, **88**, 190843. d) R. E. Diehl and R. V. Kendall, US Patent 4240822 (1980); *Chem. Abstr.*, **94**, 134160 (1980). e) H. Wamhoff, "Comprensive Heterocyclic Chemistry,"1st ed, by K. T. Potts, Pergamon Press, U.K. (1984), Vol. 5, p. 669.

4 C. D. Mudaliar and S. H. Mashraqui, *J. Chem. Res., (S)*, 174 (1994).

5 C. D. Mudaliar and S. H. Mashraqui, *Org. Prep. Proced. Int.*, **29**, 584 (1997).

6 C. D. Mudaliar and S. H. Mashraqui, *J. Chem. Res., (S)*, 98 (1992).

7 J. E. Fagel, Jr and G. W. Ewing, *J. Am. Chem. Soc.*, **73**, 4360 (1951).

8 A. R. Katritzky and J. Wu, *Synthesis*, **1994**, 597.

9 F. Krollp feiffer, H. Potz, and A. Rosenberg, *Ber. Dtsch. Chem. Ges.*, **71B**, 596 (1938).

10 J. Torres, J. L. Lavandera, P. Cabildo, R. H. Claramunt, and J. Elguero, *J. Heterocycl. Chem.*, **25**, 771 (1988).

11 J. H. Fendler, "Membrane Mimetic Chemistry," Wiley Interscience, New York, (1982).

12 R. H. Good and M. Bellas, *Res. Discl.*, **182**, 299 (1979).

13 R. H. Willey, N. R. Smith, D. M. Johnson, and J. Moffat, *J. Am. Chem. Soc.*, **76**, 4933 (1954).

14 A. De La Cruz, J. Elguero, and M. A. Goyapllar, *J. Heterocycl. Chem.*, **25**, 225 (1988).

15 A. R. Katritzky, Kuzmierkiewicz, and J. V. Greenhill, *Recl. Trav. Chim. Pays-Bas*, **110**, 369 (1991).

16 C. W. Rees and R. C. Storr, *J. Chem. Soc., Chem. Commun.*, **1969**, 1478.

17 a) H. Suschitzky and B. W. Ashton, *J. Chem. Soc.*, **1957**, 4559. b) A. P. Miller, S. African 7606, 188 (1977).