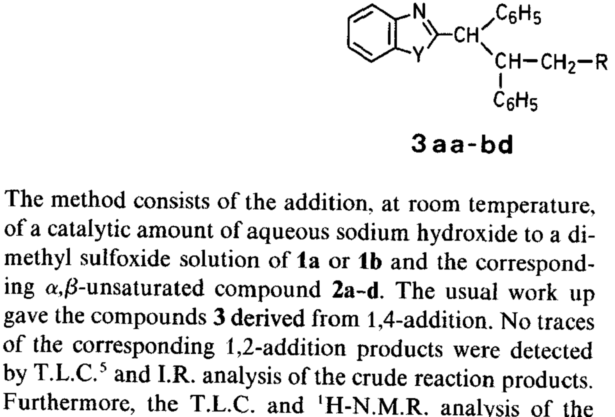
Michael Condensation of 2-Benzylbenzazoles

V. Dryanska*, C. Ivanov

Department of Chemistry, University of Sofia, Sofia 1126, Bulgaria

Recently, we reported a convenient synthesis of 1-aryl-2-(2-benzazolyl)-2-phenylethanols by the reaction of 2-benzylbenzoxazole (**1a**)[1] and 2-benzylbenzothiazole (**1b**)[2] with aromatic aldehydes when aqueous sodium hydroxide was used as catalyst. Now we wish to report the synthesis of some hitherto unknown ketones, esters, and nitriles via Michael condensation of **1a** and **1b** with α,β-unsaturated compounds **2**. As far as we know, 2-alkylbenzazoles have not been previously used as donors in Michael addition reaction[3,4].



1a Y = O
b Y = S

2a R = CO—C_6H_5
b R = $COOCH_3$
c R = $COOC_2H_5$
d R = CN

3aa-bd

The method consists of the addition, at room temperature, of a catalytic amount of aqueous sodium hydroxide to a dimethyl sulfoxide solution of **1a** or **1b** and the corresponding α,β-unsaturated compound **2a-d**. The usual work up gave the compounds **3** derived from 1,4-addition. No traces of the corresponding 1,2-addition products were detected by T.L.C.[5] and I.R. analysis of the crude reaction products. Furthermore, the T.L.C. and ^{1}H-N.M.R. analysis of the crude **3aa**, **3ba**, **3ad**, and **3bd** showed the presence of one diastereoisomer only. On the other hand, when **2b** and **2c** were used as acceptors, a mixture of the diastereomeric esters of **3ab**, **3bb**, **3ac**, and **3bc** was isolated in moderate to good yields (see Table).

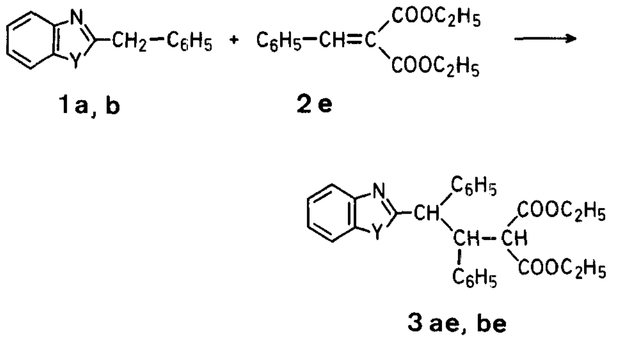
Similar reactions of **1a** and **1b** with benzylidenemalonic ester (**2e**) yielded the compounds **3ae** and **3be**, respectively. By means of fractional recrystallization, we obtained one pure form of **3ab** and **3ac** and both diastereomers of **3bb** and **3be**, respectively. Extension of the use of aqueous sodium hydroxide as catalyst for the condensation of **1a** and **1b** with 2-cyclohexenone (**2f**) was not as successful. The compounds **4a** and **4b** were obtained in low yields (12 and 11%), respectively. However, no 1,2-addition product was detected in this case, as well. When acrylonitrile (**2g**) and crotononitrile (**2h**) were reacted with **1a** under these conditions, the compounds **3ag** and **3ah** were isolated in 20% and 47% yield, respectively.

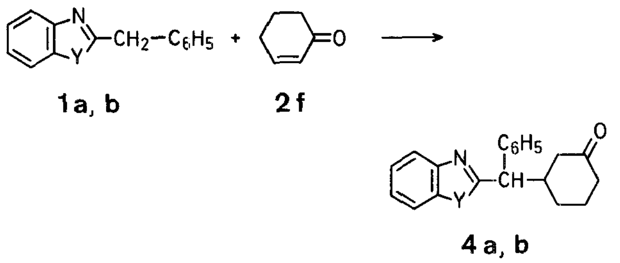
Table. Preparation of Adducts **3** and **4** by Condensation of 2-Benzylbenzazoles **1a, b** and α,β-Unsaturated Compounds **2a-h**

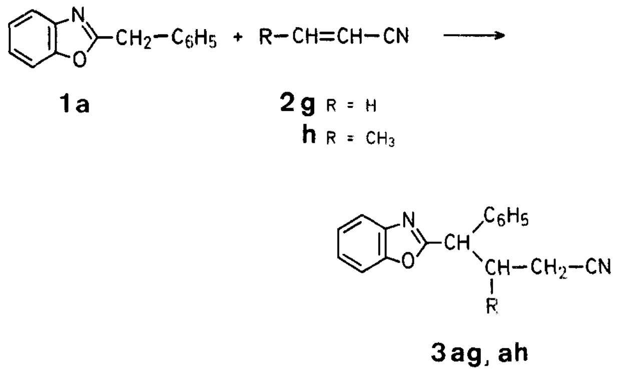
Product	Yield[a,b] [%]	m.p. [°C][c] (solvent)	Molecular formula[d]
3aa	80[e]	212-214 (benzene)	$C_{29}H_{23}NO_2$ (417.5)
3ba	79[e]	211-213 (benzene)	$C_{29}H_{23}NOS$ (433.6)
3ab[f,g]	57	105-145 (ethanol)	$C_{24}H_{21}NO_3$ (371.4)
3bb[f,h]	40	119-145 (ethanol)	$C_{24}H_{21}NO_2S$ (387.5)
3ac[f,j]	64	94-140 (ethanol)	$C_{25}H_{23}NO_3$ (385.5)
3bc[f]	60	107-125 (ethanol)	$C_{25}H_{23}NO_2S$ (401.5)
3ad	89[e]	220-221 (benzene)	$C_{23}H_{18}N_2O$ (338.4)
3bd	79[e]	199-201 (ethanol/ ethyl acetate)	$C_{23}H_{18}N_2S$ (354.5)
3ae[f]	67	84-120 (ethanol)	$C_{28}H_{27}NO_5$ (457.5)
3be[f,k]	55	92-138 (ethanol)	$C_{28}H_{27}NO_4S$ (473.6)
3ag	20	100-102 (ethanol)	$C_{17}H_{14}N_2O$ (262.3)
3ah[f,m]	47	79-103 (aq. ethanol)	$C_{18}H_{16}N_2O$ (276.3)
4a[f]	12 (18)[l]	176-179 (ethanol)	$C_{20}H_{19}NO_2$ (305.4)
4b[f]	11	150-177 (acetone)	$C_{20}H_{19}NOS$ (321.4)

[a] Yield of recrystallized product.
[b] Reaction time 24 h unless otherwise noted.
[c] Melting points are uncorrected.
[d] I.R. and ^{1}H-N.M.R. spectral data are in agreement with the structures; the N-analyses were in satisfactory agreement with the calculated values (±0.26).
[e] Reaction time shorter than 10 min.
[f] Mixture of diastereomers.
[g] m.p. of the pure form: 155-156 °C (ethanol); yield 15%.
[h] m.p. of the pure forms: 136-138 °C (6%); 152-154 °C (9%).
[j] m.p. of the pure form: 138-140 °C (24%).
[k] m.p. of the pure forms: 142-144 °C (38%); 108-109 °C (16%).
[l] Reaction time 48 h.
[m] m.p. of the pure form: 105-107 °C (14%).

0039-7881/80/0432-0317 $ 03.00







Condensation of 2-Benzylbenzoxazole (1a) and 2-Benzylbenzothiazole (1b) with α,β-Unsaturated Compounds 2; General Procedure: Aqueous sodium hydroxide (1 ml of 4% solution, 1 mmol) is added to a solution of 2-benzylbenzazole **1** (10 mmol) and the corresponding α,β-unsaturated compound **2** (10 mmol) in dimethyl sulfoxide (10 ml). The reaction mixture is left at room temperature until it completely solidifies or for maximal 24 h. Then water (100 ml) is added, the separated precipitate filtered, washed with water, and recrystallized from the solvent given in the Table. In some cases an oily product is formed after addition of water. After standing for a few days in a refrigerator, the separated solid is collected and recrystallized. In the case of **3ag** the reaction mixture is extracted with ether. After drying of the solution with sodium sulfate the ether is removed and the residue diluted with ethanol.

Received: March 26, 1979
(Revised form: November 8, 1979)

---

[1] V. Dryanska, C. Ivanov, *Commun. Dept. Chem. Bulg. Acad. Sci.* **10**, 195 (1977); *C. A.* **88**, 62322 (1978).

[2] V. Dryanska, C. Ivanov, Ts. Cholakova, *God. Sofii Univ. Khim. Fac.* **73**, in press (1980).

[3] E. D. Bergman, D. Ginsburg, R. Pappo, *Org. React.* **10**, 119 (1959).

[4] H. House, *Modern Synthetic Reactions*, W. A. Benjamin Inc., 1972, p. 595.

[5] T.L.C. was performed on silica gel plates (Silufol UV 254 - Czechoslovakia), acetone/hexane (1:4) being used as solvent system.

0039-7881/80/0432-0318 $ 03.00