Phase-Transfer-Catalyzed Cyclopropanation. Synthesis of 1,2-Dibenzoyl-3-arylcyclopropanes

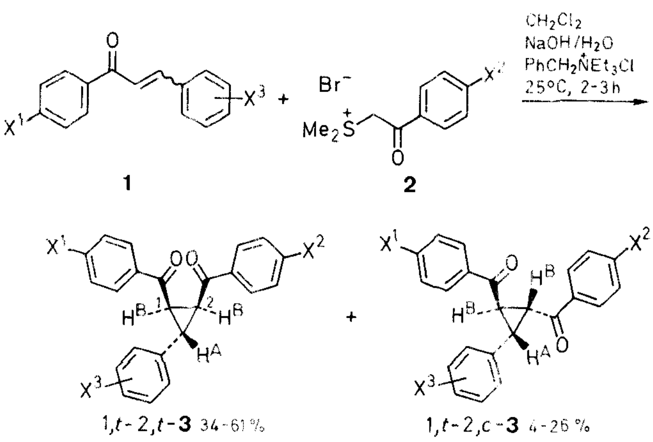
D. Bhaskar Reddy,*[,a] B. Venkataramana Reddy,[a] T. Seshamma,[a] N. Subba Reddy,[a] M. V. Ramana Reddy[b]

[a] Department of Chemistry, Sri Venkateswara University, Tirupati, 517502, India

[b] Department of Chemistry, Pondicherry Engineering College, Pondicherry, 605104, India

The 1,*t*-2,*t* and 1,*t*-2,*c*-isomers of 1,2-dibenzoyl-3-phenylcyclopropanes have been prepared by the cycloaddition of carbonyl-stabilized sulfur ylides to *trans*-chalcones under phase-transfer conditions. The configurations of the isomers were characterized by IR- and ^{1}H-NMR-spectral studies.

Reports about the applicability of phase-transfer conditions to cyclopropanation reactions are scanty, although phase-transfer catalysis has been exploited in many other reactions.[1,2] A large number of non-stabilized sulfur ylides (sulfuranes) have been used[3] as alkylidene-transfer agents for the cyclopropanation of Michael acceptors under rather vigorous reaction conditions, the yields being poor. Stabilized ylides, which are less reactive than non-stabilized ylides, have also been used for cyclopropanations under usual conditions.[4,5] Even though examples of cycloaddition of non-stabilized ylides to chalcones[6] and stabilized ylides to sulfones[7] and dibenzoylethylenes[8] under phase-transfer conditions are known, phase-transfer catalyzed reactions of carbonyl-stabilized sulfur ylides with chalcones have not been reported to our knowledge. We now report the application of phase-transfer catalysis to the synthesis of a variety of 1,2-dibenzoyl-3-arylcyclopropanes **3** by the reaction of dimethylphenacylsulfonium bromides **2** with chalcones **1** in dichloromethane/50% aqueous sodium hydroxide in the presence of benzyltriethylammonium chloride at room temperature.



Cyclpropanations of activated double bonds have earlier been performed by generating the ylide[9] *in situ* from the sulfonium salt or by preparing the stable ylide first and then adding it to the Michael acceptor.[4] However, both procedures require anhydrous conditions, are time consuming, and often give only low yields. Performance of the same reactions under phase-transfer conditions avoids the problem of generation and preservation of the ylides. Higher yields, better selectivity, milder reaction conditions, and shorter reaction times are some of the advantages of the present method.

Contrary to reports in the literature,[10] a mixture of 1,*t*-2,*t*- and 1,*t*-2,*c*-isomers of the 1,2-dibenzoyl-3-phenylcyclopropanes was obtained by this method. It has been reported[4] that 1,*t*-2*t* and 1,*t*-2,*c*-isomers are obtained in a 2:1 ratio from the reaction of dimethylsulfonium phenacylide with *trans*-chalcone under usual conditions, the stereochemistry being confirmed by NMR-spectral studies. The precursor of 1,*t*-2,*t*-isomer should be the preferred rotamer and consequently it should result as the major product. However, it has also been reported[5] that the formation of the 1,*t*-2,*c*-isomer is favored in such reactions. Nevertheless, in almost all of our reactions the 1,*t*-2,*t*-isomer was found to be the major product and the 1,*t*-2,*c*-isomer the minor one. The pure isomers were in general isolated by column chromatography; their purity was checked by TLC.

The IR spectra of all products **3** exhibited[11,12,13] medium to strong bands in the region $\nu = 1030-995\,cm^{-1}$, indicating the presence of a cyclopropane ring. They also showed strong C=O bands around $\nu = 1690-1670\,cm^{-1}$ and $\nu = 1670-1655\,cm^{-1}$, which are characteristic of the 1,*t*-2,*t*- and 1,*t*-2,*c*-isomers, respectively.[4]

The ^{1}H-NMR spectra of compounds **3** showed complex multiplets in the region $\delta = 3.20-3.60$ for the 1,*t*-2,*t*-isomers and in the regions $\delta = 3.30-3.80$ and $\delta = 4.00-4.30$ for the 1,*t*-2,*c*-isomers. The *ortho* protons of the benzoyl moieties showed a signal in the region $\delta = 7.80-8.20$ and the other aromatic protons at $\delta = 6.82-7.82$. In 1,*t*-2,*t*-**3**, the proton H^A has similar substituents *cis* to itself; hence the two protons at C-1 and C-2, i.e. H^B, are chemically nearly equivalent so that the three protons show an ABC pattern. However, in the case of 1,*t*-2,*c*-**3**,

Downloaded by: Rutgers University. Copyrighted material.

Table. 1,*t*-2,*t*- and 1,*t*-2,*c*-Isomers of 1,2-Dibenzoyl-3-arylcyclopropanes **3** Prepared

Entry	X^1	X^2	X^3	1,*t*-2,*t*		1,*t*-2,*c*		Molecular Formula[c] or Lit. mp (°C)
				Yield[a] (%)	mp (°C)[b]	Yield[a] (%)	mp (°C)[b]	
1	H	H	H	50	114–115	24	146–147	1,*t*-2,*t*: 114–116[4] 1,*t*-2,*c*: 149–150[4,5]
2	H	H	2-Cl	52	157–158	5	183–184	$C_{23}H_{17}ClO_2$ (360.8)
3	H	H	4-Cl	46	127–128	23	171–173	$C_{23}H_{17}ClO_2$ (360.8)
4	H	H	4-OMe	44	126–127	7	147–148	$C_{24}H_{20}O_3$ (356.4)
5	H	H	4-NMe_2	45	146–147	5	168–169	$C_{25}H_{23}NO_2$ (369.4)
6[d]	Cl	H	H	57	151–152	6	208–209	1,*t*-2,*c*: 209–210[5]
7	Cl	H	2-Cl	55	137–139	7	165–166	$C_{23}H_{16}Cl_2O_2$ (395.3)
8[d]	Cl	H	4-Cl	56	134–135	5	176–177	$C_{23}H_{16}Cl_2O_2$ (395.3)
9[d]	Cl	H	4-OMe	54	114–115	4	149–150	$C_{24}H_{19}ClO_3$ (390.8)
10[d]	Cl	H	4-NMe_2	52	124–125	4	174–175	$C_{25}H_{22}ClNO_2$ (403.9)
11	Br	H	H	43	129–130	18	152–153	$C_{23}H_{17}BrO_2$ (405.3)
12[d]	Br	H	4-Cl	54	132–133	8	164–165	$C_{23}H_{16}BrClO_2$ (439.7)
13[d]	Br	H	4-OMe	49	138–140	9	193–194	1,*t*-2,*c*: 195–197[5]
14[d]	MeO	H	H	47	141–143	6	160–162	$C_{24}H_{20}O_3$ (356.4)
15[d]	MeO	H	4-Cl	49	126–127	7	173–174	$C_{24}H_{19}ClO_3$ (390.8)
16[d]	MeO	H	4-OMe	44	121–122	8	150–151	$C_{25}H_{22}O_4$ (386.4)
17	Cl	Cl	H	44	128–130	21	148–150	$C_{25}H_{16}Cl_2O_2$ (419.3)
18	Cl	Cl	4-Cl	42	136–137	26	189–190	$C_{23}H_{15}Cl_3O_2$ (429.7)
19	Cl	Cl	4-OMe	42	155–156	20	173–175	$C_{24}H_{18}Cl_2O_3$ (425.3)
20	Cl	Cl	4-NMe_2	38	133–135	18	185–186	$C_{25}H_{21}Cl_2NO_2$ (438.3)
21[d]	Br	Cl	H	58	123–124	8	145–146	$C_{23}H_{16}BrClO_2$ (439.7)
22[d]	Br	Cl	4-Cl	61	139–140	10	199–200	$C_{23}H_{15}BrCl_2O_2$ (474.1)
23[d]	Br	Cl	4-OMe	53	126–128	5	172–173	$C_{24}H_{18}BrClO_3$ (469.7)
24	MeO	Cl	4-Cl	51	143–144	9	175–176	$C_{24}H_{18}Cl_2O_3$ (425.3)
25[d]	MeO	Cl	4-OMe	49	125–127	8	160–161	$C_{25}H_{21}ClO_4$ (420.9)
26	MeO	OMe	4-Cl	34	114–115	17	203–204	$C_{25}H_{21}ClO_4$ (420.9)
27	Cl	Me	H	43	145–146	22	152–153	$C_{24}H_{19}ClO_2$ (374.8)
28	Cl	Me	4-Cl	48	133–135	22	165–166	$C_{24}H_{18}Cl_2O_2$ (409.3)
29	Cl	Me	4-Me	44	143–145	15	168–169	$C_{25}H_{21}ClO_3$ (404.9)
30	MeO	Me	4-Cl	40	151–152	22	198–199	$C_{25}H_{21}ClO_3$ (404.9)
31	MeO	Me	4-OMe	36	147–148	18	175–177	$C_{26}H_{24}O_4$ (400.5)

[a] Yield of isolated product, based on **1**.

[b] Recrystallized from 2-propanol. Melting points (uncorrected) were measured with a Mel-Temp apparatus.

[c] Satisfactory microanalyses: C ± 0.22, H ± 0.15.

[d] Similar results were obtained for the inverse order of substituents X^1 and X^2.

the three cyclopropane ring protons H^A, H^B, and H^X are chemically non-equivalent and thus show an ABX pattern. The difference in chemical shift values can therefore be used as a criterion to distinguish between the 1,*t*-2,*t*- and 1,*t*-2,*c*-isomers of 1,2-dibenzoyl-3-arylcyclopropanes.[4,14]

1,2-Dibenzoyl-3-arylcyclopropanes 3; General Procedure:

A mixture of a chalcone[15] **1** (10 mmol), a dimethylphenacylsulfonium bromide[16] **2** (11 mmol), and CH_2Cl_2 (6 mL) is placed in a 100 mL conical flask equipped with a magnetic stirrer. The contents of the flask are stirred with 50% aq. NaOH (4 mL) until a clear two-phase mixture is obtained. To this, $Bzl\overset{+}{N}Et_3\ Cl^-$ (200 mg) is added and stirring is continued at room temperature for 2–3 h. The mixture is then diluted with H_2O (50 mL). The organic layer is separated, washed with H_2O (20 mL) and with brine (20 mL), and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure yields a mixture of 1,*t*-2,*c*- and 1,*t*-2,*c*-isomers of **3**. The two isomers are separated by column chromatography on silica gel (60–120 mesh, BDH) using hexane/Et_2O (3:2) as eluent. In small-scale experiments or in the case of low yields, the isomers are isolated by preparative TLC on silica gel-H using hexane/Et_2O (3:2) as eluent.

The authors thank the Regional Sophisticated Instrumentation Centre, CDRI, India, for providing microanalyses. They also wish to thank CSIR, India for the award of Senior Research Fellowship to B.V.R. and T.S.

Received: 18 August 1988; revised: 20 October 1988

(1) Weber, W.P., Gokel, G.W. *Phase-Transfer Catalysis in Organic Synthesis*, Springer Verlag, New York, 1977.

(2) Keller, W.E. *Phase-Transfer Reactions, Fluka-Compendium*, Vol. 1, 2, Georg Thieme Verlag, Stuttgart, 1986, 1987.

(3) Trost, B.M., Melvin, L.S., Jr. *Sulfur Ylides*, Academic Press, New York, 1975.

(4) Trost, B.M. *J. Am. Chem. Soc.* **1967**, *89*, 138.

(5) Tewari, R.S., Awasthi, A.K. *Indian J. Chem. Sect. B* **1980**, *19*, 155.

(6) Merz, A., Märkl, G. *Angew. Chem.* **1973**, *85*, 867; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 845.

(7) Bhaskar Reddy, D., Reddy, P.S., Reddy, B.V., Reddy, P.A. *Synthesis* **1987**, 74.

(8) Bhaskar Reddy, D., Subramanyam, V.M., Padmavathi, V. *Org. Prep. Proced. Int.* **1988**, *20*, 83.

(9) Corey, E.J., Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, *84*, 3782.

(10) Corey, E.J., Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(11) Balaji, T., Bhaskar Reddy, D. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3434.

(12) Bhaskar Reddy, D., Balaji, T., Venkataramana Reddy, B. *Phosphorus and Sulfur* **1983**, *17*, 297.

(13) Bhaskar Reddy, D., Sankaraiah, B., Balaji, T. *Indian J. Chem. Sect. B* **1980**, *19*, 563.

(14) Hayashi, Y., Takaku, M., Nozaki, H. *Tetrahedron Lett.* **1969**, *37*, 3179.

(15) Wattanasin, S., Murphy, W.S. *Synthesis* **1980**, 647.

(16) Speziale, A.J., Tung, C.C., Ratts, K.W., Yao, A. *J. Am. Chem. Soc.* **1965**, *87*, 3460.

Downloaded by: Rutgers University. Copyrighted material.